blueprint™ MEDICINES

2020 Annual Report

NASDAQ: **BPMC**

ADVANCING SCIENCE 10 CHANGING LIVES

Celebrating our first decade
of innovation in precision medicine

Dear Shareholders

This April, as we celebrate Blueprint Medicines' ten-year anniversary, we reflect on the significant progress we have achieved in our first decade. But more importantly, we look forward to the milestones ahead, as we execute on our strategy to become the world's leading precision therapy company.

Blueprint Medicines was founded in 2011 with a singular focus: to translate molecular and genomic data into transformative precision therapies for patients with cancer and hematologic disorders. Over the past decade, we have successfully executed against this goal. We have built a robust discovery engine that combines bioinformatics, expertise in structural and cell biology and a proprietary library of novel compounds to rapidly and reproducibly translate science into a broad pipeline of potential therapies. Our ability to design highly selective and potent medicines addressing challenging targets has enabled us to advance multiple programs across three areas of strategic focus — genomically defined cancers, hematologic disorders, and cancer immunotherapy. And, in 2020, we secured four regulatory approvals for our first two precision therapies in the United States and Europe to become the first company with two novel drugs discovered and approved within the first ten years of operation.

As we enter our second decade, Blueprint Medicines is in its strongest position since our inception, with the AYVAKIT™ (avapritinib) and GAVRETO® (pralsetinib) launches underway, a broad pipeline of wholly-owned or partnered precision therapies advancing through preclinical and clinical development, and sufficient capital to enable a self-sustainable financial profile. With this foundation, we are working towards the promise of precision medicine to improve and extend the lives for as many people with cancer and hematologic disorders.

To continue on this path, our efforts in 2021 will focus on three strategic priorities: accelerating the global adoption of our first two approved therapies, AYVAKIT and GAVRETO; advancing a new wave of innovative therapeutic candidates towards rapid proof-of-concept and into clinical development; and further expanding our precision medicine pipeline.

Already, we have made excellent progress toward achieving these goals. In the first quarter, our supplemental New Drug Application and Type II Marketing Authorization Application for AYVAKIT/AYVAKYT® for the treatment of advanced systemic mastocytosis (SM) were accepted for review by the U.S. Food and Drug Administration and European Medicines Agency, respectively, paving the way for planned near-term launches in a patient population with significant medical need. Advanced SM is a debilitating and often deadly disease, and we are driven by the opportunity to potentially deliver AYVAKIT as a first-in-class targeted therapy to the thousands of patients living with this condition.

We also continue to bolster our clinical pipeline and early stage research efforts. Our ongoing registration-enabling PIONEER trial in non-advanced SM has the potential to serve as the basis of AYVAKIT's next marketing authorization filing. In addition, we are investing in our next wave of potentially transformative medicines. Since the fourth quarter of 2019, we have nominated five new development candidates, including BLU-263 for the treatment of non-advanced SM, and BLU-945 and BLU-701, which serve as the pillars of our efforts to address EGFR-positive non-small cell lung cancer. At the American Association for Cancer Research (AACR) Annual Meeting in April 2021, we presented highly compelling data for each of these compounds, as well as our two newest candidates, BLU-222, a selective and potent inhibitor with first-in-class potential targeting CDK2, and BLU-852, a potential best-in-class candidate in development with our partner Roche that targets MAP4K1, a kinase believed to play a role in T-cell regulation. These data speak to the productivity of our research platform, the immense talent of our team, and our ability to provide value to patients with significant medical need.

As we continue to grow, we are cognizant also of our responsibilities to communities outside of Blueprint Medicines and to the world at-large. This means ensuring that we support initiatives that are aligned with our culture and values, such as promoting diversity — in backgrounds and experience — among our own team and across the biotechnology industry. An example this year was the creation of the Equity, Diversity and Inclusion Committee, which seeks to encourage dialogue, broaden perspectives and strengthen connections through company-wide events. We believe tools and resources such as this help employees prioritize health and wellness, celebrate diverse cultures, and foster an inclusive and collaborative spirit.

Looking ahead, I am incredibly optimistic about the future of Blueprint Medicines. Over the last decade, we have grown from a small group of enthusiastic scientists in Cambridge, Massachusetts to a diverse team of about 450 employees today, with offices in the United States and across Europe. The same entrepreneurial spirit and belief in the power of targeted therapies that drove our founders still permeates everything that we do. As a fully integrated business, we now possess the ability to capitalize on insights throughout the drug lifecycle, enabling sustained research innovation. And as always, we remain fully committed to working with urgency to solve complex problems and pursue transformative therapies that will make a difference in patients' lives.

Jeff Albers
President and Chief Executive Officer

Addressing Patient Needs in EGFR Lung Cancer

At 42 years old, Diane Legg faced the most shocking news of her life: a lung cancer diagnosis. The only thing Diane knew about lung cancer at the time was that it is one of the deadliest cancers, and her mind immediately raced to her three young boys and how raising them was the most important thing in her life. The future was uncertain, and she was fearful of the unknown.

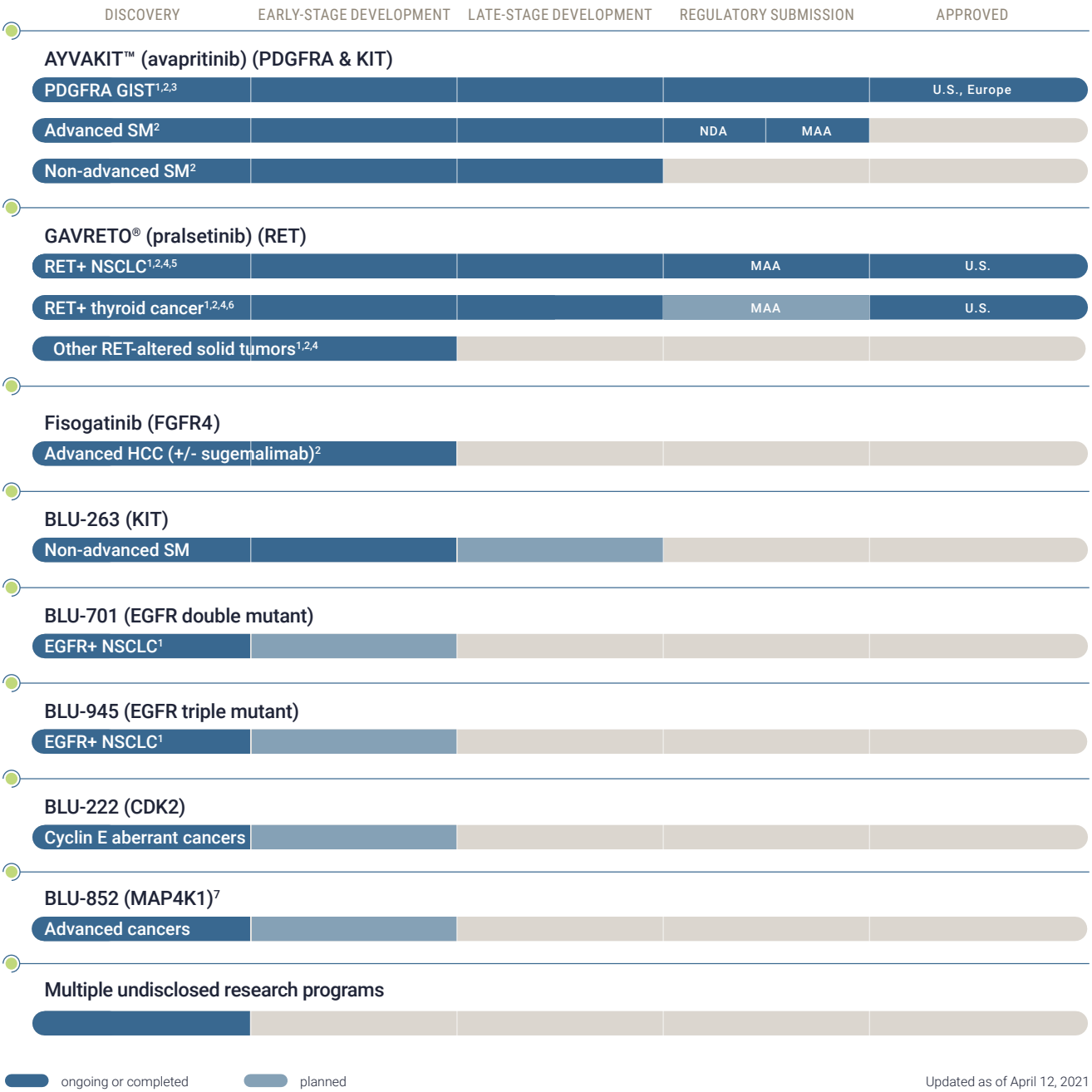
Diane began her initial treatment, and after a year and a half she was thankful to hear from her doctors that she was cancer-free. But months later, a routine scan revealed the cancer had returned, and that it was Stage 4.

Diane advocated strongly for her own biomarker testing, and after a second opinion she learned that she had a particular mutation called EGFR. Through her own research and support groups, she found out that there were targeted drugs available. But she also understood there was a risk that her cancer may eventually build a resistance to these new therapies. She was willing to try anything to survive.

Diane has been a participant in several clinical trials that are testing new targeted therapies for her EGFR mutation. She is an active lung cancer fighter, blazing the trail for other people living with EGFR-driven lung cancer to thrive.

> My hope, for people that are facing lung cancer today and in the future, is that we can identify mutations and have treatments that will allow lung cancer patients to live long, high quality lives. I hope we can treat it as a chronic disease, if not a cure.
>
> — *Diane Legg*

Rapidly expanding portfolio highlights precision therapy leadership



Updated as of April 12, 2021

1. Unresectable or metastatic disease.
2. CStone Pharmaceuticals has exclusive rights to develop and commercialize avapritinib, pralsetinib and fisogatinib in Mainland China, Hong Kong, Macau and Taiwan.
3. Approved in the U.S. for the treatment of adults with unresectable or metastatic GIST harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations. Received conditional marketing authorization in Europe under the brand name AYVAKYT® for the treatment of adults with unresectable or metastatic GIST harboring the PDGFRA D842V mutation.
4. In collaboration with Roche. Blueprint Medicines and Roche have co-exclusive rights to develop and commercialize pralsetinib in the U.S., and Roche has exclusive rights to develop and commercialize pralsetinib outside the U.S., excluding the CStone territory.
5. Received accelerated approval in the U.S. for the treatment of adults with metastatic RET fusion-positive NSCLC. Continued approval may be contingent on a confirmatory trial. The proposed indication for the MAA is locally advanced or metastatic RET fusion-positive NSCLC previously treated with platinum-based chemotherapy.
6. Received accelerated approval in the U.S. for the treatment of patients with advanced or metastatic RET-mutant medullary thyroid cancer and RET fusion-positive thyroid cancer. Continued approval may be contingent on confirmatory trials.
7. In collaboration with Roche. Blueprint Medicines and Roche are conducting activities for up to two programs under the collaboration, including the program targeting MAP4K1. For one of the programs, Blueprint Medicines has U.S. commercial rights and Roche has ex-U.S. commercialization rights. For one of the programs, Roche has worldwide commercialization rights.

GIST, gastrointestinal stromal tumors; HCC, hepatocellular carcinoma; MAA, marketing authorization application; NDA, new drug application; NSCLC, non-small cell lung cancer; SM, systemic mastocytosis.

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, 2020

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 ☐

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, 2020, 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 $4,234,191,078.

Number of shares of the registrant's common stock, par value $0.001 per share, outstanding on February 15, 2021: 57,957,641

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement for its 2021 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, 2020, are incorporated by reference into Part III of this Annual Report on Form 10-K.

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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®, GAVRETO™ 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 have limited experience as a commercial company and the marketing and sale of AYVAKIT™ (avapritinib) (marketed in Europe under the brand name AYVAKYT®), GAVRETO™ (pralsetinib) or any future approved drugs may be unsuccessful or less successful than anticipated.

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

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

- 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.

- We face substantial competition, which may result in 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 advance our drug candidates to clinical development, obtain regulatory approval for our drug candidates, including for avapritinib and pralsetinib for additional indications or in additional geographies, and ultimately commercialize them, or experience significant delays in doing so, our business will be materially harmed.

- If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

- If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals for our drug candidates and, if applicable, for any related companion diagnostic tests, we will not be able to commercialize, or may be delayed in commercializing, such drug candidates, and our ability to generate revenue will be materially impaired.

- Our drugs and drug candidates may cause undesirable side effects that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, result in restrictive distribution or result in significant negative consequences following marketing approval, if any.

- 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 are a precision therapy company with a limited operating history. We have incurred significant operating losses since our inception and anticipate that we will incur continued losses for the foreseeable future.

- We 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 pre-clinical, 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.

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

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

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

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," "predict," "project," "seek," "should," "target," "will," "would" or the negative of these words or other comparable terminology, although not all forward-looking statements contain these identifying words.

The forward-looking statements in this 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 and pralsetinib for additional indications or in additional geographies;
- our ability and plans in continuing to build out our commercial infrastructure and successfully launching, marketing and selling AYVAKIT/AYVAKYT, GAVRETO and any current and future drug candidates for which we receive marketing approval;
- the rate and degree of market acceptance of AYVAKIT, GAVRETO and any current and future drug candidates for which we receive marketing approval;
- the pricing and reimbursement of AYVAKIT, GAVRETO and any current and future drug candidates for which we receive marketing approval;
- the initiation, timing, progress and results of our pre-clinical studies and clinical trials, including our ongoing clinical trials and any planned clinical trials for avapritinib, pralsetinib, and any current and future drug candidates;
- our ability to advance drug candidates into, and successfully complete, clinical trials;
- our ability to successfully develop manufacturing processes for any of our current and future drugs or drug candidates and to secure manufacturing, packaging and labeling arrangements for development activities and commercial production;
- the implementation of our business model and strategic plans for our business, drugs, drug candidates, platform and technology;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our current and future drugs, drug candidates and technology;
- the potential benefits of our collaboration with F. Hoffmann-La Roche Ltd and Genentech, Inc. to develop and commercialize pralsetinib globally (excluding Greater China), our cancer immunotherapy collaboration with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc., and our collaboration with CStone Pharmaceuticals to develop and commercialize avapritinib, pralsetinib and fisogatinib in Greater China, as well as our ability to maintain these collaborations and establish additional strategic collaborations;
- the potential benefits of our exclusive license agreement with Clementia Pharmaceuticals, Inc. to develop and commercialize BLU-782 for fibrodysplasia ossificans progressiva;
- the development of companion diagnostic tests for our current or future drugs or drug candidates;
- our financial performance, estimates of our revenues, expenses and capital requirements and our needs for future financing, including our ability to achieve a self-sustainable financial profile;

- developments relating to our competitors and our industry;

- the actual or potential benefits of designations granted by the U.S. Food and Drug Administration, or FDA, such as orphan drug, fast track and breakthrough therapy designation or priority review; and

- the impact and scope of the COVID-19 pandemic on our business, operations, strategy, goals and anticipated milestones, including our ongoing and planned research and discovery activities, ability to conduct ongoing and planned clinical trials, clinical supply of current or future drug candidates, and the launch, marketing, sale and commercial supply of AYVAKIT, GAVRETO and any current or future drug candidates for which we receive marketing approval.

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 collaboration for pralsetinib, Roche means F. Hoffmann-La Roche Ltd and Genentech, Inc., and (ii) with respect to our cancer immunotherapy collaboration, Roche means F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc.

PART I

Item 1. Business.

Overview

We are a global precision therapy company that is inventing transformative medicines for people with cancer and hematologic disorders. Applying an approach that is both precise and agile, we create therapies that selectively target genetic drivers, with the goal of staying one step ahead across stages of disease. Since 2011, we have leveraged our research platform, including expertise in molecular targeting and world-class drug design capabilities, to rapidly and reproducibly translate science into a broad pipeline of precision therapies. We are delivering our approved medicines, AYVAKIT™/AYVAKYT® (avapritinib) and GAVRETO™ (pralsetinib), to patients in the U.S. and Europe, and we are globally advancing multiple programs for genomically defined cancers, systemic mastocytosis, and cancer immunotherapy.

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

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

Avapritinib

We are developing avapritinib for the treatment of systemic mastocytosis, or SM, a rare hematologic disorder that causes an overproduction of mast cells and the accumulation of mast cells in the bone marrow and other organs, which can lead to a wide range of debilitating symptoms and organ dysfunction and failure. Nearly all cases of SM are driven by the KIT D816V mutation, which aberrantly activates mast cells.

In December 2020, we submitted a supplemental new drug application, or NDA, to the U.S. Food and Drug Administration, or FDA, for avapritinib for the treatment of adult patients with advanced SM. In February 2021, the FDA accepted our application and set a Prescription Drug User Fee Act, or PDUFA, action date of June 16, 2021. We also submitted a Type II variation marketing authorization application, or MAA, to the European Medicines Agency, or EMA, for avapritinib for advanced SM in February 2021.

We are currently evaluating avapritinib in an ongoing registration-enabling Phase 1 clinical trial in advanced SM, which we refer to as our EXPLORER trial, and an ongoing registration-enabling Phase 2 clinical trial in advanced SM, which we refer to as our PATHFINDER trial. In September 2020, we reported positive top-line data from the EXPLORER and PATHFINDER trials. We plan to present registrational data from the PATHFINDER trial in the first half of 2021. In addition, we are evaluating avapritinib in an ongoing registration-enabling Phase 2 clinical trial in non-advanced SM, which we refer to as our PIONEER trial. In 2020, we reported data from the dose-finding portion (Part 1) of the PIONEER trial and initiated the registration-enabling Part 2 of the PIONEER trial. We expect to complete enrollment of Part 2 of the PIONEER trial in mid-2021.

The FDA has granted breakthrough therapy designation to avapritinib for (i) the treatment of advanced SM, including the subtypes of aggressive SM, SM with an associated hematologic neoplasm and mast cell leukemia, 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.

BLU-263

BLU-263 is an investigational, orally available, potent and highly selective KIT inhibitor that we are developing for the treatment of non-advanced SM and other mast cell disorders. BLU-263 is designed to have equivalent potency as avapritinib, with low off-target activity and lower penetration of the central nervous system, or CNS, relative to avapritinib based on preclinical data, which we believe will enable development of BLU-263 in a broad population of patients with non-advanced SM, including patients with lower disease burden requiring potentially life-long chronic therapy, and potentially patients with other mast cell disorders. In January 2021, we announced positive top-line results from a Phase 1 trial of BLU-263 in healthy volunteers. Based on these data, in mid-2021, we plan to initiate a Phase 2 trial of BLU-263 in patients with non-advanced SM, which we refer to as our HARBOR trial.

RET-altered Cancers — GAVRETO™ (pralsetinib)

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

Pralsetinib is approved in the U.S. with accelerated approval under the brand name GAVRETO for the treatment of (i) adult patients with metastatic RET fusion-positive NSCLC as detected by an FDA approved test, (ii) adult and pediatric patients 12 years of age and older with advanced or metastatic RET-mutant MTC who require systemic therapy, and (iii) adult and pediatric patients 12 years of age and older with advanced or metastatic RET fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate).

The EMA is currently reviewing our MAA for pralsetinib for RET fusion-positive NSCLC. If approved by the European Commission, Roche plans to launch pralsetinib in RET fusion-positive NSCLC in Europe in the first half of 2021. Roche also plans to submit a Type II variation MAA to the EMA for pralsetinib for RET-altered thyroid cancers in the second half of 2021, and to submit marketing applications for pralsetinib for RET-altered NSCLC and thyroid cancers across multiple additional global geographies in 2021. In addition, China's National Medical Products Administration, or NMPA, accepted an NDA submitted by CStone in the third quarter of 2020 for pralsetinib for the treatment of RET fusion-positive NSCLC patients previously treated with platinum-based chemotherapy.

We are currently evaluating pralsetinib in an ongoing registration-enabling Phase 1/2 clinical trial in patients with RET-altered NSCLC, MTC and other advanced solid tumors, which we refer to as our ARROW trial. Pursuant to our collaboration with Roche, we plan to co-develop pralsetinib globally in RET-altered solid tumors, including NSCLC, MTC and other thyroid cancers, as well as other solid tumors.

The FDA has granted breakthrough therapy designation to pralsetinib for (i) the treatment of patients with RET fusion-positive NSCLC that has progressed following platinum-based chemotherapy and (b) the treatment of patients with RET mutation-positive MTC that requires systemic treatment and for which there are no acceptable alternative treatments. In addition, the FDA has granted orphan drug designation to pralsetinib for the treatment of RET-rearranged NSCLC, JAK1/2-positive NSCLC or TRKC-positive NSCLC.

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

We are commercializing avapritinib for the treatment of patients with PDGFRA exon 18 mutant gastrointestinal stromal tumors, or GIST, a rare disease that is a sarcoma, or tumor of bone or connective tissue, of the gastrointestinal tract. Avapritinib is approved in the U.S. under the brand name AYVAKIT for the treatment of adults with unresectable or metastatic gastrointestinal stromal tumors harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations, and is approved in the European Union 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.

The European Commission has granted orphan medicinal product designation to avapritinib for the treatment of GIST. In addition, the NMPA accepted an NDA submitted by CStone in the first quarter of 2020 for avapritinib for the treatment of adults with unresectable or metastatic PDGFRA exon 18 mutant GIST. CStone also submitted an NDA to the Taiwan Food and Drug Administration, or the TFDA, for avapritinib for the indication of adult patients with unresectable or metastatic GIST harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations, and received priority review designation from the TFDA.

Treatment-Resistant EGFR-Mutated NSCLC

We are developing two investigational EGFR inhibitors, BLU-701 and BLU-945, with the goal of addressing the most common on-target resistance mutations to currently available EGFR-targeted therapies. While the introduction of EGFR-targeted therapies, including osimertinib, has transformed the care of patients with EGFR-driven NSCLC, treatment resistance is a significant emerging unmet medical need.

In addition to targeting EGFR resistance mutations, BLU-701 and BLU-945 were specifically designed for selectivity over wild-type EGFR and other kinases to enable potential improved tolerability and also combination strategies. In addition, in preclinical tumor models, both drug candidates have shown CNS activity, highlighting the potential to address CNS metastases which are more common in treatment-experienced NSCLC patients.

We plan to initially develop BLU-701 and BLU-945 as monotherapies and in combination with each other and other therapies to overcome treatment resistance in specific patient populations with EGFR-driven NSCLC.

EGFR-Positive Double Mutant NSCLC — BLU-701

BLU-701 is a selective and potent investigational inhibitor of double-mutant EGFR harboring either the activating L858R or exon 19 deletion mutations combined with the acquired C797S mutation, the most common on-target resistance mutation to osimertinib. We plan to initially develop BLU-701 as a monotherapy and in combination with other therapies. We plan to present foundational preclinical data for BLU-701 in the first half of 2021, and we plan to initiate a Phase 1 trial of BLU-701 in the second half of 2021.

EGFR-Positive Triple Mutant NSCLC — BLU-945

BLU-945 is a selective and potent investigational inhibitor of triple-mutant EGFR harboring either the activating L858R or exon 19 deletion mutations combined with the acquired T790M and C797S mutations, the most common on-target resistance to first-generation EGFR inhibitors and osimertinib, respectively.

In preclinical data presented in September 2020, BLU-945 inhibited triple mutant EGFR with sub-nanomolar potency and demonstrated greater than 900-fold selectivity over wild-type EGFR along with excellent overall kinome selectivity. In a triple mutant EGFR cell-line, BLU-945 potently inhibited the EGFR pathway, while osimertinib demonstrated limited activity. BLU-945 monotherapy resulted in robust anti-tumor activity in multiple cell line-derived and patient-derived xenograft models of triple mutant EGFR NSCLC. In addition, BLU-945 treatment in combination with osimertinib or gefitinib resulted in tumor regression in a triple mutant EGFR NSCLC patient-derived xenograft model, which was derived from a patient with progressive disease following five lines of prior therapy. BLU-945 was also highly active in an intracranial disease model.

Based on these preclinical proof-of-concept data, we plan to initially develop BLU-945 as a monotherapy and in combination with other agents. We plan to initiate a Phase 1 trial of BLU-945 in patients with EGFR-driven NSCLC, in the first half of 2021.

Fisogatinib — Hepatocellular Carcinoma

We are developing fisogatinib for the treatment of advanced hepatocellular carcinoma, or HCC. Fisogatinib is an investigational, orally available, potent and highly selective inhibitor that targets FGFR4, a kinase that is aberrantly activated in a defined subset of patients with HCC, the most common type of liver cancer. As part of our collaboration with CStone, we are evaluating fisogatinib as a monotherapy and in combination with sugemalimab, a clinical-stage anti-PDL1 immunotherapy being developed by CStone, for the treatment of locally advanced or metastatic HCC in an

ongoing Phase 1b/2 trial conducted in multiple clinical sites in China. The FDA has granted orphan drug designation to fisogatinib for the treatment of HCC.

Discovery Platform

We plan to continue to leverage our discovery platform to systematically and reproducibly identify kinases that are drivers of diseases in genomically defined patient populations and craft drug candidates that potently and selectively target these kinases.

In addition to our discovery programs for treatment-resistant EGFR-mutated NSCLC, we currently have the following wholly-owned discovery programs:

- *CDK2 Discovery Program.* In February 2021, we announced a discovery program targeting CDK2. CDK2, a cyclin-dependent kinase involved in cell cycle biology, is activated by its regulatory partner Cyclin E, and can drive cancer cell proliferation when Cyclin E is aberrantly expressed. Dysregulated Cyclin E is associated with multiple malignancies and has been shown to be a mechanism of resistance to targeted therapies, including CDK4/6 inhibitors.
- *Other Discovery Programs.* In addition to the discovery programs described above, we have two wholly-owned pre-development candidate programs for undisclosed kinase targets.

Under our immunotherapy collaboration with Roche, we are conducting activities for up to two discovery programs, including a development candidate for the kinase target MAP4K1. See "*—Collaborations and Licenses Summary*" below. We plan to present initial preclinical data for our MAP4K1 development candidate in the first half of 2021.

Collaborations and Licenses Summary

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

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

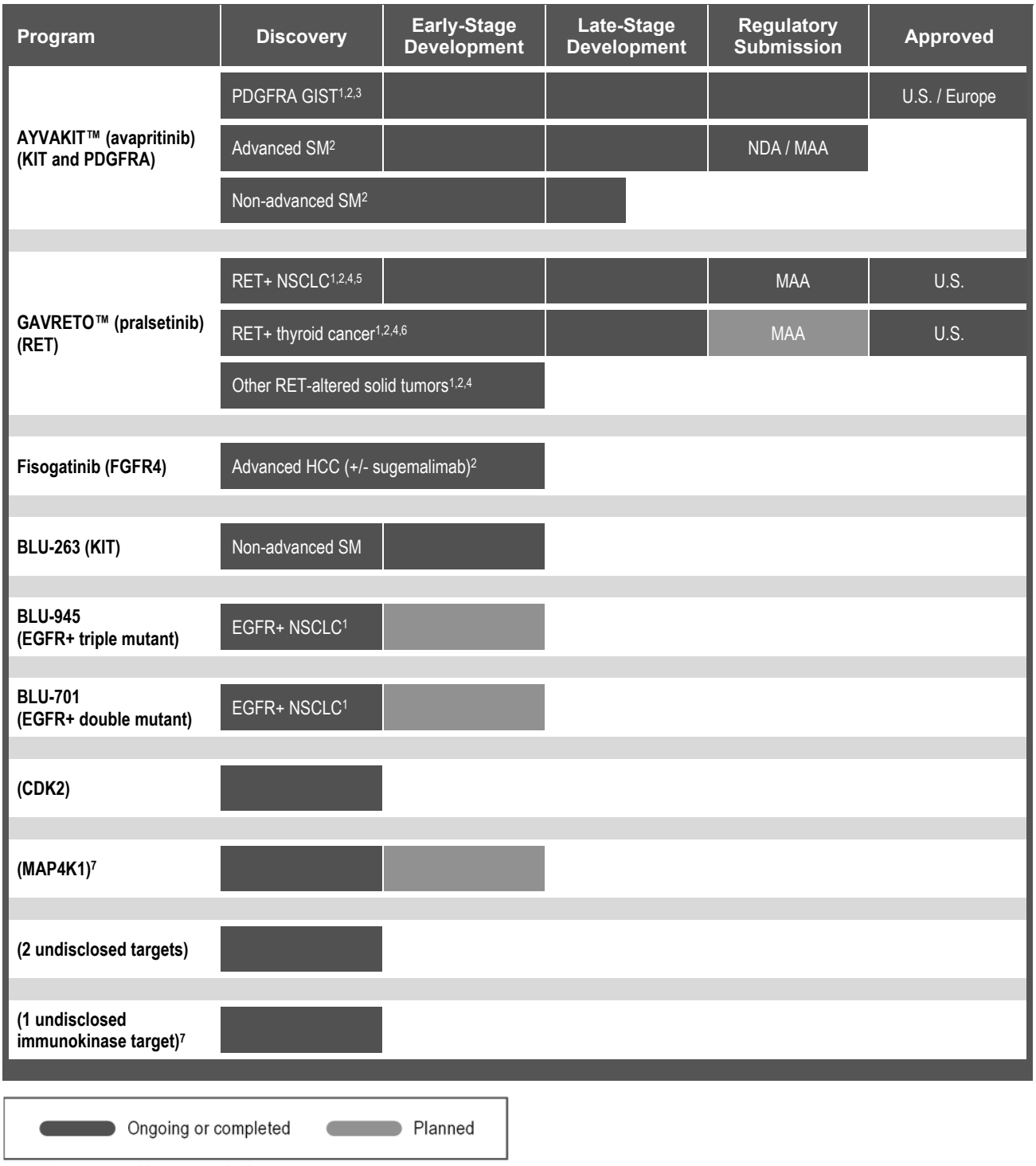
CStone. In June 2018, we entered into a collaboration with CStone to develop and commercialize avapritinib, pralsetinib and fisogatinib, including back-up forms and certain other forms, in the CStone territory either as a monotherapy or as part of a combination therapy.

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

We will continue to evaluate additional collaborations, partnerships and licenses that could maximize the value for our programs and allow us to leverage the expertise of strategic collaborators, partners and licensors, including in additional geographies where we may not have current operations or expertise. We are also focused on engaging in collaborations, partnerships and license agreements to capitalize on our discovery platform outside of our primary strategic focus area of cancer and rare diseases.

Our Pipeline

The following chart summarizes our pipeline of approved drugs and drug candidates as of February 15, 2021.



(1) Unresectable or metastatic disease.

(2) CStone has exclusive rights to develop and commercialize avapritinib, pralsetinib and fisogatinib in Mainland China, Hong Kong, Macau and Taiwan, which we refer to as the CStone territory. For more information, see "—Collaborations and Licenses" below.

(3) Approved in the U.S. for the treatment of adults with unresectable or metastatic GIST harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations. Received conditional marketing authorization in Europe under the brand name AVYAKYT® for the treatment of adults with unresectable or metastatic GIST harboring the PDGFRA D842V mutation.

(4) Roche has exclusive rights to develop and commercialize pralsetinib worldwide, excluding the U.S. and the CStone territory. We and Roche have co-exclusive rights to develop and commercialize pralsetinib in the U.S. For more information, see "—Collaborations and Licenses" below.

(5) Received accelerated approval in the U.S. for the treatment of adults with metastatic RET fusion-positive NSCLC. Continued approval may be contingent on a confirmatory trial. The proposed indication for the MAA is locally advanced or metastatic RET fusion-positive NSCLC previously treated with platinum-based chemotherapy.

(6) Received accelerated approval in the U.S. for the treatment of patients with advanced or metastatic RET-mutant medullary thyroid cancer and RET fusion-positive thyroid cancer. Continued approval may be contingent on confirmatory trials.

(7) (i) For one of the programs, Roche will receive exclusive worldwide commercialization rights and (ii) for the other program, we will retain commercialization rights in the U.S. and Roche will receive commercialization rights outside of the U.S. if Roche exercises its option. We retain worldwide rights to any programs for which Roche elects not to exercise its applicable option. For more information, see "—Collaborations and Licenses" below.

Our Strategy

As a fully-integrated, global precision therapy company focused on discovering, developing and commercializing a portfolio of precision therapies, our vision is to bring life-changing precision therapies to as many patients with cancer and hematologic disorders as possible. To achieve this goal, key elements of our strategy are as follows:

- Accelerate the global adoption of our approved medicines, AYVAKIT and GAVRETO in the U.S. and AYVAKYT in Europe, by continuing to strengthen and expand our global commercial capabilities and preparing for additional planned commercial launches in additional indications, including advanced and non-advanced SM.

- Deepen our strategic focus on SM and related mast cell disorders by seeking regulatory approvals for avapritinib for the treatment of advanced and non-advanced SM and developing BLU-263 for the treatment of non-advanced SM, as well as exploring opportunities to address the needs of additional patient populations with adjacent hematologic disorders.

- Advance the global development and commercialization of pralsetinib and to seek international regulatory approvals under the Roche pralsetinib collaboration as a treatment for RET-altered cancers.

- Advance our innovative research programs, including BLU-701 and BLU-945, our selective and potent EGFR inhibitors for treatment-resistant EGFR-driven NSCLC, and our other preclinical programs, rapidly through development with plans to seek regulatory approval.

- Expand our broad, differentiated precision medicine pipeline, with a focus on genomically defined cancers and hematologic disorders and continued internal discovery research and innovation, 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.

Our Precision Therapy Approach

Our approach is to systematically and reproducibly identify drivers of disease in genomically defined patient populations and to craft drug candidates that provide significant and durable clinical responses to patients. This approach enables us to drug known targets that have been difficult to inhibit selectively and also identify, characterize and design drug candidates to inhibit novel targets. By focusing on diseases in genomically defined patient populations, we believe that we can quickly identify the patients most likely to respond, resulting in a more efficient development path with a greater likelihood of success. To date, our approach has been enabled by our drug discovery platform consisting of two pillars: (1) a proprietary, highly-annotated library of novel compounds; and (2) a novel target discovery engine, which is a comprehensive process that interrogates kinase biology from many angles using genomics, structural biology and cell biology.

We have initially focused our efforts on kinase drug discovery and development. Kinases are enzymes that function in many signaling pathways to regulate critical cellular functions. Kinase-dependent signaling networks are present in multiple different cell types and deregulation of these networks can lead to disease pathology. Abnormal activation of kinases has been shown to drive several key activities of cancer cells, including growth, survival, metabolism, cell motility and angiogenesis. Kinases may become abnormally activated through a number of mechanisms, including when: (1) a gene mutates creating a change in the resulting protein sequence; (2) chromosomes become rearranged creating a translocation or a fusion gene; or (3) excessive amounts of protein are created due to gene duplication or dysregulation leading to overexpression. There is a strong link between genomic alterations in kinases and disease, including specific forms of cancer and rare diseases. Several kinases have been validated as oncogenes, which are genes that when altered can initiate and maintain cancer growth. Ongoing genomic analyses of tumor data sets continue to identify new roles for kinases as drivers of disease.

We believe there is substantial opportunity for developing novel and transformative therapies that target well-characterized but currently difficult-to-drug kinases as well as kinases of unknown biology which constitute the majority of the kinome, by:

- ***Crafting very selective kinase drugs.*** Due to the high degree of homology between kinases, specific targeting of a given kinase can be challenging. Many of the approved kinase drugs inhibit multiple kinases and are referred to as multi-kinase inhibitors. Due to inhibition of off-target kinases, these multi-kinase inhibitors often give rise to severe unwanted effects, which can negatively impact the ability to dose patients at sufficient levels to achieve optimal efficacy. We believe increasing selectivity will minimize off-target toxicities and will improve efficacy by enabling higher dose levels and greater target inhibition. Further, combination therapies require that the drugs have non-overlapping toxicities, which could be minimized with more selective agents.

- ***Generating novel chemical matter required to target difficult-to-drug kinases.*** Novel chemical matter is needed to address targets that are known but have proven difficult-to-drug. Pharmaceutical companies generally rely on known chemical families as the basis of drug discovery programs. Consequently, the vast majority of pharmaceutical companies have similar compound libraries. New approaches are needed to develop novel chemistry and differentiated libraries that can inhibit difficult-to-drug kinases in alternate ways.

- ***Overcoming resistance mediated by the alteration of kinase targets.*** Most approved kinase inhibitors provide only temporary disease control. Patients may relapse due to the emergence of on-target resistance mutations. Novel approaches are needed to predict and inhibit resistant mutants thus providing more durable clinical responses.

Disease Overviews

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. In advanced forms of SM, abnormal mast cells may also accumulate in 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, with nearly all patients (approximately 95%) having a KIT D816V mutation, the underlying driver of disease for most SM patients. The diagnosis, which is usually made in adulthood, involves a complex diagnostic algorithm that begins with confirmation of SM and subsequently categorizes patients into non-advanced or advanced subtypes of disease. Indolent SM, a subset of non-advanced SM, is the most common form of SM and is characterized by often severe, unpredictable and debilitating symptoms due to mast cell activation. Symptoms may include hypersensitivity reactions, including unpredictable anaphylaxis, gastrointestinal distress including severe nausea, vomiting and diarrhea, and extensive skin rashes that cause pain, discomfort and social isolation. Advanced SM

is a more rare form of SM associated with mast cell infiltration of organ systems resulting in increasingly severe impact on life expectancy, and includes three subsets: aggressive SM, or ASM, advanced SM with an associated hematologic neoplasm, SM-AHN, and mast cell leukemia, or MCL. These advanced forms of SM have a median overall survival of three to five years and are characterized by prominent organopathy and dysfunction, as well as symptoms of mast cell activation.

Advanced SM accounts for approximately 5% of the patients, and non-advanced SM, including indolent SM and an intermediate form referred to as smoldering SM, account for the remaining 95% of patients. Population studies estimate the prevalence rate of all subtypes of SM is approximately 9.6 per 100,000 people. We estimate that in the U.S., France, Germany, Italy, Spain, the United Kingdom and Japan, which we collectively refer to as the Major Markets, there are approximately 75,000 patients with SM, including 3,750 patients with advanced SM and 71,250 patients with non-advanced SM.

The current treatment paradigm for SM varies by disease subtype. Currently, there are no approved targeted therapies that address the approximately 95% of SM patients with 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 who do not harbor the KIT D816V mutation.

For patients with non-advanced SM, management is symptom-directed and includes avoidance of triggers of mast cell activation (such as insect stings). Treatments for non-advanced 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. Within non-advanced SM, key opinion leaders see the greatest degree of unmet need for a significant portion of patients who have a heavy symptom burden that current therapies fail to address.

For patients with advanced SM, treatments include midostaurin, interferon-alpha or cytoreductive agents to reduce mast cell burden or treatments aimed at addressing the associated blood disorder. Historical data have shown overall survival of approximately three to five years in patients with advanced SM.

We are developing avapritinib for the treatment of systemic mastocytosis and BLU-263 for the treatment of non-advanced SM and other mast cell disorders. Previously reported clinical data of avapritinib for patients with SM are described below. In January 2021, we announced positive top-line results of BLU-263 in a Phase 1 healthy volunteer trial. Based on the top-line results, we plan to initiate a Phase 2 trial of BLU-263 in patients with non-advanced SM in mid-2021.

Clinical Trial Data in SM

Avapritinib—Phase 1 EXPLORER Trial and Phase 2 PATHFINDER Trial

We are evaluating avapritinib for the treatment of patients with advanced SM in our registration-enabling EXPLORER and PATHFINDER clinical trials. The EXPLORER trial is an open-label, single-arm Phase 1 trial. The PATHFINDER trial is an open-label, single-arm Phase 2 trial. Both trials have completed enrollment. For both the EXPLORER and PATHFINDER trials, key endpoints include overall response rate, or ORR, duration of response, or DOR, quantitative measures of mast cell burden, patient-reported outcomes and safety.

Top-line Data Announced in September 2020

Across both trials, 85 patients were evaluable for response per the modified IWG-MRT-ECNM criteria, or IWG criteria, including 44 patients treated with a starting dose of 200 mg once daily, or QD. Top-line results were reported as of a data cutoff date of May 27, 2020 in the EXPLORER trial and a data cutoff date of June 23, 2020 in the PATHFINDER trial, with response assessments per central review completed in September 2020. Registrational endpoints are ORR and DOR based on central review. ORR was defined as complete remission with full or partial

recovery of peripheral blood counts, or CR/CRh, partial remission or clinical improvement. The confidence interval, or CI, represents the confidence interval of the reported endpoints. All reported clinical responses were confirmed.

Clinical Activity Data. In the EXPLORER trial, 53 patients were response evaluable, with a median follow-up of 27.3 months. In EXPLORER, the ORR was 76 percent (95% CI: 62%, 86%), and 36 percent of patients had a CR/CRh. The median DOR was 38.3 months (95% CI: 21.7 months, not estimable). The median overall survival, or OS, was not estimable (95% CI: 46.9 months, not estimable).

In a pre-specified interim analysis from the PATHFINDER trial, 32 patients were response evaluable, with a median follow-up of 10.4 months. The ORR was 75 percent (95% CI: 57%, 89%), and 19 percent of patients had a CR/CRh. In addition, the data showed that responses are continuing to deepen over time, at a rate consistent with the EXPLORER trial. The median DOR was not estimable (95% CI: not estimable, not estimable), and OS was not assessed due to the length of time patients have been enrolled in PATHFINDER. The top-line PATHFINDER results were based on a pre-planned analysis designed to assess the superiority of avapritinib versus the ORR per IWG criteria previously reported for the multi-kinase inhibitor midostaurin. The interim analysis achieved its primary endpoint with a p-value of p=0.0000000016.

In a pooled efficacy analysis from the 200 mg QD dose group, 44 patients were response evaluable, with a median follow-up of 10.4 months. In this group, the ORR was 68 percent, and 18 percent of patients had a CR/CRh.

Safety Data. Avapritinib was generally well-tolerated with most adverse events, or AEs, reported as Grade 1 or 2. In the EXPLORER and PATHFINDER trials, avapritinib demonstrated improved tolerability at a starting dose of 200 mg QD, compared to all doses. Across both trials, 8.1 percent of patients discontinued avapritinib due to treatment-related AEs.

Previously reported results from the EXPLORER trial showed that pre-existing severe thrombocytopenia, which occurs in approximately 10 to 15 percent of advanced SM patients based on our estimates, and starting doses of 300 mg QD or higher were contributing risk factors for intracranial bleeding, or ICB. Based on these data, we implemented treatment management guidelines in the EXPLORER and PATHFINDER trials, including exclusion criteria for pre-existing severe thrombocytopenia, routine platelet monitoring and dose interruption guidelines for emergent severe thrombocytopenia. In 76 EXPLORER and PATHFINDER trial patients without pre-existing severe thrombocytopenia treated at the 200 mg QD dose, two patients (2.6 percent) had ICB events. Both AEs were Grade 1 and asymptomatic. These safety data validate the clinical impact of the treatment management guidelines.

Phase 2 PIONEER Trial

PIONEER is a randomized, double-blind, placebo-controlled, registration-enabling trial evaluating avapritinib in patients with indolent and smoldering SM. The trial includes three parts: 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 continue 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. Part 1 has completed patient enrollment. We expect to complete enrollment of Part 2 of the PIONEER trial in mid-2021.

Data Presented at American Academy of Allergy, Asthma & Immunology Virtual Forum in March 2020

Part 1 of the PIONEER trial was designed to determine the recommended phase 2 dose, or RP2D, by evaluating three doses of avapritinib (25 mg, 50 mg and 100 mg QD) versus placebo. Key eligibility criteria include adults with indolent SM confirmed by central pathology review and moderate-to-severe symptom burden despite best supportive care medicines. Overall, 39 patients were enrolled in Part 1 across four concurrent cohorts, consisting of 10 patients each in the avapritinib dose cohorts and nine patients in the placebo cohort. Patient-reported outcomes, or PRO, data were collected using the ISM-SAF, which was designed with input from disease experts, patients and regulatory authorities to support registration. All results were as of a data cutoff date of December 27, 2019.

Baseline Patient Characteristics. Patients had high symptom burden at baseline, with a mean ISM-SAF TSS of 53 on a scale of 0 to 110. Eight patients (21 percent) had an Eastern Cooperative Oncology Group Performance Status of 2, reflecting the inability to carry out any work activities. Patients received a median of four best supportive care medicines at baseline (range: 2-9). Median serum tryptase was 45 micrograms per liter (the upper limit of normal is 11.4 micrograms per liter). A high sensitivity polymerase chain reaction assay on peripheral blood detected the KIT D816V mutation in 37 patients (95 percent).

Clinical Activity Data. Avapritinib showed broad activity across measures of mast cell burden, the patient reports outcomes, or PRO, clinical benefit measure and quality of life. The consistency of results observed across multiple measures of disease burden support the further evaluation of avapritinib in indolent SM. At 16 weeks, patients had a statistically significant reduction in ISM-SAF TSS, with a mean improvement of approximately 30 percent across all avapritinib dose cohorts compared to approximately 3 percent in the placebo cohort (p=0.001). As of the data cutoff date, 37 patients (95 percent) have remained on study with a median follow-up of 18 weeks.

Results from the 25 mg QD dose cohort show important clinical activity, including meaningful declines in serum tryptase, bone marrow mast cells and KIT D816V allele burden. Treatment with avapritinib led to consistent reductions in the ISM-SAF TSS, gastrointestinal domain, skin domain and each individual symptom. Symptom improvements in patients treated at 25 mg QD continued to deepen over time.

Mean Percent Changes in ISM-SAF at 16 Weeks (negative change = improved symptoms)		
	Avapritinib 25 mg QD	**Placebo**
TSS	-31%	-3%
Skin domain	-37%	+3%
Gastrointestinal domain	-25%	+6%
Neurological symptoms	-26%	-8%

Data from the Mastocytosis Quality of Life, or MC-QoL, questionnaire, a PRO tool developed for mast cell disorders, show improvements in quality of life for patients receiving avapritinib and support the results observed with the ISM-SAF. Patients in the 25 mg QD dose cohort had a mean reduction of 34 percent in the total MC-QoL score and improvements in all four domains assessed (symptoms, social life functioning, emotions and skin). A 7 percent increase from baseline was observed in the placebo cohort.

Safety Data. The safety profile of avapritinib supports chronic dosing in indolent SM. All doses of avapritinib were well-tolerated and no patients discontinued treatment due to AEs. No patients treated with avapritinib in the 25 mg QD dose cohort had serious AEs, Grade 3 or higher AEs, or dose modifications. In the placebo cohort, two patients (22 percent) had Grade 3 AEs, one with seizure and one with diffuse cutaneous mastocytosis; these events also met criteria for serious AEs.

Data Presented at European Academy of Allergy and Clinical Immunology Digital Congress in June 2020

Previously reported data from Part 1 of the PIONEER trial showed that treatment with avapritinib was well-tolerated and resulted in robust and clinically meaningful improvements on measures of mast cell burden, disease symptoms and patient-reported quality of life through 16 weeks. Based on these data, avapritinib 25 mg QD was selected as the RP2D. Updated data on disease symptoms through 24 weeks and new skin assessment results were reported in June 2020.

Clinical Activity Data. As of a data cutoff date of March 31, 2020, updated data from Part 1 of the PIONEER trial showed a deepening of symptom reductions in patients treated with avapritinib through 24 weeks of follow-up. The mean percent change from baseline in ISM-SAF TSS was -35 percent in patients treated with avapritinib 25 mg QD (n=10) compared to -4 percent in patients treated with placebo. In addition, the mean percent change from baseline in ISM-SAF skin domain score was -38 percent for avapritinib 25 mg QD versus +11 percent for placebo.

The updated data also showed a 60 percent response rate in patients treated with avapritinib 25 mg QD compared to a zero percent response rate in patients treated with placebo at 24 weeks, with response defined as a 30 percent or greater reduction in ISM-SAF TSS.

High resolution skin photographs were taken at baseline and every 12 weeks during treatment for patients with significant cutaneous involvement who consented to photography. To assess changes in skin disease, photographs were assessed by a blinded independent review committee and a computational image analysis algorithm. Images and data as of a cutoff of March 31, 2020 were evaluated by the independent committee.

Based on skin photography at 24 weeks or the last available assessment, results showed that skin lesions lightened in 71 percent of patients treated with avapritinib (n=17; all doses) compared to 25 percent of patients treated with placebo (n=8), per blinded review by the independent committee. In addition, the median percent change from baseline in most affected surface area was -35 percent for avapritinib (n=18; all doses) compared to -8 percent for placebo (n=8), based on a computational image analysis algorithm.

Mast cell infiltration in skin lesions was also assessed by lesional skin biopsies obtained at baseline and 12 weeks. The median percent change from baseline in mast cell infiltration was -46 percent for avapritinib (n=18; all doses) compared to +51 percent for placebo (n=7).

Safety Data. As of a data cutoff date of March 31, 2020, avapritinib 25 mg QD was well-tolerated and safety results were consistent with previously reported data, with no Grade ≥3 adverse events or discontinuations due to adverse events.

RET-Altered Cancers

RET is a receptor tyrosine kinase that activates multiple downstream pathways involved in cell proliferation and survival. RET can be activated by mutation or when a portion of the RET gene that encodes the kinase domain is joined to part of another gene creating a fusion gene that encodes an aberrantly activated RET fusion protein. RET activating mutations are implicated in advanced MTC (approximately 90% of patients), and RET fusions are implicated in several cancers, including papillary thyroid carcinoma (approximately 10- 20% of patients) and NSCLC (1-2% of patients). We estimate that in the Major Markets, there are approximately 8,900 first-and second-line patients with RET-altered NSCLC and 1,300 patients with MTC, regardless of line of therapy or alteration. In addition, oncogenic RET alterations are observed at low frequencies in colorectal, breast, pancreatic and other cancers, providing a therapeutic rationale for the use of RET inhibitors in multiple patient subpopulations.

The identification of RET fusions as drivers in some cancers prompted the use of approved multi-kinase inhibitors with RET inhibitory activity to treat patients whose tumors express a RET fusion protein. However, we believe these drugs cannot be dosed at levels required to sufficiently inhibit RET due to toxicities that result from inhibition of the primary targets. For example, currently approved therapies such as vandetanib and cabozantinib demonstrate lower objective response rates and DOR in patients with RET-altered NSCLC compared to selective kinase inhibitors targeting other kinase drivers such as EGFR, ALK and ROS1.

One of the greatest challenges in treating cancer is the ability of tumor cells to become resistant to therapy. Kinase reactivation via mutation to evade small molecule inhibition is a common mechanism of resistance. We have predicted future resistance mutations of drugs with RET inhibitory activity. Thus, there is a clear need for a selective RET inhibitor that targets both oncogenic RET fusions and activating mutations and their predicted RET resistance mutations.

Currently, pralsetinib (under the brand name GAVRETO) is the only once-daily RET-targeted therapy approved by the FDA for the treatment of certain RET-altered NSCLC and thyroid cancers in the U.S. Previously reported clinical data of pralsetinib in patients with RET-altered cancers are described below. Pursuant to our collaboration with Roche, we plan to co-develop pralsetinib globally in RET-altered solid tumors, including NSCLC, MTC and other thyroid cancers, as well as other solid tumors.

Clinical Trial Data in RET-altered NSCLC and Thyroid Cancers

GAVRETO (pralsetinib)—Phase 1/2 ARROW Trial

The ARROW trial is a Phase 1/2 open-label, registration-enabling trial designed to evaluate the safety, tolerability and efficacy of pralsetinib in adults with RET-altered cancers. The trial consists of two parts: a dose escalation portion and an expansion portion in patients treated at 400 mg QD. The dose-escalation portion of the ARROW trial is complete, and the expansion portion is actively enrolling patients at multiple sites in the United States, European Union and Asia.

Top-Line Data in RET-Altered Thyroid Cancers Announced in April 2020

Top-line efficacy data were reported for patients treated with pralsetinib who were evaluable for response assessment per RECIST 1.1, as determined by blinded independent central review. All patients received the proposed indicated dose of 400 mg QD. All results were as of a data cutoff date of February 13, 2020.

Clinical Activity Data. In 53 patients with RET-mutant MTC previously treated with cabozantinib or vandetanib, the ORR was 60 percent (95% CI: 46%,74%) with one response pending confirmation. Nearly all patients (98 percent) had tumor shrinkage. The median DOR was not reached (95% CI: not estimable, not estimable), and the 18-month DOR rate was 90 percent (95% CI: 77%, 100%).

In addition, the top-line data showed robust clinical activity in treatment-naïve patients, supporting the potential of pralsetinib across lines of therapy. In 19 patients with RET-mutant MTC who had not received prior systemic treatment, the confirmed ORR was 74 percent (95% CI: 49%, 91%), and all patients had tumor shrinkage. The median DOR was not reached (95% CI: 7 months, not estimable), with 12 of 14 responders remaining in response for up to 15 months as of the data cutoff date.

In nine patients with RET fusion-positive thyroid cancer, the confirmed ORR was 89 percent (95% CI: 52%, 100%), and all patients had tumor shrinkage. The median DOR was not reached (95% CI: 8 months, not estimable), with seven of eight responders remaining in response for up to 20 months as of the data cutoff date.

Safety Data. Top-line safety data were consistent with those previously reported. Pralsetinib was well-tolerated, and most treatment-related AEs were Grade 1 or 2. Across all patients enrolled in the ARROW trial treated at the proposed indicated dose of 400 mg QD (n=438), only 4 percent discontinued treatment with pralsetinib due to treatment-related AEs.

Data Presented at American Society of Clinical Oncology 2020 Virtual Scientific Program in May 2020

The reported data included response-evaluable populations comprising 116 patients with NSCLC who received a starting dose of 400 mg QD, including 80 patients with NSCLC previously treated with platinum-based chemotherapy and 26 patients with treatment-naïve NSCLC, 11 patients with RET fusion-positive thyroid cancer, and 12 patients with other RET fusion-positive cancers. Tumor response was assessed by blinded, independent central review using RECIST version 1.1.

Clinical Activity Data – RET Fusion-Positive NSCLC. As of a data cutoff of November 18, 2019, pralsetinib demonstrated consistent and robust clinical activity in RET fusion-positive NSCLC, regardless of prior therapy, RET fusion partner or CNS involvement.

In 80 patients who previously received platinum-based chemotherapy, the ORR was 61 percent (95% CI: 50%, 72%). Two partial responses, or PRs, were pending confirmation at the time of the data cut off and were subsequently confirmed. Five percent of patients had a complete response, or CR, and 14 percent of patients had complete regression

of target tumors. In 26 patients with no prior systemic therapy, the confirmed ORR was 73 percent (95% CI: 52%, 88%), and the CR rate was 12 percent.

Across all 116 patients, regardless of prior therapy, the median DOR was not reached (95% CI: 11 months, not reached), and the 6-month DOR was 86 percent. Overall, 74 percent of confirmed responders, including all patients with CRs, were on treatment as of the data cutoff.

Robust and durable intracranial activity was shown in nine patients with measurable CNS metastases at baseline. All patients had shrinkage of CNS metastases, with an intracranial CR rate of 33 percent. No CNS responders experienced CNS progressive events. The median CNS DOR was not reached, with ongoing treatment durations up to 12 months in patients with measurable CNS metastases. Among patients without a history of CNS metastases, none have developed new CNS metastases on study as of the data cutoff date.

Clinical Activity Data – Other RET Fusion-Positive Cancers. As of a data cutoff of February 13, 2020, pralsetinib demonstrated robust clinical activity in a range of additional RET fusion-positive cancers. In 11 patients with RET fusion-positive thyroid cancer (10 previously treated with systemic therapy), the centrally confirmed ORR was 91 percent (95% CI: 59%, 100%), and the disease control rate, or DCR, was 100 percent (95% CI: 72%, 100%). Overall, 70 percent of responders remain on therapy with ongoing treatment durations up to 22 months as of the data cutoff. Across 12 patients with other RET fusion-positive cancers previously treated with systemic therapy, the investigator-assessed ORR was 50 percent (95% CI: 21%, 79%), with one PR pending confirmation as of the data cutoff. Responses were observed in all evaluable patients with pancreatic adenocarcinoma (n=3) and cholangiocarcinoma (n=2), tumor types with a typically poor prognosis.

Safety Data. As of the data cutoff date of November 18, 2019, a total of 354 patients were enrolled in the ARROW trial at a starting dose of 400 mg QD. Overall, safety results were consistent with previously reported data. Pralsetinib was well-tolerated across tumor types, and most treatment-related AEs were Grade 1 or 2.

The most common treatment-related AEs reported by investigators (≥15 percent) were increased aspartate aminotransferase, anemia, increased alanine aminotransferase, constipation, hypertension and neutropenia. Investigator-reported Grade 3 or higher treatment-related AEs (≥5 percent) were hypertension, neutropenia and anemia. Only 4 percent of patients discontinued pralsetinib due to treatment-related AEs.

Data Presented at European Society for Medical Oncology Virtual Congress 2020 in September 2020

The presented data included response-evaluable patients with RET-mutant MTC who were previously treated with cabozantinib or vandetanib, or naïve to systemic treatment. Tumor response was assessed by blinded, independent central review using RECIST version 1.1. All patients received a pralsetinib starting dose of 400 mg QD, and results were reported as of a data cutoff date of February 13, 2020.

Clinical Activity Data – RET-Mutant MTC. Pralsetinib demonstrated broad clinical activity in patients with RET-mutant MTC with or without prior systemic therapy. In 53 patients previously treated with cabozantinib or vandetanib, the ORR was 60 percent (95% CI: 46%, 74%) with one response pending confirmation, and the DCR was 96 percent (95% CI: 87%, 100%). The median DOR was not reached (95% CI: not reached, not reached), with 94 percent of responders remaining on treatment. The median progression-free survival, or PFS, was not reached (95% CI: not reached, not reached) in patients previously treated with cabozantinib or vandetanib.

In 19 systemic treatment-naïve patients who were ineligible for standard therapy per the study protocol, the confirmed ORR was 74 percent (95% CI: 49%, 91%), and the DCR was 100 percent (95% CI: 82%, 100%). The median DOR was not reached (95% CI: 7 months, not reached), with 93 percent of responders remaining on treatment. The median PFS was not reached (95% CI: not reached, not reached) in systemic treatment-naïve patients.

Five of six patients whose tumors had a RET V804M or V804L gatekeeper mutation achieved a clinical response. Three patients previously treated with multi-kinase inhibitors had a RET M918T activating mutation and a

RET V804M or V804L gatekeeper resistance mutation at baseline, and all three of these patients had a clinical response following pralsetinib treatment.

Safety Data. The reported safety data included a total of 438 patients enrolled in the ARROW trial at a pralsetinib starting dose of 400 mg QD, regardless of tumor type. Pralsetinib was well-tolerated with safety results consistent with previously reported data. Overall, treatment-related AEs were primarily Grade 1 or 2. The most common treatment-related AEs reported by investigators (≥15 percent) were increased aspartate aminotransferase, anemia, increased alanine aminotransferase, hypertension, constipation, decreased white blood cell count, neutropenia, decreased neutrophil count and hyperphosphatemia. Investigator-reported Grade 3 or higher treatment-related AEs (≥5 percent) were hypertension, neutropenia, anemia and decreased neutrophil count. Four percent of patients discontinued pralsetinib due to treatment-related AEs.

Gastrointestinal Stromal Tumors (GIST)

GIST is a rare disease that is a sarcoma of the gastrointestinal tract. Tumors arise within cells in the wall of the gastrointestinal tract and occur most often in the stomach or small intestine. Most patients are diagnosed between the ages of 50-80 with diagnosis triggered by gastrointestinal bleeding, incidental findings during surgery or imaging, or in rare cases acute presentation due to tumor rupture or gastrointestinal obstruction. The standard workup at primary presentation includes pathologic confirmation and imaging to assess extent of disease.

The GIST treatment paradigm has advanced dramatically over the past years. Patients diagnosed with localized disease undergo potentially curative tumor resection, while imatinib is given to high risk resected patients to prolong the time to recurrence. The advent of imatinib has improved the prognosis of patients with unresectable or metastatic disease to a five-year median overall survival. Unresectable or metastatic patients typically receive imatinib, followed by sunitinib and regorafenib as the disease progresses.

GIST is a tumor type that depends on continued signaling of a single, aberrantly active kinase. About 5 to 6 percent of primary GIST cases are caused by a PDGFRA D842V mutation, the most common PDGFRA exon 18 mutation. Published data have shown poor outcomes in patients with PDGFRA D842V mutant GIST treated with imatinib and other approved therapies that do not specifically target PDGFRA mutations. Progression can occur within as little as three months, and the median overall survival is 15 months for patients with advanced disease. Currently, AYVAKIT is the only FDA-approved treatment for patients with D842V mutant PDGFRA-driven GIST.

Hepatocellular Carcinoma (HCC)

Liver cancer is the second leading cause of cancer-related deaths worldwide, and HCC accounts for most liver cancers. The highest incidence of HCC occurs in regions with endemic hepatitis B virus, or HBV, including Southeast Asia and sub-Saharan Africa. Cirrhosis is a key risk factor for HCC — the disease etiology varies by geography with the common theme of chronic conditions that lead to cirrhosis. In North America, the main risk factors for cirrhosis are infection with hepatitis C virus, or HCV, followed by HBV infection, alcohol consumption and nonalcoholic steatohepatitis. In the European Union, the main risk factors for cirrhosis are HCV, HBV and alcohol consumption. In Asia and sub-Saharan Africa, the major risk factor is chronic HBV infection.

The FGFR4 signaling pathway is a potential driver of disease in a subset of HCC patients. In these patients, FGF19 (the ligand that activates FGFR4) is overexpressed in hepatocytes, which do not normally express FGF19, leading to autocrine signaling and tumor growth. We estimate that approximately 30% of patients have FGFR4-activated HCC.

As part of our collaboration with CStone, we are evaluating fisogatinib as a monotherapy and in combination with sugemalimab for the treatment of locally advanced or metastatic HCC.

Treatment-Resistant EGFR-Mutated NSCLC

Among the 80 to 85 percent of lung cancers classified as NSCLC, it is estimated that about 10-15% of cases in the U.S. and Europe and about 40-50% of cases in Asia are caused by activating EGFR mutations. In recent years, the

introduction of EGFR targeted therapies including osimertinib has dramatically improved outcomes in patients with EGFR-mutated NSCLC. However, the emergence of tumor resistance represents an urgent medical need and there are no approved therapies for osimertinib-resistant EGFR-mutated NSCLC.

We are developing BLU-701 and BLU-945, each as a monotherapy and/or in combination with other agents, for the treatment of patients with treatment-resistant EGFR-mutated NSCLC. We plan to initiate a Phase 1 trial of BLU-701 in patients with treatment-resistant EGFR-driven NSCLC by the end of 2021, and to initiate a Phase 1 trial of BLU-945 in patients with treatment-resistant EGFR-driven NSCLC in the first half of 2021.

Collaborations and Licenses

Roche – Immunotherapy Collaboration

In March 2016, we entered into a collaboration and license agreement, or the Roche immunotherapy agreement, as may be amended from time to time, with 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. As a result of an amendment to the Roche immunotherapy agreement in the first quarter of 2021, we and Roche are currently conducting activities for up to two programs under the collaboration, including the previously announced program for the kinase target MAP4K1, which is believed to play a role in T cell regulation.

Under the Roche immunotherapy agreement, as amended, Roche was granted two option rights to obtain an exclusive license to exploit products derived from the collaboration programs in the field of cancer immunotherapy. Such option rights are triggered upon the achievement of Phase 1 proof-of-concept. For one of the collaboration programs, if Roche exercises its option, Roche will receive worldwide, exclusive commercialization rights for the licensed product. For the other collaboration program, if Roche exercises its option, we will retain commercialization rights in the U.S. for the licensed product, and Roche will receive commercialization rights outside of the U.S. for the licensed product. We will also retain worldwide rights to any products for which Roche elects not to exercise its applicable option.

Prior to Roche's exercise of an option, we have the lead responsibility for drug discovery and pre-clinical development of all collaboration programs. In addition, we have the lead responsibility for the conduct of all Phase 1 clinical trials other than those Phase 1 clinical trials for any product in combination with Roche's portfolio of therapeutics, for which Roche will have the right to lead the conduct of such Phase 1 clinical trials. Pursuant to the Roche immunotherapy agreement, the parties share the costs of Phase 1 development for each collaboration program. In addition, Roche will be responsible for post-Phase 1 development costs for each licensed product for which it retains global commercialization rights, and we and Roche will share post-Phase 1 development costs for each licensed product for which we retain commercialization rights in the U.S.

We received an upfront cash payment of $45.0 million in March 2016 upon execution of the Roche immunotherapy agreement, and through December 31, 2020, we have achieved $19.5 million in milestone payments under this collaboration. Subject to the terms of the Roche immunotherapy agreement, as amended, in addition to upfront and milestone payments received through December 31, 2020, we are eligible to receive up to approximately $323.3 million in contingent option fees and milestone payments related to specified research, pre-clinical, clinical, regulatory and sales-based milestones. In addition, for any licensed product for which Roche retains worldwide commercialization rights, we will be eligible to receive tiered royalties ranging from low double-digits to high-teens on future net sales of the licensed product. For any licensed product for which we retain commercialization rights in the U.S., we and Roche will be eligible to receive tiered royalties ranging from mid-single-digits to low double-digits on future net sales in the other party's respective territories in which it commercializes the licensed product. The upfront cash payment and any payments for milestones, option fees and royalties are non-refundable, non-creditable and not subject to set-off.

Under the Roche immunotherapy 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 Roche immunotherapy agreement, including license grants to enable each party to conduct research, development and commercialization activities pursuant to the terms of the Roche immunotherapy agreement. Following Roche's exercise

of its option with respect to the collaboration programs for which it will obtain worldwide rights, we will grant Roche an exclusive license under our intellectual property to develop and commercialize the licensed products generated through such collaboration program. Similarly, Roche will grant us an exclusive license under Roche's intellectual property to develop and commercialize licensed products in the U.S. for the collaboration programs on which we will retain rights in the U.S., with Roche receiving a license under our intellectual property to develop and commercialize such licensed products outside of the U.S.

Subject to the terms and conditions of the Roche immunotherapy agreement, we have agreed to work exclusively with Roche with respect to each collaboration target. We are not obligated to work exclusively with Roche within the field of cancer immunotherapy. In addition, subject to specified exceptions, Roche has a right of first negotiation in the event that we desire to grant any third party rights to develop or commercialize a licensed product for which we retain commercialization rights in the U.S. Roche's right of first negotiation will not apply in connection with a change of control of us, an assignment by us in accordance with the terms of the Roche immunotherapy agreement or certain agreements with contract research organizations, contract manufacturing organizations, academic institutions, not-for-profit third parties or distributors.

The Roche immunotherapy agreement will continue until the date when no royalty or other payment obligations are or will become due, unless earlier terminated in accordance with the terms of the Roche immunotherapy agreement. Prior to its exercise of its first option, Roche may terminate the Roche immunotherapy agreement at will, in whole or on a collaboration target-by-collaboration target basis, upon 120 days' prior written notice to us. Following its exercise of an option, Roche may terminate the Roche immunotherapy agreement at will, in whole, on a collaboration target-by-collaboration target basis, on a collaboration program-by-collaboration program basis or, if a licensed product has been commercially sold, on a country-by-country basis, (i) upon 120 days' prior written notice if a licensed product has not been commercially sold or (ii) upon 180 days' prior written notice if a licensed product has been commercially sold. Either party may terminate the Roche immunotherapy agreement for the other party's uncured material breach or insolvency and in certain other circumstances agreed to by the parties. In certain termination circumstances, we are entitled to retain specified licenses to be able to continue to exploit the licensed products.

Roche – Pralsetinib Collaboration

On July 13, 2020, we entered into a collaboration agreement, or the Roche pralsetinib collaboration agreement, with Roche pursuant to which we granted Roche exclusive rights to develop and commercialize pralsetinib worldwide, excluding the CStone territory, and a co-exclusive license in the U.S. to develop and commercialize pralsetinib. In addition, Roche has the right to opt in to a next-generation RET compound co-developed by Roche and us.

Under the Roche pralsetinib collaboration agreement, we received upfront cash payments of $775.0 million in the third quarter of 2020, including an upfront payment of $675.0 million and the $100.0 million equity investment by Roche described below. Through December 31, 2020, we have received $55.0 million in specified regulatory and commercialization milestones. In addition to the upfront and milestone payments received through December 31, 2020, we are eligible to receive up to $872.0 million in contingent payments, including specified development, regulatory and sales-based milestones for pralsetinib and any licensed product containing a next-generation RET compound.

In the U.S., we and Roche are working together to co-commercialize pralsetinib and will equally share responsibilities, profits and losses. In addition, we are eligible to receive tiered royalties ranging from high-teens to mid-twenties on annual net sales of pralsetinib outside the U.S., excluding the CStone territory, which we refer to as the Roche territory. We and Roche have also agreed to co-develop pralsetinib globally in RET-altered solid tumors, including NSCLC, MTC and other thyroid cancers, as well as other solid tumors. We and Roche will share global development costs for pralsetinib at a rate of 45 percent for us and 55 percent for Roche up to a specified amount of aggregate joint development costs, after which our share of global development costs for pralsetinib will be reduced by a specified percentage. We and Roche will also share specified global development costs for any next-generation RET compound co-developed under the collaboration in a similar manner.

Unless earlier terminated in accordance with its terms, the Roche pralsetinib collaboration agreement will expire on a licensed product-by-licensed product basis (i) in the U.S. upon the expiration of the gross profit sharing term for such licensed product and (ii) outside the U.S. on a country-by-country basis at the end of the applicable royalty term for such licensed product. Roche may terminate the agreement in its entirety or on a licensed product-by-licensed

product or country-by-country basis subject to certain notice periods. Either party may terminate the Roche pralsetinib collaboration agreement for the other party's uncured material breach or insolvency. Subject to the terms of the Roche pralsetinib collaboration agreement, effective upon termination of the agreement, we are entitled to retain specified licenses to be able to continue to exploit the licensed products.

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

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, including certain back-up forms and certain 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, 2020, we have received $14.0 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, 2020, we will be eligible to receive up to approximately $332.0 million in milestone payments, including $104.5 million related to development and regulatory milestones and $227.5 million related to sales-based milestones. In addition, CStone will be obligated to pay 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 will be responsible for costs related to the development of the licensed products in the CStone territory, other than specified costs related to the development of fisogatinib as a combination therapy in the CStone territory that will be shared by 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, a wholly-owned subsidiary of Ipsen S.A. 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 Phase 1 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, 2020, we have received $20.0 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 $490.0 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 on or after October 15, 2021 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.

Intellectual Property

Our commercial success depends in part on our ability to obtain and maintain proprietary or intellectual property protection for our drug and drug candidates, as well as our core technologies, including our novel target discovery engine, our proprietary compound library, 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 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 file patent applications directed to AYVAKIT/AYVAKYT, GAVRETO and our drug candidates in an effort to establish intellectual property positions regarding these new chemical entities as well as uses of these new chemical entities in the treatment of diseases and to other technologies, including patient selection markers and diagnostic discoveries that may be useful with our drug and drug candidates. We also file patent applications directed to novel fusions that we have discovered through our target discovery engine and the use of these fusions in diagnosing and treating disease. As of January 31, 2021, we owned 35 issued U.S. patents, 16 pending U.S. non-provisional patent applications, six pending U.S. provisional applications, 51 issued foreign patents, 107 foreign pending patent applications, and seven pending Patent Cooperation Treaty, or PCT, international patent applications. The foreign issued patents and patent applications are in a number of jurisdictions, including Argentina, Australia, Brazil, Canada, China, the European Union, Gulf Cooperation Council, Hong Kong, Israel, Japan, South Korea, Mexico, New Zealand,

Philippines, Russia, Singapore, South Africa, and Taiwan. Our issued patents and pending patent applications pertain to our pipeline, including our programs for avapritinib, pralsetinib, fisogatinib, BLU-263 as well as additional kinase discovery programs and novel recurrent fusions.

The intellectual property portfolios for our approved drugs and clinical-stage drug candidates as of January 31, 2021 are summarized below. 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, and by patent offices in other countries are often significantly narrowed by the time they issue, if they issue at all. We expect this to be the case with respect to our pending patent applications referred to below.

KIT and PDGFRA Program—AYVAKIT/AYVAKYT (avapritinib) and BLU-263

The intellectual property portfolio for our KIT and PDGFRA program contains patent applications directed to compositions of matter for avapritinib, BLU-263 and analogs thereof, compositions of matter for KIT and PDGFRA inhibitors with different compound families, as well as methods of use and manufacture. As of January 31, 2021, we owned 11 issued U.S. patents, 15 issued foreign patents, including one European patent validated in 38 countries, three pending U.S. non-provisional patent applications, three pending U.S. provisional applications, five pending PCT international patent applications and 22 pending foreign patent applications directed to our KIT and PDGFRA program, including avapritinib and BLU-263. The patents that have issued or will issue covering our KIT and PDGFRA program will have a statutory expiration date between 2034 and 2041. Patent term adjustments or patent term extensions could result in later expiration dates.

RET Program—GAVRETO (pralsetinib)

The intellectual property portfolio for our RET program contains patent applications directed to compositions of matter for pralsetinib and analogs and compositions of matter for RET inhibitors with different compound families, as well as methods of use. As of January 31, 2021, we owned seven issued U.S. patents, six pending U.S. non-provisional patent applications, three pending U.S. provisional applications, one pending PCT international application, 53 pending foreign patent applications and four issued foreign patents directed to our RET program, including pralsetinib. The patents that have issued or will issue covering our RET program will have a statutory expiration date between 2036 and 2041. Patent term adjustments or patent term extensions could result in later expiration dates.

FGFR4 Program — Fisogatinib

The intellectual property portfolio for our FGFR4 program contains patent applications directed to compositions of matter for fisogatinib and analogs and compositions of matter for FGFR4 inhibitors with different compound families as well as methods of use. As of January 31, 2021, we owned nine issued U.S. patents, two pending U.S. non-provisional patent applications, one pending PCT international application, 28 pending foreign patent applications and 27 issued foreign patents directed to our FGFR4 program, including fisogatinib. The patents that have issued or will issue covering our FGFR4 program will have a statutory expiration date between 2033 and 2040. Patent term adjustments or patent term extensions could result in later expiration dates.

Platform

The intellectual property portfolio directed to our platform includes patent applications directed to novel gene fusions and the uses of these fusions for detecting and treating conditions implicated with these fusions. As of January 31, 2021, we owned eight issued U.S. patents, five pending U.S. patent applications, four pending European Union patent applications and five issued European patents directed to this technology, which, if issued, will have statutory expiration dates ranging from 2034 to 2035.

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 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 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 proprietary compound library, 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 the segments of the pharmaceutical, biotechnology and other related markets that address inhibition of kinases in cancer and other rare diseases. There are other companies working to develop therapies in the field of kinase inhibition for cancer and other diseases. 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, pre-clinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved drugs than we do. Mergers and acquisitions in the pharmaceutical, biotechnology and diagnostic industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize drugs that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any drugs that we or our collaborators may develop. Our competitors also may obtain FDA or other regulatory approval for their drugs more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we or our collaborators are able to enter the market. The key competitive factors affecting the success of our drugs and our current or future drug candidates, if approved, are likely to be their efficacy, safety, convenience, price, the effectiveness of companion diagnostic tests in guiding the use of related therapeutics, 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

We are developing avapritinib for SM, including advanced SM and non-advanced SM, and we are developing BLU-263 for the treatment of non-advanced SM and other mast cell disorders. If avapritinib receives marketing approval for advanced SM, it will face competition from Novartis AG's midostaurin and imatinib. In addition, if avapritinib or BLU-263 are approved for advanced SM or non-advanced SM, they may face competition from other drug candidates in development for these indications, including those being developed by AB Science S.A., Allakos Inc. and Cogent Biosciences, Inc.

RET-altered Cancers

GAVRETO faces competition for RET fusion-positive NSCLC and RET-altered thyroid carcinoma, including MTC, from Eli Lilly and Company's selpercatinib. If pralsetinib receives marketing approval for patients with other solid tumors, it will also face competition from selpercatinib for these additional indications. In addition, pralsetinib may face competition from other drug candidates in development for RET-altered cancers, including those being developed by AstraZeneca plc, Boston Pharmaceuticals, Inc., Eisai Inc., Exelixis, Inc., GlaxoSmithKline plc, Mirati Therapeutics, Inc., Novartis AG, Pfizer Inc. Roche, Stemline Therapeutics, Inc., and Turning Point Therapeutics, Inc., as well as several approved multi-kinase inhibitors with RET activity being evaluated in clinical trials, including alectinib, apatinib, cabozantinib, dovitinib, lenvatinib, sorafenib, sunitinib and vandetinib.

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

HCC

We are developing fisogatinib for patients with advanced HCC. If fisogatinib receives marketing approval for patients with FGFR4-activated HCC, it will face competition from Bristol-Myers Squibb Company's nivolumab and

Merck & Co., Inc.'s pembrolizumab, immune checkpoint inhibitors approved by the FDA for the treatment of HCC, as well as sorafenib, cabozantinib, regorafenib and lenvatinib, multi-kinase inhibitors approved for the treatment of HCC. In addition, fisogatinib may face competition from other drug candidates in development by Abbisko Therapeutics Co., Ltd, AstraZeneca plc, Bayer AG, Celgene Corporation, Eisai Inc., H3 Biomedicine Inc., Incyte Corporation, Johnson & Johnson, Novartis AG, Sanofi S.A., Taiho Pharmaceutical Co., Ltd., U3 Pharma GmbH, a wholly-owned subsidiary of Daiichi Sankyo Company, Limited, and Xoma Ltd.

Treatment-Resistant EGFR-Mutated NSCLC

We are developing drug candidates for treatment-resistant EGFR-mutated NSCLC, which, if approved, will face competition from AstraZeneca plc's osimertinib and almonertinib, which is under collaboration between Jiangsu Hansoh Pharmaceutical Group Co., Ltd. and EQRX, Inc. and approved in China. In addition, our EGFR inhibitors may face competition from drug candidates in development for EGFR-mutated NSCLC, including those being developed by Alpha Biopharma Inc., Astellas Pharma Inc., Boehringer Ingelheim RCV GmbH & Co KG, Bridge Biotherapeutics, Inc., C4 Therapeutics, Inc., Chia Tai Tianqing Pharmaceutical Group, Daiichi Sankyo Company, Limited, Genosco Inc., Genprex, Inc., Janssen Pharmaceuticals, Inc., and Yuhan Corporation.

Commercialization

As a fully-integrated, global precision therapy company focused on discovering, developing and commercializing a portfolio of precision therapies, our vision is to bring life-changing precision therapies to as many patients with cancer and hematologic disorders as possible. We have established our own commercial organization in the U.S. and Europe in connection with our commercial launches of AYVAKIT and GAVRETO in the U.S. and AYVAKYT in Europe. We have also entered into collaborations with our partners, including CStone and Roche, for planned global commercialization activities for AYVAKIT/AYVAKYT and GAVRETO in their respective territories. We are continuing to expand our commercialization capabilities and to build our distribution capabilities to accelerate global adoption of our approved drugs and to prepare for additional planned commercial launches with an initial focus on the U.S. and Europe.

We believe our portfolio strategy focused on genomically defined cancers and hematologic disorders will allow us to efficiently commercialize approved drugs in the U.S. and Europe initially and worldwide longer-term, using a small and highly specialized sales force similar to those of other rare disease companies. 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 pre-clinical and clinical testing, as well as for commercial manufacture of any drug we may commercialize. To date, we have obtained materials for avapritinib, pralsetinib, fisogatinib, BLU-263 and BLU-945 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. Although we have negotiated manufacturing agreements with certain venders for the commercial supply of AYVAKIT/AYVAKYT and GAVRETO, 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.

Under the terms of our agreements related to the development and commercialization of companion diagnostic tests, third parties are responsible for the commercialization of companion diagnostic tests for avapritinib in order to

identify GIST patients with the PDGFRA D842V mutation, pralsetinib in order to identify NSCLC patients with RET fusions and fisogatinib in order to identify HCC patients with FGFR4 pathway activation. We generally expect to rely on third parties for the manufacture of any other companion diagnostic tests we may seek to develop.

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 pre-clinical 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 pre-clinical 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: pre-clinical and clinical. For new chemical entities, the pre-clinical 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, which support subsequent clinical testing. The conduct of the pre-clinical tests must comply with federal regulations, including GLPs, where applicable. The sponsor must submit the results of the pre-clinical 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 pre-clinical 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.

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 for oncology indications generally involve a small number of disease-affected patients who are treated with the drug candidate in escalating dose cohorts. The primary purpose of these clinical trials is to determine the MTD, or a recommended dose if the MTD is not achieved, assess the pharmacokinetic, or PK, profile, pharmacologic action, side effect tolerability and safety of the drug. Phase 1 clinical trials for oncology indications 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 adverse effects 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, its safety in use, and to establish the overall benefit/risk relationship of the drug and provide an adequate basis for physician 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. We 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 pre-clinical 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 pre-clinical and clinical testing. The application includes both negative or ambiguous results of pre-clinical 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. The FDA adjusts the PDUFA user fees on an annual basis. According to the FDA's fiscal year 2021 fee schedule, effective through September 30, 2021, the user fee for an application requiring clinical data, such as an NDA, is $2,875,842. PDUFA also imposes an annual prescription drug product program fee for human drugs ($336,432 for the current fiscal year). 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 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 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. The review and evaluation of an NDA by the FDA is extensive and time consuming and may take longer than originally planned to complete, and we may not receive a timely approval, if at all.

Before approving an NDA, the FDA will 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 due to the COVID-19 pandemic. 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, pre-clinical 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. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data.

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 pre-clinical 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 the drug may be subject to accelerated withdrawal procedures.

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.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. Furthermore, fast track designation, priority review, accelerated approval and breakthrough therapy designation, do not change the standards for approval and may not ultimately expedite the development or approval process.

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 pre-clinical 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 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. 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, 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.

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 amended by the Health Care and Education Reconciliation Act of 2010, or collectively, the Affordable Care Act. 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. Prohibitions or restrictions on sales or withdrawal of future products marketed by us could materially affect our business in an adverse way.

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 pre-clinical 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 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.

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 European Union, the European Commission, after receiving the opinion of the EMA's Committee for Orphan Medicinal Products, or COMP, grants medicinal product designation to promote the development of products that are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating conditions affecting not more than five in 10,000 persons in the European Union Community. In addition, designation is granted for products intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition and when, without incentives, it is unlikely that sales of the drug in the European Union would be sufficient to justify the necessary investment in developing the drug or biological product.

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.

In the European Union, 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 drug or biological product approval. This period may be reduced to six years if the medicinal product designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market 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. Congress has extended the PRV program through September 30, 2024, with the potential for PRVs to be granted through September 30, 2026.

Regulation of Diagnostic Tests

We expect that our drug candidates may require use of a diagnostic to identify appropriate patient populations for our products. These diagnostics, often referred to as companion diagnostic tests, are medical devices, often *in vitro* devices, which provide information that is essential for the safe and effective use of a corresponding drug. For example, we have entered into agreements with third parties to develop and commercialize companion diagnostic tests for avapritinib in order to identify GIST patients with the PDGFRA D842V mutation, pralsetinib in order to identify NSCLC patients with RET fusions and fisogatinib in order to identify HCC patients with FGFR4 pathway activation. In the U.S., the FDCA and its implementing regulations, and other federal and state statutes and regulations govern, among

other things, medical device design and development, pre-clinical and clinical testing, premarket clearance or approval, establishment registration and device listing, manufacturing, labeling, storage, advertising and promotion, sales and distribution, export and import, and post-market surveillance. Unless an exemption applies, diagnostic tests require marketing clearance or approval from the FDA prior to commercial distribution. The two primary types of FDA marketing authorization applicable to a medical device are premarket notification, also called 510(k) clearance, and premarket approval, or PMA approval. We expect that any companion diagnostic test developed for our drug candidates will utilize the PMA pathway.

PMA applications must be supported by valid scientific evidence, which typically requires extensive data, including technical, pre-clinical, clinical and manufacturing data, to demonstrate to the FDA's satisfaction the safety and effectiveness of the device. For diagnostic tests, a PMA application typically includes data regarding analytical and clinical validation studies. As part of its review of the PMA, the FDA will conduct a pre-approval inspection of the manufacturing facility or facilities to ensure compliance with the Quality System Regulation, or QSR, which requires manufacturers to follow design, testing, control, documentation and other quality assurance procedures. FDA review of an initial PMA may require several years to complete. If the FDA evaluations of both the PMA application and the manufacturing facilities are favorable, the FDA will either issue an approval letter or an approvable letter, which usually contains a number of conditions that must be met in order to secure the final approval of the PMA. If the FDA's evaluation of the PMA or manufacturing facilities is not favorable, the FDA will deny approval of the PMA or issue a not approvable letter. A not approvable letter will outline the deficiencies in the application and, where practical, will identify what is necessary to make the PMA approvable. The FDA may also determine that additional clinical trials are necessary, in which case the PMA approval may be delayed for several months or years while the trials are conducted and then the data submitted in an amendment to the PMA. Once granted, PMA approval may be withdrawn by the FDA if compliance with post approval requirements, conditions of approval or other regulatory standards is not maintained or problems are identified following initial marketing.

On August 6, 2014, the FDA issued a final guidance document addressing the development and approval process for "In Vitro Companion Diagnostic Devices." According to the guidance, for novel drugs such as our drug candidates, a companion diagnostic test device and its corresponding drug should be approved or cleared contemporaneously by FDA for the use indicated in the therapeutic product labeling. The guidance also explains that a companion diagnostic test device used to make treatment decisions in clinical trials of a drug generally will be considered an investigational device, unless it is employed for an intended use for which the device is already approved or cleared. If used to make critical treatment decisions, such as patient selection, the diagnostic device generally will be considered a significant risk device under the FDA's Investigational Device Exemption, or IDE, regulations. Thus, the sponsor of the diagnostic device will be required to comply with the IDE regulations. According to the guidance, if a diagnostic device and a drug are to be studied together to support their respective approvals, both products can be studied in the same investigational study, if the study meets both the requirements of the IDE regulations and the IND regulations. The guidance provides that depending on the details of the study plan and subjects, a sponsor may seek to submit an IND alone, or both an IND and an IDE.

In the European Economic Area, or EEA (which is comprised of the 27 Member States of the European Union plus Norway, Iceland and Liechtenstein), *in vitro* medical devices are required to conform with the essential requirements of the E.U. Directive on *in vitro* diagnostic medical devices (Directive No 98/79/EC, as amended). To demonstrate compliance with the essential requirements, the manufacturer must undergo a conformity assessment procedure. The conformity assessment varies according to the type of medical device and its classification. For low-risk devices, the conformity assessment can be carried out internally, but for higher risk devices it requires the intervention of an accredited EEA Notified Body. If successful, the conformity assessment concludes with the drawing up by the manufacturer of an EC Declaration of Conformity entitling the manufacturer to affix the CE mark to its products and to sell them throughout the EEA.

European Drug Development

In the European Union, our future drugs may 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.

Similar to the U.S., the various phases of pre-clinical and clinical research in the European Union are subject to significant regulatory controls. Although the current EU Clinical Trials Directive 2001/20/EC, or Clinical Trials Directive, has sought to harmonize the European Union clinical trials regulatory framework, setting out common rules for the control and authorization of clinical trials in the European Union, the European Union Member States have transposed and applied the provisions of the Directive differently. This has led to significant variations in the member state regimes. Under the current regime, before a clinical trial can be initiated it must be approved in each of the European Union countries where the trial is to be conducted by two distinct bodies: the National Competent Authority, or NCA, and one or more Ethics Committees, or ECs. Under the current regime all suspected unexpected serious adverse reactions to the investigated drug that occur during the clinical trial have to be reported to the NCA and ECs of the Member State where they occurred.

In April 2014, the European Union adopted a new Clinical Trials Regulation (EU) No 536/2014, or the Clinical Trials Regulation, which is set to replace the Clinical Trials Directive. It is expected that the new Clinical Trials Regulation (EU) No 536/2014 will apply following confirmation of full functionality of the Clinical Trials Information System (CTIS), the centralized European Union portal and database for clinical trials foreseen by the regulation, through an independent audit. The regulation becomes applicable six months after the European Commission publishes notice of this confirmation The Clinical Trials Regulation will overhaul the current system of approvals for clinical trials in the European Union. Specifically, the new legislation, which will be directly applicable in all member states, aims at simplifying and streamlining the approval of clinical trials in the European Union. For instance, the new Clinical Trials Regulation provides for a streamlined application procedure via a single entry point and strictly defined deadlines for the assessment of clinical trial applications.

European Drug Review and Approval

In the United Kingdom and the EEA, medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA. There are two types of marketing authorizations:

The Community MA, which is issued by the European Commission through the Centralized Procedure, based on the opinion of the Committee for Medicinal Products for Human Use, or CHMP, of the EMA and which is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of drugs, such as biotechnology medicinal drugs, orphan medicinal drugs, and medicinal drugs containing a new active substance indicated for the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases. The Centralized Procedure is optional for drugs containing a new active substance not yet authorized in the EEA, or for drugs that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the European Union.

National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for drugs not falling within the mandatory scope of the Centralized Procedure. Where a drug has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in another Member State through the Mutual Recognition Procedure. If the drug 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, or RMS. The competent authority of the RMS prepares a draft assessment report, a draft summary of the drug characteristics, or SPC, and a draft of the labeling and package leaflet, which are sent to the other Member States (referred to as the Member States Concerned) for their approval. If the Member States Concerned raise no objections, based on a potential serious risk to public health, to the assessment, SPC, labeling, or packaging proposed by the RMS, the drug is subsequently granted a national MA in all the Member States (i.e. in the RMS and the Member States Concerned).

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

European Pediatric Investigation Plan

In the EEA, MAAs 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. The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the drug 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 a marketing authorization 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.

European Chemical Entity Exclusivity

In the European Union, new chemical entities, sometimes referred to as new active substances, qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. This data exclusivity, if granted, prevents regulatory authorities in the European Union from referencing the innovator's data to assess a generic application for eight years, after which generic marketing authorization can be submitted, and the innovator's data may be referenced, but not approved for two years. The overall ten-year period will 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 held to bring a significant clinical benefit in comparison with existing therapies.

Rest of the World Regulation

For other countries outside of the European Union and the U.S., such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, 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.

Many state laws govern the privacy of personal information in specified circumstances. For example, in California the California Consumer Protection Act, or CCPA, which went into effect on January 1, 2020, establishes a new 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 of the CCPA and for businesses that fail to implement reasonable security procedures and practices to prevent data breaches. While clinical trial data and information governed by HIPAA are currently exempt from the current version of the CCPA, other personal information may be applicable and possible changes to the CCPA may broaden its scope.

European Union member states, the United Kingdom, Switzerland and other jurisdictions have also adopted data protection laws and regulations, which impose significant compliance obligations. In the EEA and the United Kingdom, 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 EU member states and the United Kingdom 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 or the United Kingdom, security breach notifications, security and confidentiality of the personal data and imposition of 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 or United Kingdom. Guidance on implementation and compliance practices are often updated or otherwise revised.

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 who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Thus, even if a drug is approved, sales of the drug will depend, in part, on the extent to which third-party payors, including government health programs in the U.S. such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage, 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 candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue. Further, due to the COVID-19 pandemic, millions of individuals have lost or will be losing employer-based insurance coverage, which may adversely affect our ability to commercialize our drugs.

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 physician usage of such drugs and have a material adverse effect on our sales, results of operations and financial condition.

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.

The American Recovery and Reinvestment Act of 2009 provides funding for the federal government to compare the effectiveness of different treatments for the same illness. The plan for the research was published in 2012 by the Department of Health and Human Services, the Agency for Healthcare Research and Quality and the National Institutes for Health, and periodic reports on the status of the research and related expenditures will be made to Congress. Although the results of the comparative effectiveness studies are not intended to mandate coverage policies for public or private payors, it is not clear what effect, if any, the research will have on the sales of our drug candidates, if any such drug or the condition that they are intended to treat is the subject of a trial. It is also possible that comparative effectiveness research demonstrating benefits in a competitor's drug could adversely affect the sales of our drug candidate. 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.

The Affordable Care Act 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, addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, 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, established annual fees and taxes on manufacturers of certain branded prescription drugs, and a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (increased to 70% pursuant to the Bipartisan Budget Act of 2018, effective as of January 1, 2019) point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D.

In addition, other legislative changes have been proposed and adopted in the U.S. since the Affordable Care Act was enacted. On August 2, 2011, the Budget Control Act of 2011 among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, started in April 2013, and, due to subsequent legislative amendments, will stay in effect through 2030 unless additional Congressional action is taken. Pursuant to the Coronavirus Aid, Relief, and Economic Security Act, also known as the CARES Act, as well as subsequent legislation, these reductions have been suspended from May 1, 2020 through March 31, 2021 due to the COVID-19 pandemic. Proposed legislation, if passed, would extend this suspension until the end of the pandemic.

The 2017 Tax Cuts and Jobs Act, or TJCA, includes a provision repealing the individual mandate, effective January 1, 2019. On December 18, 2019, the Fifth Circuit U.S. Court of Appeals held that the individual mandate is unconstitutional, and remanded the case to the lower court to reconsider its earlier invalidation of the full Affordable Care Act. On March 2, 2020, the United States Supreme Court granted the petitions for writs of certiorari to review this case, and held oral arguments on November 10, 2020. Pending a decision, the Affordable Care Act remains in effect, but it is unclear at this time what effect these developments will have on the status of the Affordable Care Act. Further, on January 20, 2017, U.S. former President Donald Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the Affordable Care Act to waive, defer, grant exemptions from, or delay the implementation of any provision of the Affordable Care Act that would impose a fiscal burden on states or a cost, fee, tax, penalty or regulatory burden on individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On October 13, 2017, former President Trump signed an Executive Order terminating the cost-sharing subsidies that reimburse insurers under the Affordable Care Act. Several state Attorneys General filed suit to stop the administration from terminating these subsidies, but on October 25, 2017, a federal judge in

California denied their request for a restraining order. On August 14, 2020, the U.S. Court of Appeals for the Federal Circuit ruled in two separate cases that the federal government is liable for the full amount of unpaid cost-sharing reduction, or CSR, payments for the years preceding and including 2017. For CSR claims made by health insurance companies for years 2018 and later, further litigation will be required to determine the amounts due, if any. Further, on June 14, 2018, the U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than $12 billion in Affordable Care Act risk corridor payments to third-party payors who argued the payments were owed to them. This decision was appealed to the U.S. Supreme Court, which on April 27, 2020, reversed the U.S. Court of Appeals for the Federal Circuit's decision and remanded the case to the U.S. Court of Federal Claims, concluding the government has an obligation to pay these risk corridor payments under the relevant formula. The effects of this gap in reimbursement on third-party payors, the viability of the ACA marketplace, providers, and potentially our business, are not yet known. While any legislative and regulatory changes will likely take time to develop, and may or may not have an impact on the regulatory regime to which we are subject, we cannot predict the ultimate content, timing or effect of any healthcare reform legislation or the impact of potential legislation on us.

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 European Union 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 European Union do not follow price structures of the U.S. and generally tend to be significantly lower.

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, state and federal anti-kickback, fraud and abuse, false claims, privacy and security and physician sunshine laws and regulations.

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. 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 civil 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. 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.

There has also been a recent trend of increased federal and state regulation of payments made to physicians and other healthcare providers. The Affordable Care Act, among other things, imposes new reporting requirements on drug manufacturers for payments made by them to physicians 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. Effective January 1, 2022, these reporting obligations will extend to include transfers of value made to certain non-physician providers such as physician assistants and nurse practitioners. Certain 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 may also be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology and Clinical Health Act and its implementing regulations, collectively referred to as HITECH, and their respective implementing regulations, including the final omnibus rule published on January 25, 2013, imposes specified requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to "business associates," defined as independent contractors or agents of covered entities that create, receive, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, 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 attorney's fees and costs associated with pursuing federal civil actions. In addition, we may be subject to state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways, thus complicating compliance efforts.

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, 2021, we had 429 full- and part-time employees globally, approximately 406 of whom are employed in the U.S. and approximately 23 are employed in foreign countries. Of those employees, 224 are engaged in research and development activities and 246 hold M.D. or Ph.D. 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 agreement applicable to our industry as required by applicable local law. We consider our relationship with our employees to be good.

Note on the COVID-19 Pandemic

The ongoing COVID-19 pandemic is having widespread, rapidly-evolving, and unpredictable impacts on global societies, economies, financial markets, and business practices. We are closely monitoring the impact of the pandemic and related developments, and our focus remains on promoting employee health and safety when continuing to advance the research and development of our drug candidates and to deliver our approved drugs to patients in need. For discussion regarding the impact of the COVID-19 pandemic on our business and financial results, see "Risk Factors" in Part I, Item 1A and "Management's Discussion and Analysis of Financial Condition and Results of Operations" in Part II, Item 7 of this Annual Report on Form 10-K.

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

We have two approved precision therapies, AYVAKIT/AYVAKYT and GAVRETO. While we have initiated the commercial launch of AYVAKIT and GAVRETO in the U.S. and AYVAKYT in Europe, we have limited experience as a commercial company, and there is limited information about our ability to successfully overcome many of the risks and uncertainties encountered by companies commercializing drugs in the biopharmaceutical industry. Marketing applications for avapritinib and pralsetinib for additional indications are currently under review or planned in the U.S. and globally. To execute our business plan, in addition to successfully marketing and selling our approved drugs, we will need to successfully:

- establish and maintain our relationships with healthcare providers who will be treating the patients who may receive our drugs and any future drugs;
- obtain and maintain adequate pricing and reimbursement for AYVAKIT/AYVAKYT, GAVRETO and any future drugs;
- gain regulatory acceptance for the development and commercialization of current or future drug candidates in our pipeline;
- maintain our existing collaborations with Roche and CStone Pharmaceuticals, or CStone;
- expand our global operations or enter into collaboration, partnerships or distribution arrangements in geographies where we may not have current operations or expertise; and
- manage our spending as costs and expenses increase due to clinical trials, marketing approvals, and commercialization.

If we are unsuccessful in accomplishing these objectives, we may not be able to successfully commercialize our current or future approved drugs, develop current or future drug candidates, expand our business or continue our operations.

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

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

- the potential efficacy and potential advantages over alternative treatments;

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

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

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

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

We cannot be sure that we will be able to 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, including due to the COVID-19 pandemic.

In the event that we are unable to effectively deploy our sales organization or distribution strategy on a timely and efficient basis, if at all, the commercialization of our 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, RET-altered cancers, EGFR-mutated NSCLC, GIST and HCC are unknown. Our projections of the number of people who have these diseases, the frequency of the genetic alterations targeted by our drugs and drug candidates and the subset of patients who have the potential to benefit from our treatment options are based on estimates. These estimates have been derived from a variety of sources, including scientific literature, surveys of clinics, patient foundations or third-party market research, and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these cancers and the number of patients may turn out to be lower than expected. Additionally, the potentially addressable patient population for our approved drugs and drug candidates may be limited or may not be amenable to treatment with our precision therapies.

Accordingly, the number of patients in the U.S., France, Germany, Italy, Spain, the United Kingdom and Japan, which we collectively refer to as the Major Markets, and elsewhere, including the number of addressable patients in those markets, may turn out to be lower than expected, patients may not be otherwise amenable to treatment with our drugs, patients treated with our drugs and drug candidates may develop mutations that confer resistance to treatment or new patients may become increasingly difficult to identify or gain access to, all of which would adversely affect our results of operations and our business.

We face substantial competition, which may result in others commercializing, developing or discovering drugs before or more successfully than we do.

The development and commercialization of new drugs is highly competitive. We face competition with respect to our drugs and current clinical-stage drug candidates, and we will face competition with respect to any drugs and drug candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. There are a number of large pharmaceutical and biotechnology companies that currently market and sell drugs or are pursuing the development of therapies in the field of kinase inhibition for cancer and other diseases. Some of these competitive drugs and therapies are based on scientific approaches that are the same as or similar to our approach, and others are based on entirely different approaches. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization. Specifically, there are a large number of companies developing or marketing treatments for cancer, including many major pharmaceutical and biotechnology companies.

We are developing avapritinib for SM, including advanced SM and non-advanced SM, and we are developing BLU-263 for the treatment of non-advanced SM and other mast cell disorders. If avapritinib receives marketing approval for advanced SM, it will face competition from Novartis AG's midostaurin and imatinib. In addition, if avapritinib or BLU-263 are approved for advanced SM or non-advanced SM, they may face competition from other drug candidates in development for these indications, including those being developed by AB Science S.A., Allakos Inc. and Cogent Biosciences, Inc.

GAVRETO faces competition for RET fusion-positive NSCLC and RET-altered thyroid carcinoma, including MTC, from Eli Lilly and Company's selpercatinib. If pralsetinib receives marketing approval for patients with other solid tumors, it will also face competition from selpercatinib for these additional indications. In addition, pralsetinib may face competition from other drug candidates in development for RET-altered cancers, including those being developed by AstraZeneca plc, Boston Pharmaceuticals, Inc., Eisai Inc., Exelixis, Inc., GlaxoSmithKline plc, Mirati Therapeutics, Inc., Novartis AG, Pfizer Inc. Roche, Stemline Therapeutics, Inc., and Turning Point Therapeutics, Inc., as well as several approved multi-kinase inhibitors with RET activity being evaluated in clinical trials, including alectinib, apatinib, cabozantinib, dovitinib, lenvatinib, sorafenib, sunitinib and vandetinib.

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

We are developing fisogatinib for patients with advanced HCC. If fisogatinib receives marketing approval for patients with FGFR4-activated HCC, it will face competition from Bristol-Myers Squibb Company's nivolumab and Merck & Co., Inc.'s pembrolizumab, immune checkpoint inhibitors approved by the FDA for the treatment of HCC, as well as sorafenib, cabozantinib, regorafenib and lenvatinib, multi-kinase inhibitors approved for the treatment of HCC. In addition, fisogatinib may face competition from other drug candidates in development by Abbisko Therapeutics Co., Ltd, AstraZeneca plc, Bayer AG, Celgene Corporation, Eisai Inc., H3 Biomedicine Inc., Incyte Corporation, Johnson & Johnson, Novartis AG, Sanofi S.A., Taiho Pharmaceutical Co., Ltd., U3 Pharma GmbH, a wholly-owned subsidiary of Daiichi Sankyo Company, Limited, and Xoma Ltd.

We are developing drug candidates for treatment-resistant EGFR-mutated NSCLC, which, if approved, will face competition from AstraZeneca plc's osimertinib and almonertinib, which is under collaboration between Jiangsu Hansoh Pharmaceutical Group Co., Ltd. and EQRX, Inc. and approved in China. In addition, our EGFR inhibitors may face competition from drug candidates in development for EGFR-mutated NSCLC, including those being developed by Alpha Biopharma Inc., Astellas Pharma Inc., Boehringer Ingelheim RCV GmbH & Co KG, Bridge Biotherapeutics, Inc., C4 Therapeutics, Inc., Chia Tai Tianqing Pharmaceutical Group, Daiichi Sankyo Company, Limited, Genosco Inc., Genprex, Inc., Janssen Pharmaceuticals, Inc., and Yuhan Corporation.

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, pre-clinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved drugs than we do. Mergers and acquisitions in the pharmaceutical, biotechnology and diagnostic industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize drugs that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any drugs that we or our collaborators may develop. Our competitors also may obtain FDA or other regulatory approval for their drugs more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we or our collaborators are able to enter the market. The key competitive factors affecting the success of all of our drug candidates, if approved, are likely to be their efficacy, safety, convenience, price, the effectiveness of any related companion diagnostic tests, the level of generic competition and the availability of reimbursement from government and other third-party payors.

Product liability lawsuits against us could cause us to incur substantial liabilities and could limit commercialization of any of our approved drugs or drug candidates that we may develop.

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

- decreased demand for any of our approved drugs or drug candidates that we may develop and commercialize;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue; and

- the inability to commercialize any of approved drugs or drug candidates that we may develop.

Although we maintain product liability insurance coverage, it may not be adequate to cover all liabilities that we may incur. We anticipate that we may need to further increase our insurance coverage as we begin additional clinical trials or if we successfully commercialize additional drug candidates. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

If we or our collaborators are unable to successfully develop and commercialize companion diagnostic tests for our drugs and drug candidates, or experience significant delays in doing so we may not realize the full commercial potential of our drugs and drug candidates.

Because we are focused on precision medicine, in which predictive biomarkers will be used to identify the right patients for our drugs and drug candidates, we believe that our success may depend, in part, on the development and commercialization of companion diagnostic tests. There has been limited success to date industrywide in developing and commercializing these types of companion diagnostic tests. To be successful, we need to address a number of scientific, technical and logistical challenges. We have entered into or plan to enter into agreements to develop and/or commercialize companion diagnostic tests with third parties for AYVAKIT/AYVAKYT in order to identify GIST patients with the PDGFRA D842V mutation, pralsetinib in order to identify NSCLC patients with RET fusions and MTC patients with RET mutations and fisogatinib in order to identify HCC patients with FGFR4 pathway activation. We have limited experience in the development and commercialization of companion diagnostic tests with third parties and may not be successful in developing and commercializing appropriate companion diagnostic tests with third parties to pair with our approved drugs or drug candidates that receive marketing approval. In addition, current commercially available diagnostic tests may become unavailable in the future. Companion diagnostic tests are subject to regulation by the FDA and similar regulatory authorities outside the U.S. as medical devices and require separate regulatory clearance or approval prior to commercialization. We are relying on third parties to design, manufacture, obtain regulatory clearance or approval for and commercialize the companion diagnostic tests for avapritinib, pralsetinib and fisogatinib, and we expect to rely in whole or in part on third parties to design, manufacture, obtain regulatory clearance or approval for and commercialize any other companion diagnostic tests for current and future drug candidates. We and our collaborators may encounter difficulties in developing and obtaining clearance or approval for the companion diagnostic tests, including issues relating to selectivity/specificity, analytical validation, reproducibility, or clinical validation. In addition, our collaborators for any companion diagnostic test that we may seek to develop:

- may not perform their respective obligations as expected or as required under our agreements with them;
- may not pursue commercialization of a companion diagnostic test even if it receives any required regulatory clearances or approvals;
- may elect not to continue the development of a companion diagnostic test based on changes in their or other third parties' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;
- may not commit sufficient resources to the marketing and distribution of a companion diagnostic test; and
- may terminate their relationship with us.

Any delay or failure by us or our collaborators to develop or obtain regulatory clearance or approval of the companion diagnostic tests could delay, prevent or revoke approval of our drug candidates. If we, or any third parties that we have engaged or may in the future engage to assist us are unable to successfully develop and commercialize companion diagnostic tests for our drugs and drug candidates, or experience delays in doing so:

- the development of our approved drugs and drug candidates may be adversely affected if we are unable to appropriately select patients for enrollment in our clinical trials;

- our drug candidates may not receive marketing approval if safe and effective use of a therapeutic drug candidate depends on an in vitro diagnostic;

- regulatory authorities may impose post-marketing requirements regarding the development and commercialization of companion diagnostic tests for our drugs and drug candidates; and

- we may not realize the full commercial potential of any of our approved drugs or drug candidates that receive marketing approval if, among other reasons, we are unable to appropriately select patients who are likely to benefit from treatment with our drugs.

As a result, our business may be materially harmed.

In addition, third party collaborators may encounter production difficulties that could constrain the supply of the companion diagnostic tests, and both they and we may have difficulties gaining acceptance of the use of the companion diagnostic tests in the clinical community. If such companion diagnostic tests fail to gain market acceptance, it would have an adverse effect on our ability to derive revenues from sales of our current and future drugs. In addition, the diagnostic company with whom we contract may decide to discontinue selling or manufacturing the companion diagnostic test that we anticipate using in connection with development and commercialization of our approved drugs and drug candidates or our relationship with such diagnostic company may otherwise terminate. We may not be able to enter into arrangements with another diagnostic company to obtain supplies of an alternative diagnostic test for use in connection with the development and commercialization of our drugs and drug candidates or do so on commercially reasonable terms, which could adversely affect and/or delay the development or commercialization of our drugs and drug candidates.

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

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

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

There are risks involved with both establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time-consuming and could delay any drug launch. If the commercial launch of a drug candidate for which we 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 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 and pralsetinib in additional indications or in additional geographies, and ultimately commercialize them, or experience significant delays in doing so, our business will be materially harmed.

Our ability to generate substantial drug revenues, if ever, will depend heavily on the successful development and commercialization of our drugs and drug candidates. Each of our drug candidates will require additional pre-clinical or clinical development, management of clinical, pre-clinical and manufacturing activities, regulatory approval in multiple jurisdictions, obtaining manufacturing supply, substantial investment and significant marketing efforts before we generate substantial revenues from sales for those drug candidates, if approved. In addition, for some of our drug candidates, in order to select patients most likely to respond to treatment and rapidly confirm mechanistic and clinical proof-of-concept, or to identify appropriate patients for our drugs or drug candidates for which we obtain approval, we may be required or we may seek to develop companion diagnostic tests, which are assays or tests to identify an appropriate patient population. Companion diagnostic tests are subject to regulation as medical devices and must themselves be cleared or approved for marketing by the FDA or certain other foreign regulatory agencies before we may commercialize our drug candidates. The success of our approved drugs and drug candidates will depend on several factors, including the following:

- successful enrollment in, and initiation and completion of, clinical trials, including our ongoing and planned clinical trials for our drugs and drug candidates;
- successful initiation and completion of pre-clinical studies for our other drug candidates;
- successful development of any companion diagnostic tests for use with our drugs and drug candidates;
- receipt of regulatory approvals from applicable regulatory authorities;
- 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 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, including avapritinib and pralsetinib for additional indications, if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside the U.S. Because the target patient populations for our drug candidates and approved drugs in clinical development for additional indications are relatively small, it may be difficult to successfully identify patients. Although we have entered into or plan to enter into third parties to develop companion diagnostic tests for use in some of our other current or future clinical trials in order to help identify eligible patients, we may experience delays in reaching, or fail to reach, agreement on acceptable terms to develop such companion diagnostic tests. Any third parties whom we engage to develop companion diagnostic tests may experience delays or may not be successful in developing such companion diagnostic tests, furthering the difficulty in identifying patients for our clinical trials. In addition, current commercially available diagnostic tests to identify appropriate patients for our clinical trials or any approved drug candidates may become unavailable in the future.

In addition, we have experienced some delays or disruptions in enrollment in our ongoing clinical trials due to the COVID-19 pandemic, and we anticipate we may experience additional delays or disruptions in the future due to the COVID-19 pandemic and changes in local site or IRB policies availabilities of site staff reprioritization of hospital resources, restricted access to healthcare professionals and testing sites and other containment measures or concerns among patients about participating in clinical trials during a pandemic. Furthermore, some of our competitors have ongoing clinical trials for drug candidates that treat the same indications as our drug candidates and approved drugs in clinical development for additional indications, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' drug candidates.

Patient enrollment may be affected by other factors including:

- the severity of the disease under investigation;
- the size of the target patient population;
- the eligibility criteria for the clinical trial;
- the availability of an appropriate genomic screening test;
- the perceived risks and benefits of the drug candidate under study;
- the efforts to facilitate timely enrollment in clinical trials;
- the patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment; and
- the proximity and availability of clinical trial sites for prospective patients.

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

If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals for our drug candidates and, if applicable, for any related companion diagnostic tests, we will not be able to commercialize, or may be delayed in commercializing, such drug candidates, and our ability to generate revenue will be materially impaired.

Our drug candidates and any companion diagnostic tests related to our approved drugs or drug candidates, including the companion diagnostic tests that we are developing or have developed for AYVAKIT/AYVAKYT in order to identify GIST patients with the PDGFRA D842V mutation, pralsetinib in order to identify NSCLC patients with RET fusions and MTC patients with RET mutations and fisogatinib in order to identify HCC patients with FGFR4 pathway activation, and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale, distribution, import and export, are subject to comprehensive regulation by the FDA and other regulatory agencies in the U.S. and by comparable authorities in other countries. Before we can commercialize any of our drug candidates, we must obtain marketing approval. We may also need marketing clearance or approval for any related companion diagnostic tests, including the companion diagnostic tests that we are developing for avapritinib and fisogatinib.

We have limited experience in filing and supporting the applications necessary to gain regulatory approvals and expect to rely on third-party CROs and/or regulatory consultants to assist us in this process. Securing regulatory approval requires the submission of extensive pre-clinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the drug candidate's safety and efficacy. Securing regulatory approval also requires the submission of information about the drug manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Should FDA determine that an inspection is necessary for approval of a marketing application and an inspection cannot be completed during the review cycle due to restrictions on travel, FDA has stated that it generally intends to issue a complete response letter. Further, if there is inadequate information to make a determination on the acceptability of a facility, FDA may defer action on the application until an inspection can be completed. Our drug candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use.

The process of obtaining regulatory approvals, if approval is obtained at all, both in the U.S. and abroad is expensive, may take many years if additional clinical trials are required and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the drug candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted NDA for a drug candidate, pre-market approval, or PMA, application for a companion diagnostic test or equivalent application types, may cause delays in the approval or rejection of an application. The FDA and comparable authorities in other countries have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional pre-clinical, clinical or other studies. We currently have marketing applications pending for avapritinib in the U.S and Europe and pralsetinib in the Europe.

Our drug candidates could be delayed in receiving, or fail to receive, regulatory approval for many reasons, including the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a drug candidate is safe and effective for its proposed indication or a related companion diagnostic test is suitable to identify appropriate patient populations;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that a drug candidate's clinical and other benefits outweigh its safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from pre-clinical studies or clinical trials;

- the data collected from clinical trials of our drug candidates may not be sufficient to support the submission of an NDA or other submission or to obtain regulatory approval in the U.S. or elsewhere;

- the FDA or comparable foreign regulatory authorities may find deficiencies with or fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies;

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

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

As of June 23, 2020, the FDA noted it is continuing to ensure timely reviews of applications for medical products during the COVID-19 pandemic in line with its user fee performance goals. On July 16, 2020, FDA noted that it is continuing to expedite oncology product development with its staff teleworking full-time. However, FDA may not be able to continue its current pace and approval timelines could be extended, including where a pre-approval inspection or an inspection of clinical sites is required and due to the COVID-19 pandemic and travel restrictions FDA is unable to complete such required inspections during the review period. In 2020, several companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. In addition, even if we were to obtain approval, regulatory authorities may approve any of our drug candidates for fewer or more limited indications than we request, may not approve the price we intend to charge for our drugs and related companion diagnostic tests, may grant approval contingent on the performance of costly post-marketing clinical trials or other post-marketing requirements, or may approve a drug candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that drug candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our drug candidates.

If we experience delays in obtaining approval or if we fail to obtain approval of our drug candidates and companion diagnostic tests related to our approved drugs and drug candidates, the commercial prospects for our approved drugs or drug candidates may be harmed and our ability to generate revenues will be materially impaired.

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 pre-clinical studies or could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other regulatory authorities. As is the case with all oncology drugs, it is likely that there may be side effects associated with the use of our drugs and drug candidates. Results of our trials could reveal a high and unacceptable severity and prevalence of these or other side effects. In such an event, our trials could be suspended or terminated, and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our drugs or drug candidates for any or all targeted indications. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete clinical trials or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

Further, our approved drugs and drug candidates could cause undesirable side effects in pre-clinical studies or clinical trials related to on-target toxicity. If on-target toxicity is observed, or if our drugs or drug candidates have characteristics that are unexpected, we may need to abandon their development or limit development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Many compounds that initially showed promise in early stage testing for treating cancer have later been found to cause side effects that prevented further development of the compound.

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

- regulatory authorities may withdraw or limit their approval of such drug;

- regulatory authorities may require the addition of labeling statements, such as a “boxed” warning or a contraindication;

- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;

- we may be required to change the way such drug is distributed or administered, conduct additional clinical trials or change the labeling of such drug;

- regulatory authorities may require a Risk Evaluation and Mitigation Strategy, or REMS, plan to mitigate risks, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools;

- we may be subject to regulatory investigations and government enforcement actions;

- we may decide to remove such drug from the marketplace;

- we could be sued and held liable for injury caused to individuals exposed to or taking our drugs and drug candidates; and

- our reputation may suffer.

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

A 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 breakthrough therapy designation for some of our current or future drug candidates. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. The FDA has granted breakthrough therapy designation to avapritinib for (i) the treatment of advanced SM, including the subtypes of aggressive SM, SM with an associated hematologic neoplasm and mast cell leukemia, and (ii) the treatment of moderate to severe indolent SM. In addition, the FDA previously granted breakthrough designation to our drugs, AYVAKIT and GAVRETO, for the treatment of certain patients with GIST and RET-altered cancers, respectively.

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our drug candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a breakthrough therapy designation for a drug candidate may not result in a faster development process, review or approval compared to other drugs and does not assure ultimate approval by the FDA. In addition, even if one or more of our drug candidates qualify as breakthrough therapies, the FDA may later decide that the drugs no longer meet the conditions for qualification. In June 2020, the FDA noted it is continuing to ensure timely reviews of applications for medical products during the COVID-19 pandemic in line with its user fee performance goals; however, the FDA may not be able to continue its current pace and review timelines could be extended.

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

The FDA has granted orphan drug designation to avapritinib for the treatment of GIST and the treatment of mastocytosis, to pralsetinib for the treatment of RET-rearranged NSCLC, JAK1/2-positive NSCLC or TRKC-positive NSCLC and to fisogatinib for the treatment of HCC. In addition, the European Commission has granted medicinal product designation to avapritinib for the treatment of GIST and the treatment of mastocytosis. As part of our business strategy, we may seek orphan drug designation for some of our other drug candidates, and we may be unsuccessful. Regulatory authorities in some jurisdictions, including the U.S. and the European Union, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a drug as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population

of fewer than 200,000 individuals annually in the U.S., or a patient population greater than 200,000 in the U.S. where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the U.S. In the U.S., orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers.

Similarly, in the European Union, the European Commission grants medicinal product designation after receiving the opinion of the European Medicines Agency, or EMA, Committee for Orphan Medicinal Products on an orphan medicinal product designation application. Orphan medicinal product designation is intended to promote the development of drugs that are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions affecting not more than 5 in 10,000 persons in the European Union and for which no satisfactory method of diagnosis, prevention, or treatment has been authorized (or the drug would be a significant benefit to those affected). In addition, designation is granted for drugs intended for the diagnosis, prevention, or treatment of a life-threatening, seriously debilitating or serious and chronic condition and when, without incentives, it is unlikely that sales of the drug in the European Union would be sufficient to justify the necessary investment in developing the drug. In the European Union, orphan medicinal product designation entitles a party to financial incentives such as reduction of fees or fee waivers.

Generally, if a drug with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the drug is entitled to a period of marketing exclusivity, which precludes the EMA or the FDA from approving another marketing application for the same drug and indication for that time period, except in limited circumstances. The applicable period is seven years in the U.S. and ten years in the European Union. The European Union exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified.

Even if we obtain orphan drug exclusivity for a drug, that exclusivity may not effectively protect the designated drug from competition because different drugs can be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

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. In addition, a designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. Moreover, orphan drug exclusive marketing rights in the U.S. may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process. While we intend to continue seek orphan drug designation for our drug candidates, we may never receive such designations. Even if we receive orphan drug designation for any of our drug candidates, there is no guarantee that we will enjoy the benefits of those designations.

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

We may not be successful in our efforts to expand our pipeline of drug candidates.

A key element of our strategy is to use our novel target discovery engine to identify kinases that are drivers of diseases in genomically defined patient populations with high unmet medical need in order to build a pipeline of drug candidates. Although our research and development efforts to date have resulted in a pipeline of drug candidates, we may not be able to continue to identify novel kinase drivers and develop drug candidates. We may also pursue

opportunities to acquire or in-license additional businesses, technologies or drugs, form strategic alliances or create joint ventures with third parties to complement or augment our existing business. However, we may not be able to identify any drug candidates for our pipeline through such acquisition or in-license.

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 pre-clinical or clinical drug candidates or programs does not have sufficient potential to warrant the allocation of resources toward such program or drug candidate. Accordingly, we may choose not to develop a potential drug candidate or elect to suspend, deprioritize or terminate one or more of our discovery programs or pre-clinical or clinical drug candidates or programs. If we suspend, deprioritize or terminate a program or drug candidate in which we have invested significant resources, we will have expended resources on a program that will not provide a full return on our investment and may have missed the opportunity to have allocated those resources to potentially more productive uses, including existing or future programs or drug candidates.

Risks Related to 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.

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

If the FDA or a comparable foreign regulatory authority approves any of our drug candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for the drug will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with current Good Manufacturing Practices, or cGMPs, and Good Clinical Practices, or GCPs, for any clinical trials that we conduct post-approval. Any regulatory approvals that we receive for our drug candidates may also be subject to limitations on the approved indicated uses for which the drug may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to

monitor the safety and efficacy of the drug. Later discovery of previously unknown problems with a drug, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of the drug, withdrawal of the drug from the market, "dear doctor" letters or drug recalls;
- fines, warning letters or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us, or suspension or revocation of marketing approvals;
- drug seizure or detention, or refusal to permit the import or export of drugs; and
- injunctions or the imposition of civil or criminal penalties.

The FDA's policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our drug candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

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, or 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.

Even if we are able to commercialize any of our approved drugs or drug candidates, if approved, such drug or drug candidate may become subject to unfavorable pricing regulations or third-party coverage and reimbursement policies, which would harm our business.

The regulations that govern regulatory approvals, pricing and reimbursement for new drugs vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a drug candidate in a particular country, but then be subject to price regulations that delay our commercial launch of the drug candidate, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the drug candidate in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more drug candidates, even if our drug candidates obtain marketing approval.

Our ability to commercialize any 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 our products will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and other third-party payors, such as private health insurers and health maintenance

organizations, decide which medications they will pay for and establish reimbursement levels. In the United States, the principal decisions about reimbursement for new medicines are typically made by the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services, or HHS. CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare and private payors tend to follow CMS to a substantial degree. The availability of coverage and extent of reimbursement by governmental and private payors is essential for most patients to be able to afford treatments. Sales of these or other products that we may identify will depend substantially, both domestically and abroad, on the extent to which the costs of our products will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health administration authorities, private health coverage insurers and other third-party payors. If coverage and adequate reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize our products. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular drugs. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for drugs. We cannot be sure that coverage will be available for any drug candidate that we commercialize and, if coverage is available, the level of reimbursement. Reimbursement may impact the demand for, or the price of, any drug candidate for which we obtain marketing approval. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any drug candidate for which we obtain marketing approval.

There may be significant delays in obtaining reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or similar regulatory authorities outside the U.S. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower-cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the U.S. Private third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any approved drugs that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize drugs and our overall financial condition.

Healthcare legislative reform measures may have a material adverse effect on our business and results of operations.

The United States has enacted or proposed legislative and regulatory changes affecting the healthcare system that could prevent or delay marketing approval of our current product candidates or any future product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product for which we obtain marketing approval. Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of our products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business. In the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs. For example, in March 2010, the ACA was passed, which substantially changes the way healthcare is financed by both governmental and private insurers, and significantly impacts the U.S. pharmaceutical industry. The ACA, among other things, made several changes to the Medicare Drug Rebate Program, establishes annual fees and taxes on manufacturers of certain branded prescription drugs, and creates a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (increased to 70% pursuant to the Bipartisan Budget Act of 2018, effective as of January 2019) point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D.

Since its enactment, there have been numerous judicial, administrative, executive, and legislative challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. For example, various portions of the ACA are currently undergoing legal and constitutional challenges in the United

States Supreme Court. Additionally, the Trump Administration issued various Executive Orders which eliminated cost sharing subsidies and various provisions that would impose a fiscal burden on states or a cost, fee, tax, penalty or regulatory burden on individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. Finally, and Congress has introduced several pieces of legislation aimed at significantly revising or repealing the ACA. Although a number of these and other proposed measures may require authorization through additional legislation to become effective, and the Biden administration may reverse or otherwise change these measures, Congress has indicated that it will continue to seek new legislative measures to control drug costs. It is unclear whether the ACA will be overturned, repealed, replaced, or further amended. We cannot predict what affect further changes to the ACA would have on our business.

In addition, there has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. HHS has already started the process of soliciting feedback on some of the Trump administration's measures and, at the same time, is immediately implementing others under its existing authority.

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 United States for our development candidates and investigational medicines, if approved, from therapies sourced from foreign countries that have placed price controls on pharmaceutical products. In the United States, the FDA issued a final guidance document outlining a pathway for manufacturers to obtain an additional National Drug Code, or NDC, for an FDA-approved drug that was originally intended to be marketed in a foreign country and that was authorized for sale in that foreign country. The market implications of the final guidance is unknown at this time. Proponents of drug reimportation may attempt to pass legislation that would directly allow reimportation under certain circumstances. Legislation or regulations allowing the reimportation of drugs, if enacted, could decrease the price we receive for any products that we may develop and adversely affect our future revenues and prospects for profitability.

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, or HIPAA, the Physician Payment Sunshine Act, HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, the federal false statements statute, federal consumer protection and unfair competition laws and similar state and foreign laws and regulations that may regulate the business or financial arrangements and relationships through which we market, sell and distribute our drugs. The number and complexity of federal, state, and

foreign laws continue to increase, and additional governmental resources are being used to enforce these laws and to prosecute companies and individuals who are believed to be violating them.

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

Ensuring that our future business arrangements with third parties comply with applicable healthcare laws and regulations could involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations, including anticipated activities to be conducted by our sales team, were to be found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, exclusion from government-funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government-funded healthcare programs.

Our future growth may depend, in part, on our ability to penetrate foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties.

Our future profitability may depend, in part, on our ability to commercialize current or future drug candidates in foreign markets for which we may rely on collaboration with third parties. We are not permitted to market or promote any of our drug candidates before we receive regulatory approval from the applicable regulatory authority in that foreign market. Even though AYVAKYT received approval in Europe, we may never receive any other foreign regulatory approval for our drug candidates. To obtain separate regulatory approval in many other countries we must comply with numerous and varying regulatory requirements of such countries regarding safety and efficacy and governing, among other things, clinical trials, manufacturing, commercial sales, pricing and distribution of our drug candidates, and we cannot predict success in these jurisdictions. If we seek to develop our drug candidates or obtain approval of our drug candidates and ultimately commercialize our drug candidates in foreign markets, we would be subject to additional risks and uncertainties, including:

- our customers' ability to obtain reimbursement for our drug candidates in foreign markets;
- our inability to directly control commercial activities because we are relying on third parties;
- the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements, including the European General Data Protection Regulation 2016/679, commonly referred to as GDPR;
- different medical practices and customs in foreign countries affecting acceptance in the marketplace;
- import or export licensing requirements;
- longer accounts receivable collection times;
- longer lead times for shipping;
- language barriers for technical training;

- reduced protection of intellectual property rights in some foreign countries;
- the existence of additional potentially relevant third-party intellectual property rights;
- foreign currency exchange rate fluctuations; and
- the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute.

Foreign sales of our drug candidates could also be adversely affected by the imposition of governmental controls, political and economic instability, trade restrictions and changes in tariffs.

Governments outside the U.S. tend to impose strict price controls, which may adversely affect our revenues, if any.

In some countries, particularly countries in the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a drug. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our drug candidate to other available therapies. If reimbursement of our drugs is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be materially harmed. In addition, in 2016, the United Kingdom referendum on its membership in the European Union resulted in a majority of United Kingdom voters voting to exit the European Union, often referred to as Brexit. Brexit has already and may continue to adversely affect European and/or worldwide regulatory conditions. Brexit could lead to legal uncertainty and potentially divergent national laws and regulations, including those related to the pricing of prescription pharmaceuticals, as the United Kingdom determines which European Union laws to replicate or replace. If the United Kingdom were to significantly alter its regulations affecting the pricing of prescription pharmaceuticals, we could face significant new costs. As a result, Brexit could impair our ability to transact business in the European Union and the United Kingdom.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

Risks Related to Our Financial Position and Need for Additional Capital

We are a precision therapy company with a limited operating history. We have incurred significant operating losses since our inception and anticipate that we will incur continued losses for the foreseeable future.

We are a precision therapy company with a limited operating history. To date, we have not yet demonstrated our ability to conduct large-scale sales and marketing activities necessary for successful commercialization. We currently have two approved precision therapies and are transitioning to a company capable of supporting commercial activities. We may not be successful in such a transition.

We commenced operations in April 2011 and we have focused substantially all of our efforts and financial resources to date on organizing and staffing our company, business planning, raising capital, establishing our intellectual property building our discovery platform, including our proprietary compound library and new target discovery engine,

identifying kinase drug targets and potential drug candidates, conducting pre-clinical studies and clinical development for our drug candidates, commencing pre-commercial activities and the commercial launches for AYVAKIT/AYVAKYT and GAVRETO, and producing the active pharmaceutical ingredient, or API, drug substance and drug product material for use in pre-clinical studies and clinical trials for our drug candidates and commercial sale of AYVAKIT/AYVAKYT and GAVRETO.

To date, we have financed our operations primarily through public offerings of our common stock, private placements of our convertible preferred and common stock, collaborations and a license agreement. Through December 31, 2020, we have received an aggregate of $2.9 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, $910.8 million in upfront payments and milestone payments under our collaborations with Roche and CStone, our license agreement with Clementia and our former collaboration with Alexion. In addition, since January 2020, we have generated limited product revenue.

Since inception, we have incurred significant operating losses, with the exception of the year ended December 31, 2020. Our net income was $313.9 million for the year ended December 31, 2020 primarily due to the collaboration revenue recorded under our collaboration with Roche for pralsetinib, and out net losses were $347.7 million and $236.6 million for the years ended December 31, 2019 and 2018, respectively. As of December 31, 2020, we had an accumulated deficit of $631.4 million.

Substantially all of our operating losses have resulted from costs incurred in connection with our research and development programs and from general and administrative costs associated with our operations. We expect to continue to incur significant expenses and operating losses over the next few years. We anticipate that our expenses will continue to increase in connection with our ongoing activities. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' equity and working capital. We expect our research and development expenses to significantly increase in connection with continuing our existing clinical trials and beginning additional clinical trials. In addition, we will incur significant sales, marketing and outsourced-manufacturing expenses in connection with the commercialization of any of our 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.

To date, we have not generated substantial revenue from drug sales. Our ability to generate substantial revenue depends on a number of factors, including, but not limited to, our ability to:

- initiate and successfully complete clinical trials that meet their clinical endpoints;
- initiate and successfully complete all safety studies required to obtain U.S. and foreign marketing approval for our drug candidates, including for avapritinib and pralsetinib for additional indications or in additional geographies;
- continue to maintain and expand commercial manufacturing capabilities or make arrangements with third-party manufacturers for clinical supply and commercial manufacturing;
- maintain and, if necessary, expand a sales, marketing and distribution infrastructure to commercialize AYVAKIT/AYVAKYT, GAVRETO and any current or future drug candidates for which we obtain marketing approval; and
- achieve market acceptance in the medical community and with third-party payors for AYVAKIT/AYVAKYT, GAVRETO and any current or future drug candidates for which we receive marketing approval.

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

marketing approval. Even if we initiate and successfully complete pivotal clinical trials of our drug candidates, and our drug candidates are approved for commercial sale, and despite expending these costs, our drug candidates may not be commercially successful. We may not achieve profitability soon after generating drug sales, if ever. If we are unable to generate drug revenue, 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. We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the research and development of, initiate or continue clinical trials of, and seek marketing approval for our drug candidates, including marketing approval for avapritinib for additional indications or in additional geographies and for pralsetinib. In addition, we expect to incur additional significant commercialization expenses for AYVAKIT/AYVAKYT, GAVRETO and other drug candidates, if approved, related to drug sales, marketing, manufacturing and distribution to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of potential collaborators or licensors. We may also need to raise additional funds if we choose to pursue additional indications or geographies for any of our approved drugs or drug candidates or otherwise expand more rapidly than we presently anticipate.

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

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

- the success of our current or future collaborations for the development and commercialization of companion diagnostic tests;

- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims; and

- the costs of continuing to expand our operations.

Accordingly, we may seek additional funding in connection with our continuing operations or business objectives. Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize any of our approved drugs or drug candidates. We cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may adversely affect the holdings or the rights of our stockholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline. We could also be required to seek funds through collaborations, partnerships, licensing arrangements or otherwise at an earlier stage than would be desirable and we may be required to relinquish rights to some of our technologies, drugs or drug candidates or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results and prospects.

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

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

Until such time, if ever, as we can generate substantial drug revenues, we expect to finance our cash needs primarily through a combination of public and private equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. We do not have any committed external source of funds, other than our collaborations with Roche and CStone and the license agreement with Clementia, which are limited in scope and duration and subject to the achievement of milestones or royalties on sales of licensed products, if any. To the extent that we raise additional capital through the sale of common stock or securities convertible or exchangeable into common stock, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that materially adversely affect the rights of our common stockholders. Debt financing, if available, would increase our fixed payment obligations and may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we raise funds through additional collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our intellectual property, future revenue streams, research programs, drugs or drug candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our drug development or future commercialization efforts or grant rights to develop and market drugs and drug candidates that we would otherwise prefer to develop and market ourselves.

Risks Related to Our Dependence on Third Parties

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

We have entered into collaborations and licenses with Roche, CStone and Clementia, for the development and commercialization of several of our drugs and drug candidates, and may enter into additional collaborations and licenses with other third parties in the future. The success of these arrangements will depend heavily on the efforts and activities of our collaborators and licensing partners. Collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations. In some situations, we may not be able to influence our collaboration partners' decisions regarding the development and collaboration of our partnered drugs and drug

candidates, and as a result, our collaboration partners may not pursue or prioritize the development and commercialization of those partnered drugs and drug candidates in a manner that is in our best interest. Disagreements between parties to a collaboration arrangement regarding clinical development and commercialization matters can lead to delays in the development process or commercializing the applicable drug candidate and, in some cases, termination of the collaboration arrangement or result in litigation or arbitration, which would be time-consuming and expensive. Licensors generally have sole discretion in determining the efforts and resources that they will apply to the licensed products.

Collaborations and licenses with pharmaceutical or biotechnology companies and other third parties often are terminated or allowed to expire by the other party. For example, in the fourth quarter of 2017, Alexion terminated our collaboration related to fibrodysplasia ossificans progressiva for convenience following a strategic review by Alexion of its research and development portfolio. Any termination or expiration of our collaboration or license agreements with Roche, CStone or Clementia, or of any future collaboration or license agreement, could adversely affect us financially or harm our business reputation.

We rely on third parties to conduct our clinical trials. 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 the clinical trials for our approved drugs and drug candidates, CROs will conduct all of the clinical trials. As a result, many important aspects of our development programs, including their conduct and timing, will be outside of our direct control. Our reliance on third parties to conduct current or future clinical trials will also result in less direct control over the management of data developed through clinical trials than would be the case if we were relying entirely upon our own staff. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. Outside parties may:

- have staffing difficulties;
- fail to comply with contractual obligations;
- experience regulatory compliance issues;

- undergo changes in priorities or become financially distressed; or
- form relationships with other entities, some of which may be our competitors.

Some of these factors may be beyond our control. For example, the performance of our CROs may also be delayed or disrupted by the ongoing COVID-19 pandemic, including due to travel or quarantine policies, availabilities of staff, exposure of CRO staff to COVID-19 or re-prioritization of CRO resources as a result of the pandemic. These factors may materially adversely affect the willingness or ability of third parties to conduct our clinical trials and may subject us to unexpected cost increases that are beyond our control. If the CROs do not perform clinical trials in a satisfactory manner, breach their obligations to us or fail to comply with regulatory requirements, the development, regulatory approval and commercialization of our approved drugs for additional indications and our drug candidates may be delayed, we may not be able to obtain regulatory approval and commercialize our drug candidates, or our development program materially and irreversibly harmed. If we are unable to rely on clinical data collected by our CROs, we could be required to repeat, extend the duration of, or increase the size of any clinical trials we conduct and this could significantly delay commercialization and require significantly greater expenditures.

If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, any clinical trials such CROs are associated with may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for or successfully commercialize our drug for additional indications or our drug candidates. As a result, we believe that our financial results and the commercial prospects for our drugs or our drug candidates in the subject indication would be harmed, our costs could increase and our ability to generate substantial revenue could be delayed.

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

The facilities used by our contract manufacturers to manufacture our drugs and drug candidates must be approved by the FDA pursuant to inspections that will be conducted after we submit our marketing applications to the FDA. We do not control the manufacturing process of, and will be completely dependent on, our contract manufacturers for compliance with cGMPs in connection with the manufacture of our drugs and drug candidates. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our drugs and drug candidates or is unable to conduct inspections necessary to approve these facilities due to delays or disruptions caused by the COVID-19 pandemic, or if the FDA or a comparable regulatory authority withdraws any such approval in the future, we may be delayed in obtaining approval of these facilities for the manufacture of our drugs and drug candidates or need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our drug candidates, if approved. Further, our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of drug candidates or drugs, if approved, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect our business and supplies of our drugs and drug candidates.

In response to the COVID-19 pandemic, in March 2020, the FDA announced its intention to postpone most inspections of foreign manufacturing facilities and products while local, national and international conditions warrant, as well as its intention to temporarily postpone routine surveillance inspections of domestic manufacturing facilities and provided guidance regarding the conduct of clinical trials which the FDA continues to update. In June 2020, the FDA noted it was conducting mission critical domestic and foreign inspections to ensure compliance of manufacturing facilities with FDA quality standards, and in July 2020, the FDA announced its goal of restarting domestic on-site inspections but with such activities depending on data about the trajectory of COVID-19 in a given state and locality and the rules and guidelines that are put in place by state and local governments. The FDA has developed a rating system to assist in determining when and where it is safest to conduct prioritized domestic inspections. Should the FDA determine that an inspection is necessary for approval and an inspection cannot be completed during the review cycle due to restrictions on travel, the FDA has stated that it generally intends to issue a complete response letter. Further, if there is inadequate information to make a determination on the acceptability of a facility, the FDA may defer action on the application until an inspection can be completed. Regulatory authorities outside the U.S. may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic and may experience delays in their regulatory activities.

We do not have long-term supply agreements with all of our contract manufacturers, and 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 contract manufacturers. In addition, we may be unable to establish or maintain any agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish and maintain agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- reliance on the third party for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreement by the third party;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how; and
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

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

Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We do not currently have arrangements in place for redundant supply for all of our bulk drug substances. If our current contract manufacturers cannot perform as agreed, we may experience shortages that require reporting to the FDA or foreign regulatory authorities and may be required to replace such manufacturers. Although we believe that there are several potential alternative manufacturers who could manufacture our approved drugs and drug candidates, we may incur added costs and delays in identifying and qualifying any such replacement.

Our current and anticipated future dependence upon others for the manufacture of our drugs or drug candidates could result in significant delays or gaps in availability of such drugs or drug candidates and may adversely affect our future profit margins and our ability to commercialize any drugs that receive marketing approval on a timely and competitive basis.

The third parties upon whom we rely for the supply of the API, drug substance and drug product used in avapritinib and pralsetinib are our sole source of supply, and the loss of any of these suppliers could significantly harm our business.

The API, drug substance and drug product used in our drug and drug candidates are supplied to us primarily from single-source suppliers. Our ability to successfully develop our drug candidates, supply our drug candidates for clinical trials and to ultimately supply our commercial drugs in quantities sufficient to meet the market demand, depends in part on our ability to obtain the API, drug substance and drug product for these drugs in accordance with regulatory requirements and in sufficient quantities for clinical testing and commercialization. Although we have entered into arrangements to establish redundant or second-source supply of some of the API, drug product or drug substance for avapritinib and pralsetinib, if any of our suppliers ceases its operations for any reason or is unable or unwilling to supply API, drug product or drug substance in sufficient quantities or on the timelines necessary to meet our needs, including as a result of the COVID-19 pandemic, it could significantly and adversely affect our business, the supply of our drug candidates or approved drugs and our financial condition.

For all of our drug candidates, we may from time to time explore opportunities to identify and qualify additional manufacturers to provide such API, drug substance and drug product prior to submission of an NDA to the FDA and/or an MAA to the EMA. We are not certain that our single-source suppliers will be able to meet our demand for their products, either because of the nature of our agreements with those suppliers, our limited experience with those suppliers or our relative importance as a customer to those suppliers. It may be difficult for us to assess their ability to timely meet our demand in the future based on past performance. While our suppliers have generally met our demand for their products on a timely basis in the past, they may subordinate our needs in the future to their other customers. In addition, we currently have sufficient supply or plans for supply to meet our anticipated global commercial and clinical development needs for our approved drugs and clinical-stage drug candidates through 2022. However, the COVID-19 pandemic could adversely impact our suppliers and result in delays or disruptions in our current or future supply chain.

Establishing additional or replacement suppliers for the API, drug substance and drug product used in our drug candidates or approved drugs, if required, may not be accomplished quickly. If we are able to find a replacement supplier, such replacement supplier would need to be qualified and may require additional regulatory approval, which could result in further delay. While we seek to maintain adequate inventory of the API, drug substance and drug product used in our drug candidates and approved drugs, any interruption or delay in the supply of components or materials, or our inability to obtain such API, drug substance and drug product from alternate sources at acceptable prices in a timely manner could impede, delay, limit or prevent our development efforts, which could harm our business, results of operations, financial condition and prospects.

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

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

Risks Related to Intellectual Property

If we are unable to adequately protect our proprietary technology or obtain and maintain patent protection for our technology and drugs or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and drugs similar or identical to ours, and our ability to successfully commercialize our technology and drugs may be impaired.

Our commercial success depends in part on our ability to obtain and maintain proprietary or intellectual property protection in the U.S. and other countries for our drugs and drug candidates, including avapritinib and pralsetinib, and our core technologies, including our novel target discovery engine and our proprietary compound library and other know-how. We seek to protect our proprietary and intellectual property position by, among other methods, filing patent applications in the U.S. and abroad related to our proprietary compounds, technologies, inventions and improvements that are important to the development and implementation of our business. We also rely on copyright, trade secrets, know-how and continuing technological innovation to develop and maintain our proprietary and intellectual property position.

We own patents and patent applications that relate to the composition of matter for avapritinib, pralsetinib, fisogatinib and BLU-263. We also own applications relating to composition of matter for KIT and PDGFRA inhibitors with multiple compound families, composition of matter for FGFR4 inhibitors with multiple compound families, and composition of matter for inhibitors of RET, including predicted RET resistance mutations, as well as methods of use for these novel compounds. The issued U.S. patent directed to avapritinib composition of matter has a statutory expiration date in 2034, the issued U.S. patent directed to pralsetinib composition of matter has a statutory expiration date in 2036, and the issued U.S. patent directed to fisogatinib composition of matter has a statutory expiration date in 2034. Patent term adjustment or patent term extension could result in a later expiration date for fisogatinib.

As of January 31, 2021, we owned 11 issued U.S. patents, 15 issued foreign patents, including one European patent validated in 38 countries, three pending U.S. non-provisional patent applications, three pending U.S. provisional applications, five pending PCT international patent applications and 22 pending foreign patent applications directed to our KIT and PDGFRA program, including avapritinib and BLU-263. The patents that have issued or will issue covering our KIT and PDGFRA program will have a statutory expiration date between 2034 and 2041. Patent term adjustments or patent term extensions could result in later expiration dates.

As of January 31, 2021, we owned seven issued U.S. patents, six pending U.S. non-provisional patent applications, three U.S. provisional patent applications, one pending PCT international application, 53 pending foreign patent applications and four issued foreign patents directed to our RET program, including pralsetinib. The patents that have issued or will issue covering our RET program will have a statutory expiration date between 2036 and 2041. Patent term adjustments or patent term extensions could result in later expiration dates.

As of January 31, 2021, we owned nine issued U.S. patents, two pending U.S. non-provisional patent applications, one pending PCT international applications, 28 pending foreign patent applications and 27 issued foreign patents directed to our FGFR4 program, including fisogatinib. The patents that have issued or will issue covering our FGFR4 program will have a statutory expiration date between 2033 and 2040. Patent term adjustments or patent term extensions could result in later expiration dates.

The intellectual property portfolio directed to our platform includes patent applications directed to novel gene fusions and the uses of these fusions for detecting and treating conditions implicated with these fusions. As of January 31, 2021, we owned eight issued U.S. patents, five pending U.S. non-provisional patent applications, four pending European Union patent applications and five issued European patents directed to this technology. Any U.S. or ex-U.S. patent issuing from the pending applications directed to this technology, if issued, will have statutory expiration dates ranging from 2034 to 2035.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation.

The degree of patent protection we require to successfully commercialize any of our approved drugs and drug candidates may be unavailable or severely limited in some cases and may not adequately protect our rights or permit us to gain or keep any competitive advantage. We cannot provide any assurances that any of our patents have, or that any of

our pending patent applications that mature into issued patents will include, claims with a scope sufficient to protect 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 patent portfolio may not provide us with adequate and continuing patent protection sufficient to exclude others from commercializing drugs similar or identical to our drugs and drug candidates, including generic versions of such drugs or drug candidates.

Other parties have developed technologies that may be related or competitive to our own, and such parties may have filed or may file patent applications, or may have received or may receive patents, claiming inventions that may overlap or conflict with those claimed in our own patent applications or issued patents, with respect to either the same methods or formulations or the same subject matter, in either case, that we may rely upon to dominate our patent position in the market. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the U.S. and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we were the first-to-file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights cannot be predicted with any certainty. For example, we are aware of patents owned by third parties that have generic composition of matter, method of inhibition and method of treatment claims that may cover fisogatinib or generic method of treatment claims that may cover pralsetinib. If the claims of any of these third-party patents are asserted against us, we do not believe fisogatinib, pralsetinib or our proposed activities related to such compounds would be found to infringe any valid claim of these patents. While we may decide to initiate proceedings to challenge the validity of these patents in the future, we may be unsuccessful, and courts or patent offices in the U.S. and abroad could uphold the validity of any such patents. If we were to challenge the validity of any issued U.S. patent in court, we would need to overcome a statutory presumption of validity that attaches to every U.S. patent. This means that in order to prevail, we would have to present clear and convincing evidence as to the invalidity of the patent's claims.

In addition, the patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. Patent prosecution is a lengthy process, during which the scope of the claims initially submitted for examination by the U.S. Patent and Trademark Office, or USPTO, have been significantly narrowed by the time they issue, if at all. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, there may be circumstances, when we do not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

Even if we acquire patent protection that we expect should enable us to maintain such competitive advantage, third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the U.S. and abroad. For example, we may be subject to a third-party submission of prior art to the USPTO challenging the priority of an invention claimed within one of our patents, which submissions may also be made prior to a patent's issuance, precluding the granting of any of our pending patent applications. We may become involved in opposition, derivation, reexamination, inter partes review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others from whom we have obtained licenses to such rights. Competitors may claim that they invented the inventions claimed in our issued patents or patent applications prior to us or may file patent applications before we do. Competitors may also claim that we are infringing on their patents and that we therefore cannot practice our technology as claimed under our patents, if issued. Competitors may also contest our patents, if issued, by showing the patent examiner that the invention was not original, was not novel or was obvious. In litigation, a competitor could claim that our patents, if issued, are not valid for a number of reasons. If a court agrees, we would lose our rights to those challenged patents.

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 patents, if issued, may not provide us with any meaningful protection or prevent competitors from designing around our patent claims to circumvent our owned or licensed patents by developing similar or alternative technologies or drugs in a non-infringing manner. For example, a third party may develop a competitive drug that provides benefits similar to one or more of our drugs and drug candidates but that has a different composition that falls outside the scope of our patent protection. If the patent protection provided by the patents and patent applications we hold or pursue with respect to our drugs and drug candidates is not sufficiently broad to impede such competition, our ability to successfully commercialize our drugs or drug candidates, if approved, could be negatively affected, which would harm our business.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our current and future drugs and use our proprietary technologies without infringing the proprietary rights and intellectual property of third parties. The biotechnology and pharmaceutical industries are characterized by extensive and frequent litigation regarding patents and other intellectual property rights. We may in the future become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our drugs, drug candidates and technology, including interference proceedings before the USPTO. Our competitors or other third parties may assert infringement claims against us, alleging that our drugs are covered by their patents. Given the vast number of patents in our field of technology, we cannot be certain that we do not infringe existing patents or that we will not infringe patents that may be granted in the future. Many companies have filed, and continue to file, patent applications related to kinase inhibitors. Some of these patent applications have already been allowed or issued, and others may issue in the future. For example, we are aware of patents owned by third parties that have generic composition of matter, method of inhibition and method of treatment claims that may cover fisogatinib or generic method of treatment claims that may cover pralsetinib. If the claims of any of these third-party patents are asserted against us, we do not believe fisogatinib, pralsetinib or our proposed activities related to such compounds would be found to infringe any valid claim of these patents. While we may decide to initiate proceedings to challenge the validity of these patents in the future, we may be unsuccessful, and courts or patent offices in the U.S. and abroad could uphold the validity of any such patents. If we were to challenge the validity of any issued U.S. patent in court, we would need to overcome a statutory presumption of validity that attaches to every U.S. patent. This means that in order to prevail, we would have to present clear and convincing evidence as to the invalidity of the patent's claims.

Since this area is competitive and of strong interest to pharmaceutical and biotechnology companies, there will likely be additional patent applications filed and additional patents granted in the future, as well as additional research and development programs expected in the future. Furthermore, because patent applications can take many years to issue and may be confidential for 18 months or more after filing, and because pending patent claims can be revised before issuance, there may be applications now pending which may later result in issued patents that may be infringed by the manufacture, use or sale of our drugs and drug candidates. If a patent holder believes any of our approved drugs or drug candidate infringes on its patent, the patent holder may sue us even if we have received patent protection for our drugs, drug candidates and technology. Moreover, we may face patent infringement claims from non-practicing entities that have no relevant drug revenue and against whom our own patent portfolio may thus have no deterrent effect.

If we are found to infringe a third party's intellectual property rights, we could be required to obtain a license from such third party to continue developing and marketing our drug candidates and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain such a license, it could be granted on non-exclusive terms, thereby providing our competitors and other third parties access to the same technologies licensed to us. Without such a license, we could be forced, including by court order, to cease developing and commercializing the infringing technology, drugs or drug candidates. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed such third-party patent rights. A finding of infringement could prevent us from commercializing our current and future drugs or force us to cease some of our business operations, which could materially harm our business.

We may become involved in lawsuits to protect or enforce our patents and other intellectual property rights, which could be expensive, time-consuming and unsuccessful.

Competitors and other third parties may infringe, misappropriate or otherwise violate our patents and other intellectual property rights. To counter infringement or unauthorized use, we may be required to file infringement claims. A court may disagree with our allegations, however, and may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the third-party technology in question. Further, such third parties could counterclaim that we infringe their intellectual property or that a patent we have asserted against them is invalid or unenforceable. In patent litigation in the U.S., defendant counterclaims challenging the validity, enforceability or scope of asserted patents are commonplace. In addition, third parties may initiate legal proceedings against us to assert such challenges to our intellectual property rights. The outcome of any such proceeding is generally unpredictable. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Patents may be unenforceable if someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution. It is possible that prior art of which we and the patent examiner were unaware during prosecution exists, which could render our patents invalid. Moreover, it is also possible that prior art may exist that we are aware of but do not believe is relevant to our current or future patents, but that could nevertheless be determined to render our patents invalid.

An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly. If a defendant were to prevail on a legal assertion of invalidity or unenforceability of our patents covering any of our approved drugs or drug candidates, we would lose at least part, and perhaps all, of the patent protection covering such drug or drug candidate. Competing drugs may also be sold in other countries in which our patent coverage might not exist or be as strong. If we lose a foreign patent lawsuit, alleging our infringement of a competitor's patents, we could be prevented from marketing our drugs in one or more foreign countries. Any of these outcomes would have a materially adverse effect on our business.

Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Litigation or other legal proceedings relating to intellectual property claims, with or without merit, is unpredictable and generally expensive and time-consuming and is likely to divert significant resources from our core business, including distracting our technical and management personnel from their normal responsibilities. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities.

We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing upon or misappropriating or from successfully challenging our intellectual property rights. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

Obtaining and maintaining patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. In addition, periodic maintenance fees on issued patents often must be paid to the USPTO and foreign patent agencies over the lifetime of the patent. While an unintentional lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we fail to maintain the patents and patent applications covering our drugs, 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.

Changes to the patent law in the U.S. and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our drugs and drug candidates.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve both technological and legal complexity and is therefore costly, time-consuming and inherently uncertain. Recent patent reform legislation in the U.S. and other countries, including the Leahy-Smith America Invents Act, or Leahy-Smith Act, signed into law on September 16, 2011, could increase those uncertainties and costs. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art and provide more efficient and cost-effective avenues for competitors to challenge the validity of patents. In addition, the Leahy-Smith Act has transformed the U.S. patent system into a “first-to-file” system. The first-to-file provisions, however, only became effective on March 16, 2013. Accordingly, it is not yet clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could make it more difficult to obtain patent protection for our inventions and increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could harm our business, results of operations and financial condition.

The U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition, there have been recent proposals for additional changes to the patent laws of the U.S. and other countries that, if adopted, could impact our ability to obtain patent protection for our proprietary technology or our ability to enforce our proprietary technology. Depending on future actions by the U.S. Congress, the U.S. courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position may be harmed.

In addition to the protection afforded by patents, we rely upon unpatented trade secret protection, unpatented know-how and continuing technological innovation to develop and maintain our competitive position. With respect to the building of our proprietary compound library, we consider trade secrets and know-how to be our primary intellectual property. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our collaborators, scientific advisors, employees and consultants, and invention assignment agreements with our consultants and employees. We may not be able to prevent the unauthorized disclosure or use of our technical know-how or other trade secrets by the parties to these agreements, however, despite the existence generally of confidentiality agreements and other contractual restrictions. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. If any of the collaborators, scientific advisors, employees and consultants who are parties to these agreements breaches or violates the terms of any of these agreements, we may not have adequate remedies for any such breach or violation, and we could lose our trade secrets as a result. Enforcing a claim that a third party illegally obtained and is using our trade secrets, like patent litigation, is expensive and time-consuming, and the outcome is unpredictable. In addition, courts outside the U.S. are sometimes less willing to protect trade secrets.

Our trade secrets could otherwise become known or be independently discovered by our competitors. Competitors could purchase our drugs and drug candidates and attempt to replicate some or all of the competitive advantages we derive from our development efforts, willfully infringe our intellectual property rights, design around our protected technology or develop their own competitive technologies, 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 business, results of operations and future growth prospects could be materially and adversely affected by the COVID-19 pandemic.

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

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

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

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

Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on the research and development, clinical, business development, financial and legal expertise of 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, 2021, we had 429 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 conditions could adversely affect our business, financial condition or results of operations.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. For example, the COVID-19 pandemic has caused extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn could result in a variety of risks to our business, including, weakened demand for our drug candidates and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption, or cause our customers to delay making payments for our services.

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

We or the third parties upon whom we depend may be adversely affected by earthquakes or other natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Earthquakes or other natural disasters could severely disrupt our operations, and have a material adverse effect on our business, results of operations, financial condition and prospects. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as clinical trial sites or the manufacturing facilities of our third-party contract manufacturers, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, could have a material adverse effect on our business.

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

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

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

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

We rely upon a variety of Internet service providers, third-party hosting facilities and cloud computing platform providers to support our business. Failure to maintain the security, confidentiality, accessibility or integrity of data stored on such systems could damage our reputation in the market, cause us to lose revenue or market share, increase our service costs, cause us to incur substantial costs, subject us to liability for damages and/or fines and divert our resources from other tasks, any one of which could materially adversely affect our business, financial condition, results of

operations and prospects. Any damage to, or failure of, such systems, or communications to and between such systems, could result in interruptions in our operations. If our security measures or those of our third-party data center hosting facilities, cloud computing platform providers, or third-party service partners, are breached, and unauthorized access is obtained to our data or our information technology systems, we may incur significant legal and financial exposure and liabilities.

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

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

Privacy and data security have become significant issues in the U.S., Europe and in many other jurisdictions where we conduct or may in the future conduct our operations. The regulatory framework for the collection, use, safeguarding, sharing and transfer of information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally, virtually every jurisdiction in which we operate has established its own data security and privacy frameworks with which we must comply. On May 25, 2018, the European General Data Protection Regulation 2016/679, which is commonly referred to as GDPR, took effect. The GDPR applies to any company established in the European Union as well as any company outside the European Union that collects or otherwise processes personal data in connection with the offering goods or services to individuals in the European Union or the monitoring of their behavior. The GDPR enhances data protection obligations for processors and controllers of personal data, including, for example, expanded disclosures about how personal information is to be used, limitations on retention of information, mandatory data breach notification requirements and onerous new obligations on services providers. The GDPR imposes additional obligations and risk upon our business and substantially increase the penalties to which we could be subject in the event of any non-compliance, including fines of up to €20 million or 4% of total worldwide annual turnover, whichever is higher. Given the breadth and depth of changes in data protection obligations, preparing for and complying with the GDPR requirements has required and will continue to require significant time, resources and a review of our technologies, systems and practices, as well as those of any third-party collaborators, service providers, contractors or consultants that process or transfer personal data collected in the European Union. If enacted, we will be subject to the EU ePrivacy Regulation, which is a proposed regulation of privacy and electronic communications. In addition, we are subject to the California Consumer Privacy Act, or CCPA, which took effect on January 1, 2020 and imposes sweeping privacy and security obligations on many companies doing business in California and provides for substantial fines for non-compliance and, in some cases, a private right of action to consumers who are victims of data breaches involving their unredacted or unencrypted personal information. While there is currently an exception for protected health information that is subject to HIPAA and clinical trial regulations, as currently written, the CCPA may impact our business activities. The CCPA became enforceable as of July 1, 2020, but there continues to be uncertainty about how the law will be interpreted and enforced. The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could lead to government enforcement actions and significant penalties against us and could have a material adverse effect on our business, financial condition or results of operations.

Our employees, principal investigators, CROs and consultants may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading.

We are exposed to the risk that our employees, principal investigators, CROs and consultants may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violate the regulations of the FDA and other regulatory authorities, including those laws requiring the reporting of true, complete and accurate information to such authorities; healthcare fraud and abuse laws and regulations in the U.S. and abroad; or laws that require the reporting of financial information or data accurately. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Activities subject to these laws also involve the improper use of information obtained in the course of clinical trials or creating

fraudulent data in our pre-clinical studies or clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of conduct applicable to all of our employees, but it is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. In addition, we are subject to the risk that a person could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

We may acquire or in-license businesses, technologies or 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. In recent years, many such changes have been made and changes are likely to continue to occur in the future. We cannot predict whether, when, in what form, or with what effective dates, tax laws, regulations and rulings may be enacted, promulgated or decided, which could result in an increase in our, or our stockholders', tax liability or require changes in the manner in which we operate in order to minimize increases in our tax liability. For example, in December 2017, the U.S. enacted the Tax Cuts and Jobs Act of 2017, or TCJA. The TCJA significantly reformed the Internal Revenue Code of 1986, as amended, and among other things, included changes to U.S. federal tax rates, imposed significant additional limitations on the deductibility of interest and net operating loss carryforwards and allows for the expensing of capital expenditures. Our net deferred tax assets and liabilities were revalued as of December 31, 2017 at the newly enacted U.S. corporate rate, and the impact was recognized in our tax expense in the year of enactment but was offset by a corresponding reduction to the valuation allowance. Additionally, in March 2020, the U.S. enacted the CARES Act, which included certain changes in tax law intended to stimulate the U.S. economy in light of the COVID-19 pandemic, including delaying the effective date of the net operating loss restrictions imposed by the TJCA, temporarily relaxing (but not eliminating) the TJCA's interest deductibility limitations, and making temporary beneficial changes to the payroll tax regime. We continue to examine the impact this tax reform legislation may have on our business. The impact of these and other future changes in tax laws is uncertain and could have an adverse effect on our business, cash flow, financial condition or results of operations.

Risks Related to Our Common Stock

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

Our stock price has been and may in the future be subject to substantial volatility. For example, our stock traded within a range of a high price of $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 15, 2021. As a result of this volatility, our stockholders could incur substantial losses.

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

- the success of commercialization of our drugs and drug candidates, if approved;
- the success of competitive drugs or technologies;
- results of clinical trials of our drug candidates or those of our competitors;
- regulatory or legal developments in the U.S. and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our drug candidates or clinical development programs;
- the results of our efforts to discover, develop, acquire or in-license additional drug candidates or drugs;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- natural disasters, epidemic or pandemic disease outbreaks, including the COVID-19 pandemic, trade wars, political unrest or other similar events;
- general economic, industry and market conditions; and
- the other factors described in this “Risk Factors” section.

Future sales or issuances of common stock or other equity related securities may also adversely affect the market price of our common stock. For example, In July 2020, we entered into a sales agreement with Cowen through which we may, from time to time, issue and sell shares of our common stock having an aggregate offering price of up to $250.0 million, subject to the terms and conditions of the sales agreement. In the three months ended December 31, 2020, we issued and sold 1,784,926 shares of our common stock under the sales agreement at an average price of $112.05 per share for net and gross proceeds of $194.7 million and $200.0 million, respectively. If we seek authorization to 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. If any of our stockholders brought a lawsuit against us, we could incur substantial costs defending the lawsuit. Such a lawsuit could also divert the time and attention of our management.

If equity research analysts publish negative evaluations of or downgrade our common stock, the price of our common stock could decline.

The trading market for our common stock relies in part on the research and reports that equity research analysts publish about us or our business. We do not control these analysts. If one or more of the analysts covering our business downgrade their evaluations of our common stock, the price of our common stock could decline. If one or more of these analysts cease to cover our common stock, we could lose visibility in the market for our common stock, which in turn could cause our common stock price to decline.

Our executive officers, directors, principal stockholders and their affiliates maintain the ability to exercise significant influence over our company and all matters submitted to stockholders for approval.

Our executive officers, directors and stockholders who own more than 5% of our outstanding common stock, together with their affiliates and related persons, beneficially own shares of common stock representing a significant percentage of our capital stock. As a result, if these stockholders were to choose to act together, they would be able to influence our management and affairs and the outcome of matters submitted to our stockholders for approval, including the election of directors and any sale, merger, consolidation, or sale of all or substantially all of our assets. This concentration of voting power could delay or prevent an acquisition of our company on terms that other stockholders may desire. In addition, this concentration of ownership might adversely affect the market price of our common stock by:

- delaying, deferring or preventing a change of control of us;
- impeding a merger, consolidation, takeover or other business combination involving us; or
- discouraging a potential acquiror from making a tender offer or otherwise attempting to obtain control of us.

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our amended and restated certificate of incorporation and amended and restated bylaws may delay or prevent an acquisition of us or a change in our management. These provisions include a classified board of directors, a prohibition on actions by written consent of our stockholders and the ability of our board of directors to issue preferred stock without stockholder approval. In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of stockholders owning in excess of 15% of our outstanding voting stock to merge or combine with us. Although we believe these provisions collectively provide for an opportunity to obtain greater value for stockholders by requiring potential acquirors to negotiate with our board of directors, they would apply even if an offer rejected by our board were considered beneficial by some stockholders. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management.

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

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

because our principal executive offices are located in Massachusetts. In addition, our bylaws provide that any person or entity purchasing or otherwise acquiring any interest in shares of our common stock is deemed to have notice of and consented to the Delaware forum provision and the federal forum provision.

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

Future sales of our common stock, including by us or our directors and executive officers or shares issued upon the exercise of currently outstanding options, could cause our stock price to decline.

A substantial portion of our outstanding common stock can be traded without restriction at any time. In addition, a portion of our outstanding common stock is currently restricted as a result of federal securities laws, but can be sold at any time subject to applicable volume limitations. As such, sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, by us or others, could reduce the market price of our common stock or impair our ability to raise adequate capital through the sale of additional equity securities. In addition, we have a significant number of shares that are subject to outstanding options. The exercise of these options and the subsequent sale of the underlying common stock could cause a further decline in our stock price. These sales also might make it difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate. We cannot predict the number, timing or size of future issuances or the effect, if any, that any future issuances may have on the market price for our common stock.

We have incurred and will continue to incur increased costs as a result of operating as a public company, and our management is required to devote substantial time to new compliance initiatives and corporate governance practices.

As a public company, we have incurred and expect to continue to incur significant legal, accounting and other expenses. In addition, the Sarbanes-Oxley Act of 2002 and rules subsequently implemented by the Securities and Exchange Commission, or SEC, and Nasdaq have imposed various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and make some activities more time-consuming and costlier.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we are required to furnish an annual report by our management on our internal control over financial reporting. To achieve compliance with Section 404 within the prescribed period, we have been and will continue to be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting.

Despite our efforts, there is a risk that in the future neither we nor our independent registered public accounting firm will be able to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404 or that we will not be able to comply with the requirements of Section 404 in a

timely manner. If this were to occur, the market price of our stock could decline and we could be subject to sanctions or investigations by the SEC or other regulatory authorities, which would require additional financial and management resources. Furthermore, investor perceptions of our company may suffer if deficiencies are found, and this could cause a decline in the market price of our stock. Irrespective of compliance with Section 404, any failure of our internal control over financial reporting could have a material adverse effect on our stated operating results and harm our reputation. If we are unable to implement these requirements effectively or efficiently, it could harm our operations, financial reporting, or financial results and could result in an adverse opinion on our internal control over financial reporting from our independent registered public accounting firm.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be the sole source of gain for our stockholders.

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be the sole source of gain for our stockholders for the foreseeable future.

Our ability to utilize our net operating loss carryforwards and certain other tax attributes may be limited.

Under Section 382 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an "ownership change" (generally defined as a greater than 50% change (by value) in the ownership of its equity over a three-year period), the corporation's ability to use its pre-change net operating loss carryforwards and certain other pre-change tax attributes to offset its post-change income may be limited. We analyzed shifts in the stock ownership to determine if its net operating losses and tax credit carryforwards may be subject to limitation under Sections 382 and 383. Based on this analysis, we determined that it is more likely than not that an ownership change occurred on the following dates: March 24, 2011; April 5, 2011; November 10, 2014; and February 7, 2017. As a consequence of these ownership changes, our net operating loss carryforwards allocable for the period preceding each ownership change are subject to limitations under Section 382. In addition, pursuant to the TCJA (as modified by the CARES Act), we may not use net operating loss carry-forwards generated in taxable years beginning after December 31, 2017 to reduce our taxable income in any year beginning after December 31, 2020 by more than 80%, and we may not carry back any net operating losses generated in taxable years beginning after December 31, 2020 to prior years. These new rules apply regardless of the occurrence of an ownership change.

Item 1B. Unresolved Staff Comments.

Not applicable.

Item 2. Properties.

Our headquarters are located at 45 Sidney Street in Cambridge, Massachusetts where we occupy approximately 99,833 rentable square feet of office and laboratory space under a lease that commenced on October 1, 2017 and will expire on November 30, 2029. On September 19, 2018, we entered into an amendment to the lease agreement to expand the rentable square footage from approximately 99,833 square feet to approximately 139,216 square feet. Pursuant to the lease amendment, the rent commencement date for the expansion premises was July 1, 2019. The initial term of the lease with respect to the expansion premises commenced on March 1, 2019 and will expire on November 30, 2029, unless terminated sooner.

We also lease our former corporate headquarters at 38 Sidney Street in Cambridge, Massachusetts under a lease that will expire on October 31, 2022. The lease agreement provides us with an option to extend the lease for five additional years. In the first quarter of 2018, we fully subleased these premises, and the term of the existing sublease will expire on February 28, 2021.

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.

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

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, 2021, there were approximately 11 holders of record of our common stock. This number does not include beneficial owners whose shares are held by nominees in street name.

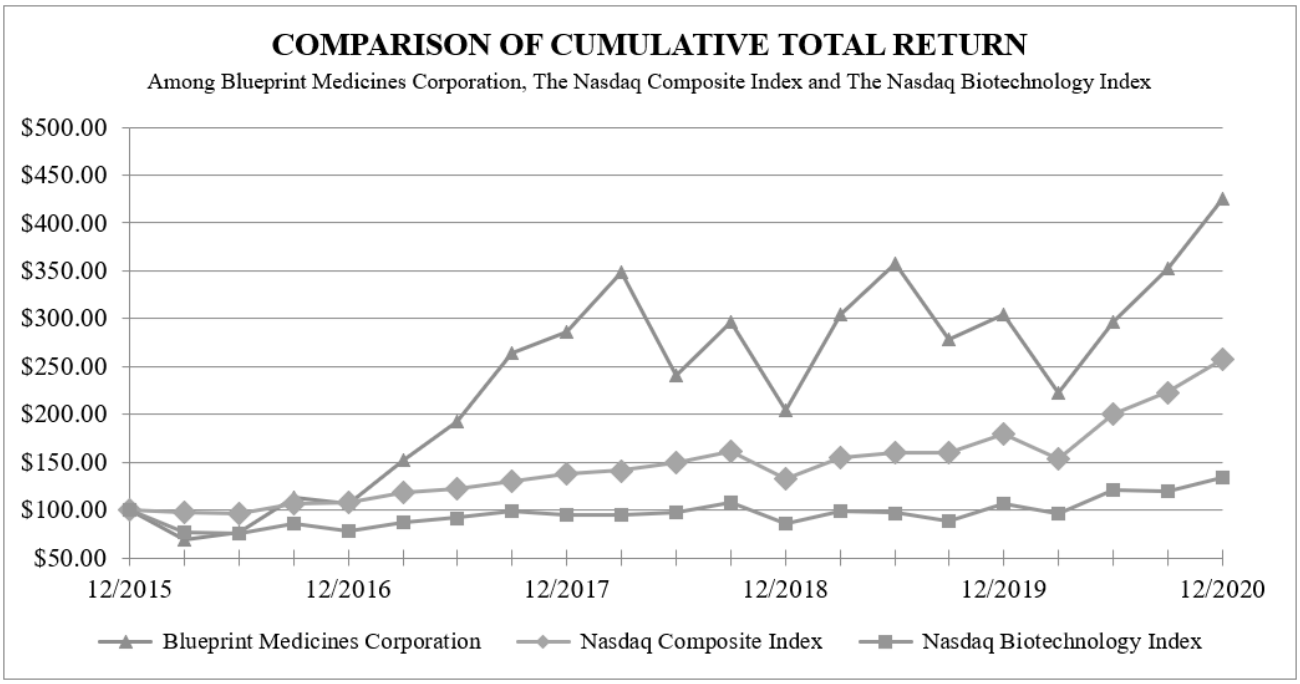
Dividends

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, 2020. 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.



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.

Overview

We are a global precision therapy company that is inventing transformative medicines for people with cancer and hematologic disorders. Applying an approach that is both precise and agile, we create therapies that selectively target genetic drivers, with the goal of staying one step ahead across stages of disease. Since 2011, we have leveraged our research platform, including expertise in molecular targeting and world-class drug design capabilities, to rapidly and reproducibly translate science into a broad pipeline of precision therapies. We are delivering our approved medicines, AYVAKIT™/AYVAKYT® (avapritinib) and GAVRETO™ (pralsetinib), to patients in the U.S. and Europe, and we are globally advancing multiple programs for genomically defined cancers, systemic mastocytosis, and cancer immunotherapy.

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

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

Avapritinib

We are developing avapritinib for the treatment of systemic mastocytosis, or SM, a rare hematologic disorder that causes an overproduction of mast cells and the accumulation of mast cells in the bone marrow and other organs, which can lead to a wide range of debilitating symptoms and organ dysfunction and failure. Nearly all cases of SM are driven by the KIT D816V mutation, which aberrantly activates mast cells.

In December 2020, we submitted a supplemental new drug application, or NDA, to the U.S. Food and Drug Administration, or FDA, for avapritinib for the treatment of adult patients with advanced SM. In February 2021, the FDA accepted our application and set a Prescription Drug User Fee Act, or PDUFA, action date of June 16, 2021. We also submitted a Type II variation marketing authorization application, or MAA, to the European Medicines Agency, or EMA, for avapritinib for advanced SM in February 2021.

We are currently evaluating avapritinib in an ongoing registration-enabling Phase 1 clinical trial in advanced SM, which we refer to as our EXPLORER trial, and an ongoing registration-enabling Phase 2 clinical trial in advanced SM, which we refer to as our PATHFINDER trial. In September 2020, we reported positive top-line data from the EXPLORER and PATHFINDER trials. We plan to present registrational data from the PATHFINDER trial in the first half of 2021. In addition, we are evaluating avapritinib in an ongoing registration-enabling Phase 2 clinical trial in non-advanced SM, which we refer to as our PIONEER trial. In 2020, we reported data from the dose-finding portion (Part 1) of the PIONEER trial and initiated the registration-enabling Part 2 of the PIONEER trial. We expect to complete enrollment of Part 2 of the PIONEER trial in mid-2021.

The FDA has granted breakthrough therapy designation to avapritinib for (i) the treatment of advanced SM, including the subtypes of aggressive SM, SM with an associated hematologic neoplasm and mast cell leukemia, 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.

BLU-263

BLU-263 is an investigational, orally available, potent and highly selective KIT inhibitor that we are developing for the treatment of non-advanced SM and other mast cell disorders. BLU-263 is designed to have equivalent potency as avapritinib, with low off-target activity and lower penetration of the central nervous system, or CNS, relative to avapritinib based on preclinical data, which we believe will enable development of BLU-263 in a broad population of patients with non-advanced SM, including patients with lower disease burden requiring potentially life-long chronic therapy, and potentially patients with other mast cell disorders. In January 2021, we announced positive top-line results from a Phase 1 trial of BLU-263 in healthy volunteers. Based on these data, in mid-2021, we plan to initiate a Phase 2 trial of BLU-263 in patients with non-advanced SM, which we refer to as our HARBOR trial.

RET-altered Cancers — GAVRETO™ (pralsetinib)

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

Pralsetinib is approved in the U.S. with accelerated approval under the brand name GAVRETO for the treatment of (i) adult patients with metastatic RET fusion-positive NSCLC as detected by an FDA approved test, (ii) adult and pediatric patients 12 years of age and older with advanced or metastatic RET-mutant MTC who require systemic therapy, and (iii) adult and pediatric patients 12 years of age and older with advanced or metastatic RET fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate).

The EMA is currently reviewing our MAA for pralsetinib for RET fusion-positive NSCLC. If approved by the European Commission, Roche plans to launch pralsetinib in RET fusion-positive NSCLC in Europe in the first half of 2021. Roche also plans to submit a Type II variation MAA to the EMA for pralsetinib for RET-altered thyroid cancers in the second half of 2021, and to submit marketing applications for pralsetinib for RET-altered NSCLC and thyroid cancers across multiple additional global geographies in 2021. In addition, China's National Medical Products Administration, or NMPA, accepted an NDA submitted by CStone in the third quarter of 2020 for pralsetinib for the treatment of RET fusion-positive NSCLC patients previously treated with platinum-based chemotherapy.

We are currently evaluating pralsetinib in an ongoing registration-enabling Phase 1/2 clinical trial in patients with RET-altered NSCLC, MTC and other advanced solid tumors, which we refer to as our ARROW trial. Pursuant to our collaboration with Roche, we plan to co-develop pralsetinib globally in RET-altered solid tumors, including NSCLC, MTC and other thyroid cancers, as well as other solid tumors.

The FDA has granted breakthrough therapy designation to pralsetinib for (i) the treatment of patients with RET fusion-positive NSCLC that has progressed following platinum-based chemotherapy and (b) the treatment of patients with RET mutation-positive MTC that requires systemic treatment and for which there are no acceptable alternative treatments. In addition, the FDA has granted orphan drug designation to pralsetinib for the treatment of RET-rearranged NSCLC, JAK1/2-positive NSCLC or TRKC-positive NSCLC.

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

We are commercializing avapritinib for the treatment of patients with PDGFRA exon 18 mutant gastrointestinal stromal tumors, or GIST, a rare disease that is a sarcoma, or tumor of bone or connective tissue, of the gastrointestinal tract. Avapritinib is approved in the U.S. under the brand name AYVAKIT for the treatment of adults with unresectable or metastatic gastrointestinal stromal tumors harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations, and is approved in the European Union 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.

The European Commission has granted orphan medicinal product designation to avapritinib for the treatment of GIST. In addition, the NMPA accepted an NDA submitted by CStone in the first quarter of 2020 for avapritinib for the treatment of adults with unresectable or metastatic PDGFRA exon 18 mutant GIST. CStone also submitted an NDA to the Taiwan Food and Drug Administration, or the TFDA, for avapritinib for the indication of adult patients with unresectable or metastatic GIST harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations, and received priority review designation from the TFDA.

Treatment-Resistant EGFR-Mutated NSCLC

We are developing two investigational EGFR inhibitors, BLU-701 and BLU-945, with the goal of addressing the most common on-target resistance mutations to currently available EGFR-targeted therapies. While the introduction of EGFR-targeted therapies, including osimertinib, has transformed the care of patients with EGFR-driven NSCLC, treatment resistance is a significant emerging unmet medical need.

In addition to targeting EGFR resistance mutations, BLU-701 and BLU-945 were specifically designed for selectivity over wild-type EGFR and other kinases to enable potential improved tolerability and also combination strategies. In addition, in preclinical tumor models, both drug candidates have shown CNS activity, highlighting the potential to address CNS metastases which are more common in treatment-experienced NSCLC patients.

We plan to initially develop BLU-701 and BLU-945 as monotherapies and in combination with each other and other therapies to overcome treatment resistance in specific patient populations with EGFR-driven NSCLC.

EGFR-Positive Double Mutant NSCLC — BLU-701

BLU-701 is a selective and potent investigational inhibitor of double-mutant EGFR harboring either the activating L858R or exon 19 deletion mutations combined with the acquired C797S mutation, the most common on-target resistance mutation to osimertinib. We plan to initially develop BLU-701 as a monotherapy and in combination with other therapies. We plan to present foundational preclinical data for BLU-701 in the first half of 2021, and we plan to initiate a Phase 1 trial of BLU-701 in the second half of 2021.

EGFR-Positive Triple Mutant NSCLC — BLU-945

BLU-945 is a selective and potent investigational inhibitor of triple-mutant EGFR harboring either the activating L858R or exon 19 deletion mutations combined with the acquired T790M and C797S mutations, the most common on-target resistance to first-generation EGFR inhibitors and osimertinib, respectively.

In preclinical data presented in September 2020, BLU-945 inhibited triple mutant EGFR with sub-nanomolar potency and demonstrated greater than 900-fold selectivity over wild-type EGFR along with excellent overall kinome selectivity. In a triple mutant EGFR cell-line, BLU-945 potently inhibited the EGFR pathway, while osimertinib demonstrated limited activity. BLU-945 monotherapy resulted in robust anti-tumor activity in multiple cell line-derived and patient-derived xenograft models of triple mutant EGFR NSCLC. In addition, BLU-945 treatment in combination with osimertinib or gefitinib resulted in tumor regression in a triple mutant EGFR NSCLC patient-derived xenograft model, which was derived from a patient with progressive disease following five lines of prior therapy. BLU-945 was also highly active in an intracranial disease model.

Based on these preclinical proof-of-concept data, we plan to initially develop BLU-945 as a monotherapy and in combination with other agents. We plan to initiate a Phase 1 trial of BLU-945 in patients with EGFR-driven NSCLC, in the first half of 2021.

Fisogatinib — Hepatocellular Carcinoma

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

Discovery Platform

We plan to continue to leverage our discovery platform to systematically and reproducibly identify kinases that are drivers of diseases in genomically defined patient populations and craft drug candidates that potently and selectively target these kinases.

In addition to our discovery programs for treatment-resistant EGFR-mutated NSCLC, we currently have the following wholly-owned discovery programs:

- *CDK2 Discovery Program.* In February 2021, we announced a discovery program targeting CDK2. CDK2, a cyclin-dependent kinase involved in cell cycle biology, is activated by its regulatory partner Cyclin E, and can drive cancer cell proliferation when Cyclin E is aberrantly expressed. Dysregulated Cyclin E is associated with multiple malignancies and has been shown to be a mechanism of resistance to targeted therapies, including CDK4/6 inhibitors.
- *Other Discovery Programs.* In addition to the discovery programs described above, we have two wholly-owned pre-development candidate programs for undisclosed kinase targets.

Under our immunotherapy collaboration with Roche, we are conducting activities for up to two discovery programs, including a development candidate for the kinase target MAP4K1. See "*—Collaborations and Licenses Summary*" below. We plan to present initial preclinical data for our MAP4K1 development candidate in the first half of 2021.

Collaborations and Licenses

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

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

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

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

We will continue to evaluate additional collaborations, partnerships and licenses that could maximize the value for our programs and allow us to leverage the expertise of strategic collaborators, partners and licensors, including in additional geographies where we may not have current operations or expertise. We are also focused on engaging in collaborations, partnerships and license agreements to capitalize on our discovery platform outside of our primary strategic focus area of cancer and rare diseases.

Note on the COVID-19 Pandemic

Due to the continued evolution and uncertain global impacts of the COVID-19 pandemic, we cannot precisely determine or quantify the impact this pandemic will have on our business, operations and financial performance. In 2020, we initially established a work-from-home policy for all employees, other than those performing or supporting business-critical activities, such as certain members of our laboratory and facilities staff. While the majority of employees continue to work from home, we have continued to evaluate and update this policy for each of our locations and field-based employees based on guidance from federal, state and local government authorities and the severity of the pandemic. For our ongoing and planned clinical trials, while we anticipate and have experienced some delays or disruptions due to the COVID-19 pandemic, in particular with respect to activation of additional clinical trial sites and patient enrollment rates, we have continued to work with any impacted clinical trial sites to ensure study continuity, enable medical monitoring, facilitate study procedures and maintain clinical data and records, including the use of local laboratories for testing and tumor imaging, home delivery of study drug and remote data and records monitoring. In addition, we currently have sufficient supply or plans for supply to meet our anticipated global commercial and clinical development needs for our approved drugs and clinical-stage drug candidates through 2022. However, depending on the duration and impact of the COVID-19 pandemic on local and global supply chains, our suppliers could be adversely impacted, which may result in delays or disruptions in our current or future supply chain. For our commercial activities for AYVAKIT/AYVAKYT and GAVRETO, we are committed to continuing to serve the needs of healthcare providers, patients and other stakeholders during this critical time, including by conducting commercial and medical affairs field activities across our portfolio in virtual formats where possible. We will continue to assess the duration, scope and severity of the COVID-19 pandemic and the existing and potential impacts on our business, operations and financial performance, and we will continue to work closely with our third-party vendors, collaborators and other parties in order to seek to advance our pipeline of targeted therapies as quickly as possible, while making the health and safety of our employees and their families, healthcare providers, patients and communities a top priority. Please refer to our Risk Factors in Part I, Item 1A of this Annual Report on Form 10-K for further discussion of risks related to the COVID-19 pandemic.

Financial Operations Overview

To date, we have financed our operations primarily through public offerings of our common stock, private placements of our convertible preferred and common stock, collaborations and a license agreement. Through December 31, 2020, we have received an aggregate of $2.9 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, $910.8 million in upfront and milestone payments under our collaborations with Roche and CStone, our license agreement with Clementia and our former collaboration with Alexion Pharma Holding, or Alexion. In addition, since January 2020, we have generated limited product revenue.

Since inception, we have incurred significant operating losses, with the exception of the year ended December 31, 2020. Our net income was $313.9 million for the year ended December 31, 2020 primarily due to the collaboration revenue recorded under our collaboration with Roche for pralsetinib. Our net losses were $347.7 million and $236.6 million for the years ended December 31, 2019 and 2018, respectively. As of December 31, 2020, we had an accumulated deficit of $631.4 million. We expect to continue to incur significant expenses and operating losses over the next few years. We anticipate that our expenses will continue to increase in connection with our ongoing activities, particularly as we:

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

- continue to discover, validate and develop additional drug candidates or development candidates, including our discovery programs for treatment-resistant EGFR-mutated NSCLC and our CDK2 discovery program;

- continue to manufacture increasing quantities of drug substance and drug product material for use in pre-clinical studies, clinical trials and commercialization;

- conduct development and commercialization activities for companion diagnostic tests for our drugs and drug candidates;

- conduct research and development activities under our collaborations with Roche and CStone;

- maintain, expand and protect our intellectual property portfolio;

- acquire or in-license additional businesses, technologies, drugs or drug candidates, form strategic alliances or create joint ventures with third parties; 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 FDA granted accelerated approval to pralsetinib under the brand name GAVRETO for the treatment of adult patients with metastatic RET fusion-positive NSCLC as detected by an FDA approved test, and the European Commission granted conditional marketing authorization to avapritinib under the brand name AYVAKYT as a monotherapy for the treatment of adult patients with unresectable or metastatic GIST harboring the PDGFRA D842V mutation.

For the year ended December 31, 2020, our revenue primarily consisted of sales of AYVAKIT/AYVAKYT, GAVRETO and collaboration revenue under our collaborations with Roche and CStone. Collaboration revenue for the year ended December 31, 2020 primarily includes amounts that were recognized related to upfront payments, milestone payments, the equity premium from Roche, and amounts due to us for supply of inventory (under our collaboration agreements) and research and development services.

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

Cost of sales

Our cost of sales includes the cost of producing and distributing inventories that are related to product revenue during the respective period, including salary related and stock-based compensation expense for employees involved with production and distribution, freight, and indirect overhead costs. In addition, shipping and handling costs for product shipments are recorded in cost of sales as incurred.

Prior to receiving FDA approval for AYVAKIT and GAVRETO in January 2020 and September 2020, respectively, we manufactured inventory to be sold upon commercialization and recorded approximately $36.3 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 a prior period and are therefore excluded from the

cost of goods sold for the year ended December 31, 2020. We estimate our cost of goods sold as a percentage of net product revenue will continue to be positively impacted as we sell through certain inventory that was previously expensed prior to FDA approval. We expect to utilize zero cost inventory for an extended period of time.

Expenses

Research and Development Expenses

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

- employee-related expenses including salaries, benefits, and stock-based compensation expense;
- expenses incurred under agreements with third parties that conduct research and development, pre-clinical activities, clinical activities and manufacturing on our behalf;
- expenses incurred under agreements with third parties for the development and commercialization of companion diagnostic tests;
- the cost of consultants 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 pre-clinical study materials, clinical trial materials and commercial supply materials; and
- facilities, depreciation, and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance, and other operating costs in support of research and development activities.

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

The successful development of our drug candidates is highly uncertain. As such, at this time, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the remainder of the development of these drug candidates. We are also unable to predict when, if ever, material net cash inflows will commence from 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 commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for AYVAKIT/AYVAKYT, GAVRETO and our drug candidates;
- commercializing AYVAKIT/AYVAKYT, GAVRETO and our drug candidates, if and when approved, whether alone or in collaboration with others;

- market acceptance of AYVAKIT/AYVAKYT, GAVRETO and any future drug we may commercialize; and

- continued acceptable safety profile of the drugs following approval.

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

Research and development activities are central to our business model. Drug candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect research and development costs to increase significantly for the foreseeable future as our drug candidate development programs progress and as we conduct and continue our clinical trials to evaluate our approved drugs for additional indications. However, we do not believe that it is possible at this time to accurately project total program-specific expenses through commercialization. There are numerous factors associated with the successful commercialization of any of our 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.

A significant portion of our research and development expenses have been external expenses, which we track on a program-by-program basis following nomination as a development candidate. Our internal research and development expenses are primarily personnel-related expenses, including stock-based compensation expense. Except for internal research and development expenses related to collaboration agreements, we do not track our internal research and development expenses on a program-by-program basis as they are deployed across multiple projects under development.

The following table summarizes our external research and development expenses by program for the years ended December 31, 2020, 2019 and 2018. Other development and pre-development candidate expenses, unallocated expenses and internal research and development expenses have been classified separately.

	Year Ended December 31,		
	2020	2019	2018
		(in thousands)	
Avapritinib external expenses	$ 77,074	$ 98,146	$ 83,417
Pralsetinib external expenses	63,066	78,689	44,099
Fisogatinib external expenses	4,190	6,496	10,167
BLU-263 external expenses	14,138	4,575	—
BLU-701/945 external expenses	14,549	5,397	2,791
Other development and pre-development candidate expenses and unallocated expenses	55,409	62,741	53,917
Internal research and development expenses	98,434	75,406	49,230
Total research and development expenses	$ 326,860	$ 331,450	$ 243,621

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

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

collaboration with CStone, development activities under our collaboration for pralsetinib with Roche and development activities for companion diagnostic tests for current and future drug candidates.

Selling, General and Administrative Expenses

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

Interest Income (Expense), net

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

Other Income (Expense), net

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

Income Tax Expense

Income tax expense consists primarily of income taxes related to the taxable income generated from our collaboration with Roche for pralsetinib and our product sales in the state jurisdictions where we conduct business.

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. Actual results may differ from these estimates under different assumptions or conditions. On an ongoing basis, we evaluate our judgments and estimates in light of changes in circumstances, facts and experience. The effects of material revisions in estimates, if any, will be reflected in the consolidated financial statements prospectively from the date of change in estimates.

Our critical accounting policies are those policies that require the most significant judgments and estimates in the preparation of our financial statements. Management has determined that our most critical accounting policies are those relating to revenue recognition, accounts receivable, inventory, accrued research and development expenses, available-for-sale investments, stock-based compensation and leases.

Revenue Recognition

We account for contracts with customers in accordance with ASC Topic 606, *Revenue from Contracts with Customers*, ASC 606. We recognize revenue when our customer obtains control of promised goods or services, in an amount that reflects the consideration which we expect to receive in exchange for those goods or services. To determine revenue recognition for arrangements that we determine are within the scope of ASC 606, we perform 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) we satisfy a performance obligation. We only apply the five-step model to contracts when it is probable that we will collect the consideration we are entitled to in exchange for the goods or services we transfer to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, we assess the goods or services promised within each contract and determine those that are performance obligations and assess whether each promised good or service is distinct. We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

Product Revenue

We generated product revenue from sales of AYVAKIT and GAVRETO 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, we entered into arrangements with payors that provide for government mandated rebates, discounts and allowances with respect to the utilization of our products.

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

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

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

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

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

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

Collaboration Revenue

At contract inception, we analyze our collaboration 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 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, we first determine 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. We evaluate 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 our products and product candidates in a collaboration arrangement, where we are the principal on sales transactions with third parties, we recognize revenue, cost of sales and operating expenses on a gross basis in their respective lines in our consolidated statements of operations and comprehensive income (loss). Where we are not the principal on sales transactions with third parties, we record our share of the revenues, cost of sales and operating expenses on a net basis as revenue (expenses) from the collaboration arrangement in our consolidated statements of operations and comprehensive income (loss).

For elements accounted within scope of ASC 606, to determine the appropriate amount of revenue to be recognized for the arrangements, we perform 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) we satisfy each performance obligation. As part of the accounting for these arrangements, we 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. We use judgment to determine whether milestones or other variable consideration, except for 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 we recognize revenue as or when the performance obligations under the contract are satisfied.

Exclusive Licenses. If the license to our intellectual property is determined to be distinct from the other promises or performance obligations identified in the arrangement, we recognize 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, we consider 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, we consider 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, we utilize 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. We evaluate 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 we record in future periods.

Research and Development Services. The promises under our collaboration agreements may include research and development services to be performed by our employees on behalf of the partner. Payments or reimbursements resulting from our research and development efforts are recognized as revenue when the services are performed and presented on a gross basis because we are 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. We evaluate 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. We allocate 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, we evaluate whether the milestones are considered probable of being achieved and estimate 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 our control or the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. We evaluate 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, we reevaluate 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 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, we recognize 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. To date, we have not recognized any royalty revenue resulting from any of our licensing arrangements.

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. If we transfer goods or services to a customer before the customer pays consideration or before payment is due, we record a contract asset as unbilled accounts receivable on the consolidated balance sheets.

Accounts Receivable

Accounts receivables arise from product sales and amounts due from our collaboration partners. The amount from product sales represents amounts due from specialty pharmacy providers in the U.S. and in the European Union. We monitor economic conditions and the financial performance and credit worthiness of our counterparties to identify facts or circumstances that may indicate that our receivables are at risk of collection. We provide reserves against

accounts receivable for estimated losses that may result from a customer's inability to pay based on the composition of our accounts receivable, 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.

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. We classify our inventory costs as long-term when we expect to utilize the inventory beyond the normal operating cycle and include these costs in other assets in the consolidated balance sheets.

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

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

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.

Available-for-Sale Investments

We classify marketable securities with a remaining maturity when purchased of greater than three months as available-for-sale. Marketable securities with a remaining maturity date greater than one year are classified as non-current. Available-for-sale securities are maintained by an investment manager and mainly consist of U.S. Treasury securities and U.S. government agency securities. Available-for-sale 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). We review our 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 or other factors. If the decline in fair value is due to credit-related factors, a loss is recognized in net income, whereas if the decline in fair value is not due to credit-related factors, the loss is recorded in other comprehensive income (loss).

Stock-Based Compensation

We account for stock-based compensation awards in accordance with ASC 718, *Compensation –Stock Compensation,* which we refer to as ASC 718. We expense the fair value of stock-based 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. We estimate the fair value of options granted to employees at the date of grant using the Black-Scholes option-pricing model that requires management to apply judgment and make estimates, including:

- expected volatility, which is calculated based a blend of our reported volatility data for the length of time that market data is available for our stock and the historical data for a representative group of publicly traded companies, for which historical information is available. For these analyses, we select companies with comparable characteristics to ours including enterprise value, risk profiles, position within the industry, and with historical share price information sufficient to meet the expected life of the stock-based awards. We compute the historical volatility data using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of our stock-based awards. We intend to consistently apply this process using representative companies until a sufficient amount of historical information regarding the volatility of our own share price becomes available;

- 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 we calculate using the simplified method, as prescribed by the Securities and Exchange Commission Staff Accounting Bulletin No. 107, Share-Based Payment, as we have insufficient historical information regarding our 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 we never paid cash dividends and do not expect to pay any cash dividends in the foreseeable future.

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 award 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 our 2015 employee stock purchase plan, as amended, or 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 our 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.

Leases

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

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

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

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

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.

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

Results of Operations

Comparison of Years Ended December 31, 2020 and 2019

The following table summarizes our results of operations for the years ended December 31, 2020 and 2019, together with the changes in those items in dollars and as a percentage:

	Year Ended December 31,			
	2020	2019	Dollar Change	% Change
		(in thousands)		
Revenues:				
Product revenue, net	$ 22,134	$ —	$ 22,134	100 %
Collaboration revenue	771,601	66,512	705,089	1,060
Total revenue	793,735	66,512	727,223	1,093
Cost and operating expenses:				
Cost of sales	425	—	425	100
Research and development	326,860	331,450	(4,590)	(1)
Selling, general and administrative	157,743	96,388	61,355	64
Total cost and operating expenses	485,028	427,838	57,190	13
Other income (expense):				
Interest income (expense), net	6,599	13,732	(7,133)	(52)
Other income (expense), net	(366)	(100)	266	266
Total other income (expense)	6,233	13,632	(7,399)	(54)
Income (loss) before income taxes	314,940	(347,694)	662,634	191
Income tax expense	1,058	—	1,058	100
Net income (loss)	$ 313,882	$ (347,694)	$ 661,576	190 %

Product Revenue, Net

Product revenue, net was $22.1 million for the year ended December 31, 2020. We started generating revenue from sales of AYVAKIT in the first quarter of 2020 following FDA approval of AYVAKIT for the treatment of adults with unresectable or metastatic GIST harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations. In September 2020, the European Commission granted conditional marketing authorization to 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. For the year ended December 31, 2020, we recorded net product revenue from the sale of AYVAKIT/AYVAKYT for a total of $21.2 million. We started generating revenue from sales of GAVRETO in the third quarter of 2020 following the initial FDA approval of GAVRETO. GAVRETO was originally approved for the treatment of adult patients with metastatic RET fusion-positive NSCLC and subsequently approved for adult and pediatric patients 12 years of age and older with advanced or metastatic RET-mutant MTC who require systemic therapy, or with advanced or metastatic RET fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate). For the year ended December 31, 2020, we recorded net product revenue from the sale of GAVRETO for a total of $0.9 million.

Collaboration Revenue

Collaboration revenue increased by $705.1 million from $66.5 million for the year ended December 31, 2019 to $771.6 million for the year ended December 31, 2020. For the year ended December 31, 2020, our collaboration revenue mainly consisted of $753.1 million in revenue under our collaboration agreement with Roche for pralsetinib, $14.6 million revenue under our cancer immunotherapy collaboration with Roche, and $3.6 million in revenue under our CStone collaboration. Revenue recognized under our collaboration with Roche for pralsetinib for the year ended December 31, 2020 consisted of $695.7 million upfront cash payment including the $20.7 million premium associated with the $100.0 million equity investment by Roche, $55.0 million in specified regulatory and commercialization milestone payments and $2.4 million associated with services related to Roche territory-specific activities. We recognized $14.6 million in revenue under our cancer immunotherapy collaboration with Roche for the year ended December 31, 2020, which was primarily related to the amortization of the total $64.5 million of upfront and milestone payments received as of such period. Revenue recognized under our CStone collaboration for the year ended

December 31, 2020 primarily consisted of $2.0 million in milestone revenue related to a development milestone that was achieved during the year and $1.6 million associated with drug supply related to CStone territory-specific activities.

Collaboration revenue for the year ended December 31, 2019 consisted of $46.2 million revenue under the Clementia license agreement, $12.1 million in revenue under our CStone collaboration and $8.2 million revenue under our cancer immunotherapy collaboration with Roche. Revenue recognized under the Clementia license agreement for the year ended December 31, 2019 consisted of a $25.0 million upfront payment received, a $20.0 million cash milestone payment due and paid in the third quarter of 2020 and a $1.2 million inventory transfer. Revenue recognized under our CStone collaboration for the year ended December 31, 2019 primarily consisted of $12.0 million in milestone revenue related to several development and regulatory milestones that were achieved during the year. We recognized $8.2 million in revenue under our cancer immunotherapy collaboration with Roche for the year ended December 31, 2019, which was primarily related to the amortization of the total $63.0 million of upfront and milestone payments received during such period.

Cost of sales

Cost of sales was $0.4 million for the year ended December 31, 2020 and was related to manufacturing costs associated with our product sales. Costs associated with the manufacture of our drugs prior to FDA approval were recorded as research and development expenses and, therefore, are not included in cost of sales during such period.

Research and Development Expense

Research and development expense decreased by $4.6 million from $331.5 million for the year ended December 31, 2019 to $326.9 million for the year ended December 31, 2020. The decrease in research and development expense was primarily related to $20.5 million reimbursement from the global development cost sharing arrangement under our collaboration with Roche for pralsetinib and approximately $12.6 million in decreased expenses associated with clinical and commercial manufacturing activities. This decrease in research and development expense was primarily offset by an increase of approximately $18.7 million in personnel expense, primarily due to an increase in headcount, which was driven by growth in the clinical and manufacturing organizations and an increase of $5.0 million in stock-based compensation expense.

Selling, general and Administrative Expense

Selling, general and administrative expense increased by $61.4 million from $96.4 million for the year ended December 31, 2019 to $157.7 million for the year ended December 31, 2020. The increase in selling, general and administrative expense was primarily related to increased costs and personnel expenses, including an increase of $15.8 million in stock-based compensation expense, associated with building our commercial infrastructure and to support the overall growth of our business, as well as an increase of $17.5 million in commercial expenses to build our commercial infrastructure for commercialization of AYVAKIT/AYVAKYT and GAVRETO. The increase in selling, general and administrative expense was partially offset by a $10.6 million reimbursement in connection with the commercialization of GAVRETO in the U.S. under our collaboration with Roche for pralsetinib.

Interest Income (Expense), Net

Interest income (expense), net decreased by $7.1 million from $13.7 million for the year ended December 31, 2019 to $6.6 million for the year ended December 31, 2020. The decrease was primarily due to a lower rate of return on investments caused by the severe liquidity crisis in the capital markets resulting from the COVID-19 pandemic.

Other Income (Expense), Net

Other expense, net increased by less than $0.3 million from $0.1 million for the year ended December 31, 2019 to $0.4 million for the year ended December 31, 2020. The increase was primarily related to changes in foreign currency exchange rates.

Income Tax Expense

Income tax expense consisted of $1.1 million for the year ended December 31, 2020, related to the income taxes provisions associated with the taxable income generated from our collaboration with Roche for pralsetinib and our product sales in certain state jurisdictions.

Comparison of Years Ended December 31, 2019 and 2018

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

	Year Ended December 31,			
	2019	2018	Dollar Change	% Change
	(in thousands)			
Collaboration revenue	$ 66,512	$ 44,521	$ 21,991	49 %
Operating expenses:				
Research and development	331,450	243,621	87,829	36
Selling, general and administrative	96,388	47,928	48,460	101
Total operating expenses	427,838	291,549	136,289	47
Other income (expense):				
Interest income (expense), net	13,732	10,566	3,166	30
Other income (expense), net	(100)	(180)	(80)	(44)
Total other income (expense)	13,632	10,386	3,246	31
Net loss	$ (347,694)	$ (236,642)	$ 111,052	47 %

Collaboration Revenue

Collaboration revenue increased by $22.0 million from $44.5 million for the year ended December 31, 2018 to $66.5 million for the year ended December 31, 2019. Collaboration revenue for the year ended December 31, 2019 consisted of $46.2 million revenue under the Clementia license agreement, $12.1 million in revenue under our CStone collaboration and $8.2 million revenue under our cancer immunotherapy collaboration with Roche. Revenue recognized under the Clementia license agreement for the year ended December 31, 2019 consisted of a $25.0 million upfront payment received, a $20.0 million cash milestone payment due and paid in the third quarter of 2020 and a $1.2 million inventory transfer. Revenue recognized under our CStone collaboration for the year ended December 31, 2019 primarily consisted of $12.0 million in milestone revenue related to several development and regulatory milestones that were achieved during the year. We recognized $8.2 million in revenue under our cancer immunotherapy collaboration with Roche for the year ended December 31, 2019, which was primarily related to the amortization of the total $63.0 million of upfront and milestone payments received as of such period.

Collaboration revenue for the year ended December 31, 2018 was related to the CStone collaboration and cancer immunotherapy collaboration with Roche. We entered into the CStone agreement on June 1, 2018 and recognized collaboration revenue of $40.0 million from the upfront payment under the CStone agreement for the year ended December 31, 2018. We recognized $4.5 million in collaboration revenue under the cancer immunotherapy agreement with Roche for the year ended December 31, 2018, which was primarily related to amortization of the total $55.0 million upfront and milestone payments received as of such period.

Research and Development Expense

Research and development expense increased by $87.8 million from $243.6 million for the year ended December 31, 2018 to $331.5 million for the year ended December 31, 2019. The increase in research and development expense was primarily related to $35.3 million in increased expenses for external clinical activities related to avapritinib, pralsetinib and BLU-782 and $31.3 million in increased personnel expense, primarily due to an increase in headcount, which was driven by growth in the clinical and manufacturing organizations and an increase of $11.6 million in stock-based compensation expense.

General and Administrative Expense

General and administrative expense increased by $48.5 million from $47.9 million for the year ended December 31, 2018 to $96.4 million for the year ended December 31, 2019. The increase in general and administrative expense was primarily related to increased costs and personnel expenses, including an increase of $12.5 million in stock-based compensation expense, associated with building our commercial infrastructure and to support the overall growth of our business globally.

Interest Income (Expense), Net

Interest income (expense), net increased by $3.2 million from $10.6 million for the year ended December 31, 2018 to $13.7 million for the year ended December 31, 2019. The increase was primarily related to higher average investment balances and a higher rate of return on investments.

Other Income (Expense), Net

Other income (expense), net, decreased by $0.1 million from $0.2 million of expense for the year ended December 31, 2018 to $0.1 million of expense for the year ended December 31, 2019. The decrease was primarily related to changes in foreign currency exchange rates.

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 a license agreement. Through December 31, 2020, we have received an aggregate of $2.9 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, $910.8 million in upfront payments and milestone payments under our collaborations with Roche and CStone, our license agreement with Clementia and our former collaboration with Alexion. In addition, since January 2020, we have generated limited product revenue.

As of December 31, 2020, we had cash, cash equivalents and marketable securities of $1,549.7 million.

Cash Flows

The following table provides information regarding our cash flows for the years ended December 31, 2020, 2019 and 2018:

	Year Ended December 31,		
(in thousands)	**2020**	**2019**	**2018**
Net cash provided by (used in) operating activities	$ 387,035	$ (278,015)	$ (175,009)
Net cash used in investing activities	(434,249)	(16,466)	(161,088)
Net cash provided by financing activities	617,759	340,638	4,454
Net increase (decrease) in cash and cash equivalents	$ 570,545	$ 46,157	$ (331,643)

Net Cash Provided by (Used in) Operating Activities. For the year ended December 31, 2020, compared to the same period in 2019, the $665.1 million increase in net cash provided by operating activities was primarily due to the increased net income during this period of $661.6 million, which was driven by the $753.1 million collaboration revenue recognized under our collaboration agreement with Roche for pralsetinib.

For the year ended December 31, 2019, compared to the same period in 2018, the $103.0 million increase in net cash used in operating activities was primarily due to the increase in net loss during this period of $110.0 million, which

was driven by increased payroll and payroll-related expenses and spending on pre-clinical, clinical and pre-commercial activities, partially offset by upfront and milestone payments received during year ended December 31, 2019. The net cash flows provided by operating activities for year ended December 31, 2019 reflect a $25.0 million upfront payment received under the Clementia agreement, an aggregate of $10.0 million in milestone payments received under the CStone agreement and an $8.0 million milestone payment received under the cancer immunotherapy agreement with Roche.

Net Cash Used in Investing Activities. For the year ended December 31, 2020, compared to the same period in 2019, the $417.8 million increase in net cash used in investing activities was primarily due to an increase in net purchases of available-for-sale investments.

For the year ended December 31, 2019, compared to the same period in 2018, the $144.6 million decrease in net cash used in investing activities was primarily due a decrease in net purchases of available-for-sale investments.

Net Cash Provided by Financing Activities. For the year ended December 31, 2020, compared to the same period in 2019, the $277.1 million increase in net cash provided by financing activities was primarily due to the $175.7 million increase in proceeds received from our common stock offerings net of issuance costs, the $79.3 million received from the issuance of common stock related to the collaboration agreement with Roche for pralsetinib, and a $22.0 million increase in net proceeds received from stock option exercises and the issuance of common stock under our employee stock purchase plan.

For the year ended December 31, 2019, compared to the same period in 2018, the $336.2 million increase in net cash provided by financing activities was primarily due to a $327.5 million increase in net proceeds received from our April 2019 follow-on public offering, and a $6.9 million increase in net proceeds received from stock option exercises and the issuance of common stock under our employee stock purchase plan.

Funding Requirements

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

As of December 31, 2020, we had cash, cash equivalents and marketable securities of $1,549.7 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 many factors, including:

- the success of our commercialization efforts and market acceptance for AYVAKIT/AYVAKYT, GAVRETO or any of our current or future drug candidates for which we receive marketing approval;

- the costs of maintaining, expanding or contracting for sales, marketing and distribution capabilities in connection with commercialization of AYVAKIT/AYVAKYT, GAVRETO and any of our current or future drug candidates for which we receive marketing approval;

- the costs of securing manufacturing, packaging and labeling arrangements for development activities and commercial production, including active pharmaceutical ingredient, or API, drug substance and drug product material for use in pre-clinical studies, clinical trials, our compassionate use program and for use as commercial supply, as applicable;

- the scope, progress, results and costs of drug discovery, pre-clinical development, laboratory testing and clinical trials for our approved drugs and drug candidates;

- the costs, timing and outcome of regulatory review of marketing applications for our drug candidates, including seeking marketing approval for avapritinib and pralsetinib for additional indications or in additional geographies;

- the success of our collaborations with Roche and CStone and our license agreement with Clementia, as well as our ability to establish and maintain additional collaborations, partnerships or licenses on favorable terms, if at all;

- the achievement of milestones or occurrence of other developments that trigger payments under our existing collaboration or license agreements, or any collaboration, partnership or license agreements that we may enter into in the future;

- the extent to which we are obligated to reimburse, or entitled to reimbursement of, research and development, clinical or other costs under future collaboration agreements, if any;

- the extent to which we acquire or in-license other approved drugs, drug candidates or technologies and the terms of any such arrangements;

- the success of our current or future collaborations for the development and commercialization of companion diagnostic tests;

- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims; and

- the costs of continuing to expand our operations.

Identifying potential drug candidates, conducting pre-clinical development and testing and clinical trials and, for any drug candidates that receive marketing approval, establishing and maintaining commercial infrastructure is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain additional marketing approvals, including for avapritinib and pralsetinib in additional indications or in additional geographies, and achieve substantial revenues for any of our drugs that receive marketing approval, including for AYVAKIT/AYVAKYT and GAVRETO. In addition, our drugs and any current or future drug candidates that receive marketing approvals, including avapritinib and pralsetinib for additional indications or in additional geographies, may not achieve commercial success. Accordingly, we may need to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all.

Until such time, if ever, as we can generate substantial drug revenues, we expect to finance our cash needs primarily through a combination of public and private equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. We do not have any committed external source of funds, other than our collaborations with Roche and CStone and the license agreement with Clementia, which are limited in scope and duration and subject to the achievement of milestones or royalties on sales of licensed products, if any. To the extent that we raise additional capital through the sale of common stock or securities convertible or exchangeable into common stock, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that materially adversely affect the rights of our common stockholders. Debt financing, if available, would increase our fixed payment obligations and may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we raise funds through additional collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our intellectual property, future revenue streams, research programs, drugs or drug candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our drug development or future commercialization efforts or grant rights to develop and market drug and drug candidates that we would otherwise prefer to develop and market ourselves.

Contractual Obligations

Our contractual obligations primarily consist of our obligations under non-cancellable operating leases and unconditional purchase obligations related to certain commercial manufacturing agreements.

The following table summarizes our significant contractual obligations as of payment due date by period at December 31, 2020:

	Payments Due by Period				
(in thousands)	**Total**	**Less than 1 Year**	**1 to 3 Years**	**3 to 5 Years**	**More than 5 Years**
Minimum purchase obligations .	$ 30,875	$ 7,465	$ 12,330	$ 11,080	$ -
Operating lease obligations.	126,179	14,879	27,700	26,758	56,842
Total	$ 157,054	$ 22,344	$ 40,030	$ 37,838	$ 56,842

In the normal course of business, we enter into agreements with contract research organizations for clinical trials and clinical supply manufacturing and with vendors for pre-clinical research studies, synthetic chemistry and other services and products for operating purposes. We have not included these payments in the table of contractual obligations above since 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.

We also have obligations to make future payments to third parties that become due and payable on the achievement of certain milestones, including future payments to third parties with whom we have entered into agreements to develop and commercialize companion diagnostic tests for certain of our drug candidates. We have not included these commitments on our balance sheet or in the table above because the achievement and timing of these milestones is not fixed and determinable.

Off-Balance Sheet Arrangements

We did not have, during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under applicable SEC rules.

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

As of December 31, 2020 and 2019, we had cash, cash equivalents and marketable securities of $1,549.7 million and $548.0 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, which is affected by changes in the general level of U.S. interest rates, including recent changes resulting from the impact of the COVID-19 pandemic. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, we believe an immediate 10% change in interest rates would not have a material effect on the fair market value of our investment portfolio. We have the ability to hold our investments until maturity, and therefore, we would not expect our operating results or cash flows to be affected to any significant degree by the effect of a change in market interest rates on our investment portfolio.

We are also exposed to market risk related to changes in foreign currency exchange rates, including recent changes resulting from the impact of the COVID-19 pandemic. From time to time, we contract with vendors that are located in Asia and Europe, which are denominated in foreign currencies. We are subject to fluctuations in foreign currency rates in connection with these agreements. We do not currently hedge our foreign currency exchange rate risk. As of December 31, 2020 and 2019, we held limited funds and future obligations denominated in foreign currencies.

Inflation generally affects us by increasing our cost of labor, clinical trial and manufacturing costs. We do not believe that inflation had a material effect on our business, financial condition or results of operations during the years ended December 31, 2020 and 2019.

Item 8. Financial Statements and Supplementary Data.

The financial statements 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, 2020. Based upon such evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that, as of December 31, 2020, 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, 2020 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, 2020.

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 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, 2020, 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, 2020, 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 Blueprint Medicines Corporation as of December 31, 2020 and 2019, the related consolidated statements of operations and comprehensive income (loss), stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2020, and the related notes and our report dated February 17, 2021 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 17, 2021

Changes in Internal Control over Financial Reporting

No change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the three months ended December 31, 2020 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

None.

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 2021 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 2021 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 2021 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 2021 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 2021 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-39 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			Filing Date
		Form	File No.	Exhibit Number	
1.1	Sales Agreement, dated as of July 30, 2020, by and between Blueprint Medicines Corporation and Cowen and Company, LLC	10-Q	001-37359	1.1	July 31, 2020
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 April 30, 2020, of the Registrant	10-Q	001-37359	3.1	May 6, 2020
4.1	Specimen Common Stock Certificate	S-1/A	333-202938	4.1	April 20, 2015
4.2	Second Amended and Restated Investors' Rights Agreement, dated as of November 7, 2014, by and among the Registrant and the Investors listed therein	S-1	333-202938	4.4	March 23, 2015
4.3	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	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
10.8	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
10.9#	Employment Agreement, dated November 6, 2015, by and between the Registrant and Jeffrey W. Albers	10-Q	001-37359	10.2	November 9, 2015
10.10#	Employment Agreement, dated November 6, 2015, by and between the Registrant and Anthony L. Boral	10-Q	001-37359	10.4	November 9, 2015
10.11#	First Amendment to Employment Agreement, dated January 11, 2021, by and between Blueprint Medicines Corporation and Anthony L. Boral, M.D., Ph.D.	8-K	001-37359	10.1	January 11, 2021
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#	Employment Agreement, dated September 6, 2016, by and between the Registrant and Tracey L. McCain	10-Q	001-37359	10.3	November 10, 2016
10.15#	Employment Agreement, dated November 9, 2016, by and between the Registrant and Marion Dorsch	8-K	001-37359	10.1	November 14, 2016
10.16#	Employment Agreement, dated October 10, 2017, by and between the Registrant and Christopher Murray	10-Q	001-37359	10.1	October 31, 2017
10.17#	Employment Agreement, dated November 22, 2017, by and between the Registrant and Michael Landsittel	8-K	001-37359	10.1	November 22, 2017
10.18#	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
10.19#	Employment Agreement, dated October 29, 2018, by and between the Registrant and Christina Rossi	8-K	001-37359	10.1	October 29, 2018
10.20#	Employment Agreement, dated March 6, 2019, by and between the Registrant and Ariel Hurley	8-K	001-37359	10.1	March 8, 2019
10.21#	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

10.22#	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
10.23#	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
10.24†	Collaboration and License Agreement, effective March 14, 2016, by and among F. Hoffmann-La Roche Ltd, Hoffmann-La Roche Inc. and the Registrant, as amended by Amendment to Collaboration and License Agreement, effective April 15, 2016	10-Q/A	001-37359	10.2	July 22, 2016
10.25†	Second Amendment to Collaboration and License Agreement, effective April 27, 2016, by and among F. Hoffmann-La Roche Ltd, Hoffmann-La Roche Inc. and the Registrant	10-Q	001-37359	10.1	August 9, 2016
10.26	Third Amendment to Collaboration and License Agreement, effective August 4, 2016, by and among F. Hoffmann-La Roche Ltd, Hoffmann-La Roche Inc. and the Registrant	10-Q	001-37359	10.1	November 10, 2016
10.27†	Fourth Amendment to Collaboration and License Agreement, effective February 25, 2019, by and among F. Hoffmann-La Roche Ltd, Hoffmann-La Roche Inc. and the Registrant	10-K	001-37359	10.26	February 26, 2019
10.28††	Fifth Amendment to Collaboration and License Agreement, effective June 28, 2019, by and among F. Hoffmann-La Roche Ltd, Hoffmann-La Roche Inc. and the Registrant	8-K	001-37359	10.1	July 3, 2019
10.29††	Sixth Amendment to Collaboration and License Agreement, effective November 1, 2019, by and among F. Hoffmann-La Roche Ltd, Hoffmann-La Roche Inc. and the Registrant	10-Q	001-37359	10.2	November 5, 2019
10.30††	Seventh Amendment to Collaboration and License Agreement, effective December 17, 2019, by and among F. Hoffmann-La Roche Ltd, Hoffmann-La Roche Inc. and the Registrant	8-K	001-37359	10.1	December 20, 2019
10.31††	Eighth Amendment to Collaboration and License Agreement, effective April 30, 2020, by and among F. Hoffmann-La Roche Ltd, Hoffmann-La Roche Inc. and the Registrant	10-Q	001-37359	10.1	May 6, 2020
10.32††	Ninth Amendment to Collaboration and License Agreement, effective January 8, 2021, by and among F. Hoffmann-La Roche Ltd, Hoffmann-La Roche Inc. and the Registrant				*
10.33††	Collaboration Agreement, dated as of July 13, 2020, by and among F. Hoffmann-La Roche Ltd, Genentech, Inc. and the Registrant	10-Q	001-37359	10.1	July 30, 2020
10.34†	License and Collaboration Agreement, dated June 1, 2018, between the Registrant and CStone Pharmaceuticals	10-Q	001-37359	10.1	August 1, 2018

10.35††	License Agreement, effective October 15, 2019, by and between the Registrant and Clementia Pharmaceuticals, Inc.	10-Q	001-37359	10.1	November 5, 2019
10.36	Form of Indemnification Agreement entered into between the Registrant and its directors	S-1	333-202938	10.11	March 23, 2015
10.37	Form of Indemnification Agreement entered into between the Registrant and its officers	S-1	333-202938	10.12	March 23, 2015
10.38	Senior Executive Cash Incentive Bonus Plan	10-K	001-37359	10.15	March 11, 2016
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				+
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.

† 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 17, 2021

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

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/ Jeffrey W. Albers Jeffrey W. Albers	President, Chief Executive Officer and Director *(Principal Executive Officer)*	February 17, 2021
/s/ Michael Landsittel Michael Landsittel	Chief Financial Officer *(Principal Financial Officer)*	February 17, 2021
/s/ Ariel Hurley Ariel Hurley	Vice President, Finance and Controller *(Principal Accounting Officer)*	February 17, 2021
/s/ Daniel S. Lynch Daniel S. Lynch	Chairman of the Board	February 17, 2021
/s/ Nicholas Lydon Nicholas Lydon, Ph.D.	Director	February 17, 2021
/s/ Alexis Borisy Alexis Borisy	Director	February 17, 2021
/s/ Mark Goldberg Mark Goldberg, M.D.	Director	February 17, 2021
/s/ Charles A. Rowland, Jr. Charles A. Rowland, Jr.	Director	February 17, 2021
/s/ George Demetri George Demetri, M.D.	Director	February 17, 2021
/s/ Lonnel Coats Lonnel Coats	Director	February 17, 2021
/s/ Lynn Seely Lynn Seely, M.D.	Director	February 17, 2021

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 as of December 31, 2020 and 2019, the related consolidated statements of operations and comprehensive income (loss), stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2020, 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, 2020 and 2019, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2020, 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, 2020, 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 17, 2021 expressed an unqualified opinion thereon.

Adoption of ASC 842

As discussed in Note 2 to the consolidated financial statements, the Company changed its method of accounting for leases effective January 1, 2019 due to the adoption of Accounting Standards Update (ASU) 2016-02, Leases (Topic 842), and the related amendments.

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 matters communicated below are matters arising from the current period audit of the financial statements that were communicated or required to be communicated to the audit committee and that: (1) relate to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of critical audit matters 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 matters below, providing separate opinions on the critical audit matters or on the accounts or disclosures to which they relate.

Roche – Pralsetinib Collaboration

Description of the Matter

As discussed in Note 10 to the consolidated financial statements, the Company recognized $753 million in revenue under the collaboration and stock purchase agreement with F. Hoffmann-La Roche Ltd and Genentech, Inc., a member of the Roche Group (collectively, "Roche"). The Company determined that there were four material components of the Roche agreement: (i) licenses granted to Roche to develop and commercialize pralsetinib worldwide, excluding the CStone territory (pralsetinib license); (ii) the Roche territory-specific commercialization activities for pralsetinib, including manufacturing Roche territory activities; (iii) the parties' joint development activities for pralsetinib worldwide, excluding the CStone territory; and (iv) the parties' joint commercialization activities for pralsetinib in the U.S. The Company accounts for the pralsetinib license and Roche territory-specific components pursuant to ASC 606, Revenue from Contracts with Customers, and the joint development and commercialization activities components under ASC 808, Collaborative Arrangements.

Auditing management's identification of performance obligations for the pralsetinib license and Roche territory-specific components pursuant to ASC 606 was challenging as the contract includes implicit and explicit goods and services. Significant judgment was required in the evaluation of whether the identified promised goods and services meet the criteria of being distinct and capable of being distinct within the context of the contract or represent a material right.

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 identifying performance obligations and material rights in its contracts with customers.

To test the identification of performance obligations and material rights, we assessed, among other things, the stated terms of the Company's arrangement with Roche. We also conducted meetings with personnel at the Company responsible for negotiating the contract and overseeing the delivery of the performance obligation in order to understand the nature of the explicit and implicit promised goods and services as well as understand whether promises were capable of being distinct and distinct in the context of the contract. We reviewed the Company's analyses to support their assessment that there is no separate material right in connection with the development and commercial supply of pralsetinib. Finally, we assessed the Company's analyses to support their conclusion of the amount of revenue to recognize in 2020 under ASC 606 Revenue.

Accrued Clinical Trial Expenses

Description of the Matter

As discussed in Note 2 to the consolidated financial statements, the Company records costs for clinical trial activities based upon estimates of costs incurred through the balance sheet date that have yet to be invoiced by the contract research organizations and other vendors.

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 17, 2021

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

	December 31, 2020	December 31, 2019
Assets		
Current assets:		
Cash and cash equivalents	$ 684,636	$ 113,938
Marketable securities	187,213	369,616
Accounts receivable	7,096	663
Unbilled accounts receivable	18,213	22,749
Inventory	8,581	—
Prepaid expenses and other current assets	22,020	9,820
Total current assets	927,759	516,786
Marketable securities	677,873	64,406
Property and equipment, net	34,129	38,361
Operating lease right-of-use assets, net	67,539	72,753
Restricted cash	5,168	5,166
Other assets	5,925	10,222
Total assets	$ 1,718,393	$ 707,694
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	4,370	4,793
Accrued expenses	105,938	88,706
Current portion of operating lease liabilities	7,935	6,823
Current portion of deferred revenue	12,559	6,160
Total current liabilities	130,802	106,482
Operating lease liabilities, net of current portion	81,669	89,126
Deferred revenue, net of current portion	28,599	39,913
Other long-term liabilities	7,235	7,814
Total liabilities	248,305	243,335
Commitments (Note 18)		
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; 57,793,533 and 49,272,223 shares issued and outstanding at December 31, 2020 and December 31, 2019, respectively	58	49
Additional paid-in capital	2,106,600	1,412,083
Accumulated other comprehensive loss	(5,214)	(2,535)
Accumulated deficit	(631,356)	(945,238)
Total stockholders' equity	1,470,088	464,359
Total liabilities and stockholders' equity	$ 1,718,393	$ 707,694

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

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

	Year Ended December 31,		
	2020	2019	2018
Revenues:			
Product revenue, net	$ 22,134	$ —	$ —
Collaboration revenue	771,601	66,512	44,521
Total revenues	793,735	66,512	44,521
Cost and operating expenses:			
Cost of sales	425	—	—
Research and development	326,860	331,450	243,621
Selling, general and administrative	157,743	96,388	47,928
Total cost and operating expenses	485,028	427,838	291,549
Other income (expense):			
Interest income, net	6,599	13,732	10,566
Other expense, net	(366)	(100)	(180)
Total other income	6,233	13,632	10,386
Income (loss) before income taxes	314,940	(347,694)	(236,642)
Income tax expense	1,058	—	—
Net income (loss)	$ 313,882	$ (347,694)	$ (236,642)
Other comprehensive income (loss):			
Unrealized losses on pension benefit obligations	(2,843)	(2,985)	—
Unrealized gains on available-for-sale investments	441	671	105
Currency translation adjustments	(278)	(40)	(16)
Comprehensive income (loss)	$ 311,202	$ (350,048)	$ (236,553)
Net income (loss) per share — basic	$ 5.76	$ (7.27)	$ (5.39)
Net income (loss) per share — diluted	$ 5.59	$ (7.27)	$ (5.39)
Weighted-average number of common shares used in net income (loss) per share — basic	54,534	47,829	43,867
Weighted-average number of common shares used in net income (loss) per share — diluted	56,168	47,829	43,867

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	Accumulated Other Comprehensive	Accumulated	Stockholders'
	Shares	Amount	Capital	Loss	Deficit	Equity
Balance at December 31, 2017	43,577,526	$ 43	$ 979,784	$ (269)	$ (355,588)	$ 623,970
Issuance of common stock under stock plan	445,622	1	5,586	—	—	5,587
Purchase of common stock under ESPP	13,878	—	750	—	—	750
Stock-based compensation expense	—	—	30,534	—	—	30,534
Adoption of new accounting standard	—	—	—	—	(5,314)	(5,314)
Other comprehensive gain	—	—	—	89	—	89
Other	—	—	35	—		35
Net income (loss)	—	—	—	—	(236,642)	(236,642)
Balance at December 31, 2018	44,037,026	$ 44	$ 1,016,689	$ (180)	$ (597,544)	$ 419,009
Issuance of common stock under stock plan	552,311	1	12,130	—	—	12,131
Purchase of common stock under ESPP	20,724	—	1,148	—	—	1,148
Stock-based compensation expense	—	—	54,653	—	—	54,653
Follow on offering, net of issuance costs	4,662,162	4	327,462	—	—	327,466
Other comprehensive loss	—	—	—	(2,354)	—	(2,354)
Net income (loss)	—	—	—	—	(347,694)	(347,694)
Balance at December 31, 2019	49,272,223	$ 49	$ 1,412,082	$ (2,534)	$ (945,238)	$ 464,359
Issuance of common stock under stock plan	952,205	1	33,282	—	—	33,283
Purchase of common stock under ESPP	38,516	1	2,153	—	—	2,154
Stock-based compensation expense	—	—	76,602	—	—	76,602
Follow on offering and at-the-market offerings, net of issuance costs	6,495,070	6	503,176	—	—	503,182
Issuance of common stock related to collaboration agreement	1,035,519	1	79,305	—	—	79,306
Other comprehensive loss	—	—	—	(2,680)	—	(2,680)
Net income (loss)	—	—	—	—	313,882	313,882
Balance at December 31, 2020	57,793,533	$ 58	$ 2,106,600	$ (5,214)	$ (631,356)	$ 1,470,088

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,		
	2020	2019	2018
Cash flows from operating activities			
Net income (loss)	$ 313,882	$ (347,694)	$ (236,642)
Adjustments to reconcile net income (loss) to net cash provided by (used in) operating activities:			
Depreciation and amortization	6,559	5,259	4,246
Noncash lease expense	5,791	4,991	—
Stock-based compensation	75,526	54,653	30,534
Accretion of premiums and discounts on investments	466	(4,949)	(4,381)
Other	429	—	(6)
Changes in assets and liabilities:			
Accounts receivable	(6,387)	(599)	349
Unbilled accounts receivable	4,536	(22,597)	(151)
Inventory	(6,707)	—	—
Prepaid expenses and other current assets	(12,620)	(3,338)	6,086
Other assets	1,440	20	(4,242)
Accounts payable	(791)	1,448	(445)
Accrued expenses	16,214	36,980	24,804
Deferred revenue	(4,915)	(94)	5,479
Deferred rent	—	—	(640)
Operating lease liabilities	(6,388)	(2,095)	—
Net cash provided by (used in) operating activities	387,035	(278,015)	(175,009)
Cash flows from investing activities			
Purchases of property and equipment	(3,159)	(14,013)	(12,677)
Purchases of investments	(969,437)	(738,387)	(801,236)
Maturities of investments	538,347	735,934	652,825
Net cash used in investing activities	(434,249)	(16,466)	(161,088)
Cash flows from financing activities			
Principal payments on loan payable	—	—	(1,528)
Proceeds from common stock offerings, net of issurance costs	503,189	327,466	—
Net proceeds from stock option exercises and employee stock purchase plan	35,265	13,288	6,425
Proceeds from issuance of common stock related to collaboration agreement	79,305	—	—
Other financing activities	—	(116)	(443)
Net cash provided by financing activities	617,759	340,638	4,454
Net increase (decrease) in cash, cash equivalents, and restricted cash	570,545	46,157	(331,643)
Cash, cash equivalents and restricted cash at beginning of period	119,604	73,429	405,072
Effect of exchange rate changes on cash, cash equivalents and restricted cash	(345)	18	—
Cash, cash equivalents and restricted cash at end of period	$ 689,804	$ 119,604	$ 73,429
Supplemental cash flow information			
Property and equipment purchases unpaid at period end	$ 141	$ 958	$ 912
Cash paid for interest	$ —	$ 5	$ 267
Cash paid for taxes, net	$ 778	$ 185	$ 123

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

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

	December 31,		
	2020	2019	2018
Cash and cash equivalents	$ 684,636	$ 113,938	$ 68,064
Restricted cash included in prepaid expenses and other current assets	—	500	211
Restricted cash	5,168	5,166	5,154
Total cash, cash equivalents, and restricted cash shown in consolidated statements of cash flows	$ 689,804	$ 119,604	$ 73,429

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 precision therapy company focused on genomically defined cancers and hematologic disorders. The Company's approach is to leverage its novel target discovery engine to systematically and reproducibly identify kinases that are drivers of diseases and to craft highly selective and potent drug candidates that may provide significant and durable clinical responses for patients without adequate treatment options.

The Company has two approved precision therapies and is globally advancing multiple programs for genomically defined cancers, systemic mastocytosis, and cancer immunotherapy. The Company is devoting substantially all of its efforts to research and development for current and future drug candidates and commercialization of AYVAKIT/AYVAKYT, GAVRETO and any current or future drug candidates that obtain marketing approval.

The Company is subject to a number of risks similar to those of other companies transitioning to a commercial stage, 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 out-license certain of its research and development programs or future commercialization efforts.

On January 27, 2020, the Company closed a follow-on public offering of 4,710,144 shares of its common stock at a price to the public of $69.00 per share and received net proceeds of $308.4 million, after deducting underwriting discounts and commissions and offering expenses paid by the Company.

On July 30, 2020, the Company entered into a sales agreement 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 $250.0 million through Cowen as sales agent (the ATM Facility). Cowen may sell the shares under such sales agreement by any method that is deemed to be an "at the market offering" as defined in Rule 415 of the Securities Act of 1933, as amended, including sales made directly on the Nasdaq Global Select Market or any other trading market for our common stock. During the year ended December 31, 2020, the Company issued and sold 1,784,926 shares of its common stock under the ATM Facility and received gross proceeds and net proceeds of $200.0 million and $194.7 million, respectively.

As of December 31, 2020, the Company had cash, cash equivalents and marketable securities of $1,549.7 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 Update (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.

Due to the shares issued and sold in the follow-on public offerings completed in April 2019 and in January 2020 and the shares issued and sold under the ATM Facility in the year ended December 31, 2020, there were significant increases in shares outstanding in the years ended December 31, 2020 and 2019, which impacts the year-over-year comparability of the Company's net income (loss) per share calculations.

Use of Estimates

The preparation of financial statements in conformity with GAAP requires the Company's management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Actual results could differ from those estimates. Management considers many factors in selecting appropriate financial accounting policies and in developing the estimates and assumptions that are used in the preparation of the financial statements. Management must apply significant judgment in this process. Management's estimation process often may yield a range of potentially reasonable estimates and management must select an amount that falls within that range of reasonable estimates. Estimates are used in the following areas, among others: revenue recognition, inventory, operating lease right-of-use assets, operating lease liabilities, stock-based compensation expense, accrued expenses, and income taxes. The length of time and full extent to which the COVID-19 pandemic will directly or indirectly impact the Company's business, results of operations and financial condition, including revenues, expenses, reserves and allowances, manufacturing, clinical trials, research and development costs and employee-related amounts, will depend on future developments that are highly uncertain, subject to change and difficult to predict, including as a result of new information that may emerge concerning COVID-19 and the actions taken to contain or treat COVID-19, as well as the economic impact thereof on local, regional, national and international customers and markets. The Company considers the impact of COVID-19 while establishing the estimates within its consolidated financial statements and there may be changes to those estimates in future periods. Actual results may differ from these estimates.

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.

Product revenue

The Company generated product revenue from sales of AYVAKIT and GAVRETO 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 the Company's current contractual and statutory requirements, specific known market events and trends, industry data and forecasted customer buying and payment patterns. The amount of variable consideration that is included in the transaction price may be constrained and is included in net product revenues only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period. Actual amounts of consideration ultimately received may differ from the Company's estimates. If actual results vary from the Company's estimates, the Company adjusts these estimates, which would affect net product revenue and earnings in the period such variances become known.

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

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

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

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

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

Collaboration revenue

At contract inception, the Company analyzes its collaboration 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 income (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, except for 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 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. To date, the Company has not recognized any royalty revenue resulting from any of its licensing arrangements.

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. If the Company transfer goods or services to a customer before the customer pays consideration or before payment is due, the Company records a contract asset as unbilled accounts receivable on the consolidated balance sheets.

For a complete discussion of accounting for collaboration revenues, see Note 10, *Collaboration and License Agreements*.

Accounts Receivable, net

Accounts receivable arise from product sales and amounts due from the Company's collaboration partners. The amount from product sales represents amounts due from specialty distributors and specialty pharmacy providers in the U.S. and in the European Union. The Company monitors economic conditions and the financial performance and credit worthiness of its counterparties to identify facts or circumstances that may indicate that its receivables are at risk of collection. The Company provides reserves against accounts receivable for estimated losses that may result from a customer's inability to pay based on the composition of its accounts receivable, 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 year ended December 31, 2020, the Company did not record any expected credit losses related to outstanding accounts receivable.

Inventory

Inventories are stated at the lower of cost or estimated net realizable value with cost based on the first-in first-out method. Inventory that can be used in either the production of clinical or commercial products is expensed as research and development costs when identified for use in clinical trials. 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, 2020 and 2019.

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, 2020, cash equivalents were comprised of money market funds with less than 90 days from the date of purchase. As of December 31, 2019, cash equivalents were comprised of money market funds and U.S. treasury obligations with maturities less than 90 days from the date of purchase. Cash equivalents are reported at fair value.

Available-for-Sale Investments

The Company classifies marketable debt securities with a remaining maturity when purchased of greater than three months available-for-sale, and marketable debt securities with a remaining maturity date greater than one year 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). The Company 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 or other factors. If the decline in fair value is due to credit-related factors, a loss is recognized in net income, whereas if the decline in fair value is not due to credit-related factors, the loss is recorded in other comprehensive income (loss).

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 cancer 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, 2020 and 2019, advertising costs totaled $9.4 million and $3.3 million, respectively. The advertising cost for the year ended December 31, 2018 was minimal.

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 estimated remaining useful life of its long-lived assets may warrant revision or that the carrying value of these assets may be impaired. The Company has not recognized any impairment charges through December 31, 2020.

Leases

Beginning January 1, 2019, 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 our consolidated balance sheets and to recognize those lease payments on a straight-line basis in our 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 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 is calculated based on a blend of the Company's reported volatility data for the length of time that market data is available for the Company's stock and the historical data for a representative group of publicly traded companies, for which historical information is available. For these analyses, the Company selects companies with comparable characteristics to itself including enterprise value, risk profiles, position within the industry, and with historical share price information sufficient to meet the expected life of the stock-based awards. The Company computes the historical volatility data using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of its stock-based awards. The Company intends to consistently apply this process using representative companies until a sufficient amount of historical information regarding the volatility of its own share price becomes available;

- 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.

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.

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.

Reclassifications

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

Concentrations of Credit Risk and Off-Balance-Sheet Risk

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, investments, 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, 2020 and 2019, 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 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.

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, or decision-making group, in making decisions on how to allocate resources and assess performance. The Company's chief operating decision maker is the chief executive officer. The Company and the chief operating decision maker view 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.

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.

Credit Losses

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments - Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments* (ASU 2016-13). The FASB subsequently issued amendments to ASU 2016-13, which had the same effective date and transition date of January 1, 2020. These standards require an entity to measure and recognize expected credit losses for certain financial instruments, including trade receivables, as an allowance that reflects the entity's current estimate of credit losses expected to be incurred. For available-for-sale debt securities with unrealized credit losses, the standard requires allowances to be recorded through net income instead of directly reducing the amortized cost of the investment under the previous other-than-temporary impairment model. The Company adopted the new standard on a prospective basis on January 1, 2020. The adoption of this standard did not have a material impact on the Company's consolidated financial position and results of operations or a significant impact on its internal controls.

Fair Value Measurements

In August 2018, the FASB issued ASU No. 2018-13*, Fair Value Measurement (Topic 820): Disclosure Framework Changes to the Disclosure Requirements for Fair Value Measurement*. This standard modifies certain disclosure requirements on fair value measurements. The Company adopted the new standard on January 1, 2020 and the adoption did not have a material impact on the related disclosures.

Collaborative Arrangements

In November 2018, the *FASB* issued ASU No. 2018-18*, Collaborative Arrangements (Topic 808): Clarifying the Interaction between Topic 808 and Topic 606.* This update clarifies that transactions between collaborative arrangement participants should be accounted for as revenue under ASC 606 when the collaborative arrangement participant is a customer in the context of a unit of account, consistent with the unit of account guidance in ASC 606. The update also requires that in a transaction with a collaborative arrangement participant that is not directly related to sales to third parties, presenting that transaction together with revenue recognized under ASC 606 is precluded if the collaborative arrangement participant is not a customer. The Company adopted the new standard on January 1, 2020. The adoption of this standard did not have a material impact on the Company's consolidated financial position and results of operations or a significant impact on its internal controls.

Internal-Use Software

In August 2018, the FASB issued ASU No. 2018-15*, Intangibles-Goodwill and Other-Internal-Use Software (Subtopic 350-40): Customer's Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement That Is a Service Contract*, which clarifies the accounting for implementation costs in cloud computing arrangements. The standard is effective for interim and annual periods beginning after December 15, 2019, with early adoption permitted, and can be adopted prospectively or retrospectively. The Company adopted the new standard on January 1, 2020 on a prospective basis. The adoption of this standard did not have a material impact on the Company's consolidated financial position and results of operations or a significant impact on its internal controls. However, the adoption of this standard

resulted in an increase in capitalized assets related to qualifying cloud computing arrangement implementation costs incurred after the adoption date.

Income Taxes

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

Defined Benefit Plans

In August 2018, the FASB issued No. ASU 2018-14, *Compensation – Retirement Benefits – Defined Benefit Plans – General (Subtopic 715-20): Disclosure Framework – Changes to the Disclosure Requirements for Defined Benefit Plans*, which amends ASC 715 to add, remove, and clarify disclosure requirements related defined benefit pension and other postretirement plans. The amendments in ASU 2018-14 are effective for the fiscal years ending after December 15, 2020. The Company adopted this amendment as of January 1, 2020 and the adoption did not have a material impact on the related disclosures.

3. Marketable Securities

Marketable securities consisted of the following at December 31, 2020 and 2019 (in thousands):

December 31, 2020	**Amortized Cost**	**Unrealized Gain**	**Unrealized Losses**	**Fair Value**
Marketable securities, available-for-sale:				
U.S. government agency securities	$ 746,770	$ 513	$ (14)	$ 747,269
U.S. treasury obligations	117,368	449	—	117,817
Total	$ 864,138	$ 962	$ (14)	$ 865,086

December 31, 2019	**Amortized Cost**	**Unrealized Gain**	**Unrealized Losses**	**Fair Value**
Marketable securities, available-for-sale:				
U.S. government agency securities	$ 128,156	$ 160	$ (4)	$ 128,312
U.S. treasury obligations	305,360	358	(8)	305,710
Total	$ 433,516	$ 518	$ (12)	$ 434,022

As of December 31, 2020 and 2019, the Company held 8 and 11 securities, respectively, that were in an unrealized loss position. The aggregate fair value of securities held by the Company in an unrealized loss position for less than twelve months as of December 31, 2020 and 2019 were $125.7 million and $82.1 million, respectively, and there were no securities held by the Company in an unrealized loss position for more than twelve months. The Company has the intent and ability to hold such securities until recovery. As a result, the Company did not record any charges for credit-related impairments for its marketable debt securities for the years ended December 31, 2020 and 2019.

As of December 31, 2020, 65 securities with an aggregate fair value of $677.9 million had remaining maturities between one year and five years. As of December 31, 2019, 9 securities with an aggregate fair value of $64.4 million had remaining maturities greater than one year.

4. Fair Value of Financial Instruments

The following table summarizes the Company's cash equivalents and marketable securities measured at fair value on a recurring basis as of December 31, 2020 (in thousands):

Description	December 31, 2020	Active Markets (Level 1)	Observable Inputs (Level 2)	Unobservable Inputs (Level 3)
Cash equivalents:				
Money market funds	$ 420,567	$ 420,567	$ —	$ —
Marketable securities, available-for-sale:				
U.S. government agency securities	747,269	—	747,269	—
U.S. treasury obligations	117,817	117,817	—	—
Total	$ 1,285,653	$ 538,384	$ 747,269	$ —

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

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

5. Product Revenue Reserves and Allowances

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

For the year ended December 31, 2020, the Company generated aggregate net product revenue of $22.1 million from sales of AYVAKIT/AYVAKYT and GAVRETO. The following table summarizes activity in each of the product revenue allowance and reserve categories for the year ended December 31, 2020 (in thousands):

	Total
Beginning balance at January 1, 2020	$ —
Provision related to sales in the current period	2,515
Adjustment related to prior periods sales	—
Credits and payments made	(1,323)
Ending balance at December 31, 2020	$ 1,192

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

	As of December 31,	
	2020	2019
Reduction of accounts receivable, net	$ 227	$ —
Component of accrued expenses	966	—
Total revenue-related reserves	$ 1,192	$ —

6. Inventory

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

	As of December 31,	
	2020	2019
Work in process	$ 9,488	$ —
Finished goods	914	—
Total	$ 10,402	$ —

Balance sheet classification

	As of December 31,	
	2020	2019
Inventory	$ 8,581	$ —
Other assets	1,821	—
Total	$ 10,402	$ —

Inventory amounts written down as a result of excess, obsolescence, unmarketability or other reasons are charged to cost of sales and was zero for the year ended December 31, 2020. Long-term inventory, which primarily consists of work in process, is included in other assets in the consolidated balance sheets.

7. Restricted Cash

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

8. Property and Equipment, Net

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

	Estimated Useful Life (Years)	As of December 31,	
		2020	2019
Lab equipment	5	$ 11,418	$ 8,975
Furniture and fixtures	4	3,420	3,512
Computer equipment	3	1,513	1,558
Leasehold improvements	Term of lease	36,946	36,627
Software	3	412	417
Construction-in-progress		151	956
Total cost		53,860	52,045
Less: accumulated depreciation and amortization		(19,731)	(13,684)
Total		$ 34,129	$ 38,361

Property, plant and equipment are recorded at historical cost, net of accumulated depreciation. Depreciation expense for the years ended December 31, 2020, 2019 and 2018 was $6.6 million, $5.3 million and $4.2 million, respectively.

9. Accrued Expenses

Accrued expenses consist of the following (in thousands):

	As of December 31,	
	2020	2019
External research and development	$ 60,255	$ 59,420
Employee compensation	27,622	13,519
Accrued professional fees	10,986	12,042
Revenue-related reserves	966	—
Other	6,109	3,725
Total	$ 105,938	$ 88,706

10. Collaboration and License Agreements

Roche – Pralsetinib Collaboration

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

Under the Roche pralsetinib collaboration agreement, the Company received an upfront cash payment of $675.0 million in the third quarter of 2020, and through December 31, 2020, the Company has received $55.0 million in specified regulatory and commercialization milestones. In addition to upfront and milestone payments received through December 31, 2020, the Company is eligible to receive up to $872.0 million in contingent payments, including specified development, regulatory and sales-based milestones for pralsetinib and any licensed product containing a next-generation RET compound.

In the U.S., the Company and Roche are working together to co-commercialize pralsetinib and will equally share responsibilities, profits and losses. In addition, the Company is eligible to receive tiered royalties ranging from high-teens to mid-twenties on annual net sales of pralsetinib outside the U.S., excluding Greater China (the Roche territory). The Company and Roche have also agreed to co-develop pralsetinib globally in RET-altered solid tumors, including non-small cell lung cancer, medullary thyroid carcinoma and other thyroid cancers, as well as other solid tumors. The Company and Roche will share global development costs for pralsetinib at a rate of 45 percent for the Company and 55 percent for Roche up to a specified amount of aggregate joint development costs, after which the Company's share of global development costs for pralsetinib will be reduced by a specified percentage. The Company and Roche will also share specified global development costs for any next-generation RET compound co-developed under the collaboration in a similar manner.

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

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

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

The Company determined that the Roche pralsetinib collaboration agreement contained four material components: (i) licenses granted to Roche to develop and commercialize pralsetinib worldwide, excluding the CStone territory (pralsetinib license); (ii) the Roche territory-specific commercialization activities for pralsetinib, including manufacturing (Roche territory activities); (iii) the parties' joint development activities for pralsetinib worldwide, excluding the CStone territory; and (iv) the parties' joint commercialization activities for pralsetinib in the U.S. The Company considered the guidance in ASC 606 to determine which of the components of the Roche pralsetinib collaboration agreement are performance obligations with a customer and concluded that the pralsetinib license and the Roche territory activities are within the scope of ASC 606 because Roche is the Company's customer in those transactions.

The Company evaluated the Roche pralsetinib license under ASC 606 and concluded that the pralsetinib license is a functional intellectual property license and is a distinct performance obligation. The Company determined that Roche benefited from the pralsetinib license at the time of grant, and therefore the related performance obligation is satisfied at a point in time.

The Company evaluated the Roche territory activities under ASC 606 and identified one material promise associated with manufacturing activities related to development and commercial supply of pralsetinib in the Roche territory for up to 24 months. Given that Roche is not obligated to purchase any minimum amount or quantities of the development and commercial supply from the Company, the Company concluded that, for the purpose of ASC 606, the provision of manufacturing activities related to development and commercial supply of pralsetinib in Roche territory was an option but not a performance obligation of the Company at the inception of the Roche collaboration agreement and will be accounted for if and when exercised. The Company also concluded that there is no separate material right in connection with the development and commercial supply of pralsetinib, as the expected pricing was not issued at a significant and incremental discount. Therefore, the manufacturing activities were excluded as performance obligations at the outset of the arrangement. Additionally, the Company is entitled to sales milestones and royalties from Roche upon future sales of pralsetinib in the Roche territory, and revenue will be recognized when the related sales occur. Costs that are incurred associated with the Roche territory activities are reimbursable from Roche and will be recognized as revenue.

For the purposes of ASC 606, the transaction price of the Roche collaboration agreement as of 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. During the year ended December 31, 2020, the Company achieved $55.0 million in specified regulatory and commercialization milestones and added the $55.0 million to the estimated transaction price of the Roche pralsetinib agreement. The other potential milestone payments that the Company is eligible to receive under the Roche pralsetinib agreement have been excluded from the transaction price, as all the remaining milestone amounts were fully constrained based on the probability of achievement. The Company will re-evaluate the transaction price at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur, and if necessary, the Company will adjust its estimate of the transaction price, and any addition to the transaction price would be recognized as revenue when it becomes probable that inclusion would not lead to a significant revenue reversal.

The following table summarizes revenue recognized under the Roche pralsetinib collaboration during the years ended December 31, 2020 and 2019 (in thousands):

	Year Ended December 31,	
	2020	2019
Upfront license revenue	$ 695,694	$ —
License milestone revenue	55,000	—
Services related to Roche territory-specific activities.	2,406	—
Total Roche pralsetinib collaboration revenue	$ 753,100	$ —

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

During the year ended December 31, 2020, the Company recorded a $10.6 million reduction in selling, general and administrative expenses in connection with the commercialization of GAVRETO in the U.S. and a $20.5 million reduction in research and development expenses in connection with global development activities for pralsetinib.

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

	As of December 31,	
	2020	2019
Unbilled accounts receivable	$ 17,600	$ —

Clementia

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

Under the Clementia agreement, the Company received an upfront cash payment of $25.0 million and through December 31, 2020, the Company has received $20.0 million cash milestone payments. Subject to the terms of the Clementia agreement, in addition to the upfront and milestone payments received through December 31, 2020, the Company is eligible to receive up to $490.0 million in potential development, regulatory and sales-based milestone payments for licensed products. In addition, Clementia is obligated to pay to the Company royalties on aggregate annual worldwide net sales of licensed products at tiered percentage rates ranging from the low- to mid-teens, subject to adjustment in specified circumstances under the Clementia agreement, and Clementia purchased specified manufacturing inventory from the Company for a total of $1.5 million.

Unless earlier terminated in accordance with the terms of the Clementia agreement, the agreement will expire on a country-by-country, licensed product-by-licensed product basis on the date when no royalty payments are or will become due. Clementia may terminate the agreement at any time on or after the second anniversary of the effective date

of the agreement upon at least 12 months' prior written notice to the Company, which cannot be delivered before the first anniversary of the effective date. Either party may terminate the agreement for the other party's uncured material breach or insolvency and in certain other circumstances agreed to by the parties. In certain termination circumstances, the Company is entitled to retain specified licenses to be able to continue to exploit the Clementia licensed products.

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

The Company determined that the transaction price as of the outset of the arrangement was $46.5 million, which consisted of the upfront amount of $25.0 million, the $20.0 million cash milestone payment due in the third quarter of 2020, the purchase of existing manufacturing inventory of $1.2 million and the purchase of in-process manufacturing inventory of $0.3 million. The other potential milestone payments that the Company is eligible to receive were excluded from the transaction price, as all milestone amounts were fully constrained based on the probability of achievement. The transaction price was allocated to the three performance obligation on a relative stand-alone selling price basis. The Company satisfies the performance obligations upon delivery of the license and completion of the technology transfer and inventory transfers.

During the year ended December 31, 2019, the Company completed the delivery of the license, the technology transfer and the transfer of existing manufacturing inventory and recognized a total of $46.2 million as revenue. During the year ended December 31, 2020, the Company completed the transfer of the in-process manufacturing inventory and recognized revenue of $0.3 million accordingly. There was no revenue deferred as a contract liability associated with the Clementia agreement as of December 31, 2020 and 2019.

CStone Pharmaceuticals

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

The Company received an upfront cash payment of $40.0 million, and through December 31, 2020, the Company has received $14.0 million in milestone payments under this collaboration. Subject to the terms of the CStone agreement, in addition to the upfront and milestone payments received through December 31, 2020, the Company will be eligible to receive up to approximately $332.0 million in additional milestone payments, including $104.5 million related to development and regulatory milestones and $227.5 million related to sales-based milestones. In addition, CStone will be obligated to pay the Company tiered percentage royalties on a licensed product-by-licensed product basis ranging from the mid-teens to low twenties on annual net sales of each licensed product in the CStone territory, subject to adjustment in specified circumstances. CStone will be responsible for costs related to the development of the licensed products in the CStone territory, other than specified costs related to the development of fisogatinib as a combination therapy in the CStone territory that will be shared by the Company and CStone.

Pursuant to the terms of the CStone agreement, CStone 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 after June 1, 2019, and CStone may terminate the CStone agreement with respect to a licensed product for convenience at any time by providing written notice to the Company following the occurrence of specified events. In addition, the Company may terminate the CStone agreement under specified circumstances if CStone or certain other parties challenges the Company's patent rights or any joint collaboration patent rights or if CStone or its affiliates do not conduct any material development or commercialization activities with respect to one or more licensed products for a specified period of time, subject to specified exceptions. Either party may terminate the CStone agreement for the other party's uncured material breach or insolvency. In certain termination circumstances, the parties are entitled to retain specified licenses to be able to continue to exploit the licensed products, and in the event of termination by CStone for the Company's uncured material breach, the Company will be obligated to pay CStone a low single digit percentage royalty on a licensed product-by-licensed product basis on annual net sales of such licensed product in the CStone territory, subject to a cap and other specified exceptions.

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

A summary of manufacturing and research and development services related to the global development activities net of cost sharing payments during the years ended December 31, 2020, 2019 and 2018 is as follows (in thousands):

	Year Ended December 31,		
	2020	2019	2018
Manufacturing and research and development services related to global development activities net of cost sharing payments	$ 3,060	$ 3,286	$ 496

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 as of the outset of the arrangement, which was allocated to the three performance obligations. The potential milestone payments that the Company is eligible to receive were excluded from the transaction price, as all milestone amounts were fully constrained based on the probability of achievement. The Company satisfied the performance obligations upon delivery of the licenses, initial know-how transfers and product trademark and recognized the upfront payment of $40.0 million as revenue during the second quarter of 2018.

During the years ended December 31, 2020 and 2019, cash consideration associated with achieved development milestones of $2.0 million and $12.0 million, respectively, were added to the estimated transaction price for the CStone agreement and recognized as revenue in such periods. The Company will continue to reevaluate the transaction price at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur, and if necessary, the Company will adjust its estimate of the transaction price, and any addition to the transaction price would be recognized as revenue when it becomes probable that inclusion would not lead to a significant revenue reversal.

A summary of revenue recognized under the CStone agreement during the years ended December 31, 2020, 2019 and 2018 is as follows (in thousands):

	Year Ended December 31,		
	2020	2019	2018
License milestone revenue	$ 2,000	$ 12,000	$ 40,000
Manufacturing services related to CStone territory-specific activities	1,630	144	—
Total CStone collaboration revenue	$ 3,630	$ 12,144	$ 40,000

The following table presents the receivables including the contract assets associated with the CStone agreement as of December 31, 2020 and 2019 (in thousands):

	As of December 31,	
	2020	2019
Accounts receivable, net	$ 563	$ 663
Unbilled accounts receivable	$ —	$ 2,749

As of December 31, 2020, the Company had $6.5 million of deferred revenue as a contract liability associated with the CStone collaboration. This contract liability resulted from advance payments made by CStone in connection with commercial supply of avapritinib and pralsetinib for the CStone territory. There was no revenue deferred as a contract liability at December 31, 2019.

Roche – Immunotherapy Collaboration

In March 2016, the Company entered into a collaboration and license agreement (as amended, the Roche immunotherapy agreement) with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc. (collectively, Roche) for the discovery, development and commercialization of small molecule therapeutics targeting kinases believed to be important

in cancer immunotherapy (including the kinase target MAP4K1, which is believed to play a role in T cell regulation), as single products or possibly in combination with other therapeutics.

Under the Roche immunotherapy agreement, Roche was originally granted up to five option rights to obtain an exclusive license to exploit products derived from the collaboration programs in the field of cancer immunotherapy. Such option rights are triggered upon the achievement of Phase 1 proof-of-concept. As a result of amendments to the Roche immunotherapy agreement in the fourth quarter of 2019 and subsequently in the first quarter of 2021, the Company and Roche are currently conducting activities for up to two programs under the collaboration. For one of the two collaboration programs, if Roche exercises its option, Roche will receive worldwide, exclusive commercialization rights for the licensed product. For the other collaboration program, if Roche exercises its option, the Company will retain commercialization rights in the U.S. for the licensed product, and Roche will receive commercialization rights outside of the U.S. for the licensed product. The Company will also retain worldwide rights to any products for which Roche elects not to exercise its applicable option.

Prior to Roche's exercise of an option, the Company will have the lead responsibility for drug discovery and pre-clinical development of all collaboration programs. In addition, the Company will have the lead responsibility for the conduct of all Phase 1 clinical trials other than those Phase 1 clinical trials for any product in combination with Roche's portfolio of therapeutics, for which Roche will have the right to lead the conduct of such Phase 1 clinical trials. Pursuant to the Roche immunotherapy agreement, the parties will share the costs of Phase 1 development for each collaboration program. In addition, Roche will be responsible for post-Phase 1 development costs for each licensed product for which it retains global commercialization rights, and the Company and Roche will share post-Phase 1 development costs for each licensed product for which the Company retains commercialization rights in the U.S.

The Company received an upfront cash payment of $45.0 million in March 2016 upon execution of the Roche immunotherapy agreement, and through December 31, 2020, the Company has achieved $19.5 million in milestone payments under this collaboration. Subject to the terms of the Roche immunotherapy agreement, as amended, in addition to upfront and milestone payments received through December 31, 2020, the Company is eligible to receive up to approximately $323.3 million in contingent option fees and milestone payments related to specified research, pre-clinical, clinical, regulatory and sales-based milestones. In addition, for any licensed product for which Roche retains worldwide commercialization rights, the Company will be eligible to receive tiered royalties ranging from low double-digits to high-teens on future net sales of the licensed product. For any licensed product for which the Company retains commercialization rights in the U.S., the Company and Roche will be eligible to receive tiered royalties ranging from mid-single-digits to low double-digits on future net sales in the other party's respective territories in which it commercializes the licensed product. The upfront cash payment and any payments for milestones, option fees and royalties are non-refundable, non-creditable and not subject to set-off.

The Roche immunotherapy agreement will continue until the date when no royalty or other payment obligations are or will become due, unless earlier terminated in accordance with the terms of the Roche immunotherapy agreement. Prior to its exercise of its first option, Roche may terminate the Roche immunotherapy agreement at will, in whole or on a collaboration target-by-collaboration target basis, upon 120 days' prior written notice to the Company. Following its exercise of an option, Roche may terminate the Roche immunotherapy agreement at will, in whole, on a collaboration target-by-collaboration target basis, on a collaboration program-by-collaboration program basis or, if a licensed product has been commercially sold, on a country-by-country basis, (i) upon 120 days' prior written notice if a licensed product has not been commercially sold or (ii) upon 180 days' prior written notice if a licensed product has been commercially sold. Either party may terminate the Roche immunotherapy agreement for the other party's uncured material breach or insolvency and in certain other circumstances agreed to by the parties. In certain termination circumstances, the Company is entitled to retain specified licenses to be able to continue to exploit the licensed products.

The Company assessed this arrangement in accordance with ASC 606 upon the adoption of the new standard on January 1, 2018, and concluded that the contract counterparty, Roche, is a customer prior to the exercise, if any, of an option by Roche. The Company identified the following material promises under the arrangement: (1) a non-transferable, sub-licensable and non-exclusive license to use the Company's intellectual property and collaboration compounds to conduct research activities; (2) research and development activities through Phase 1 clinical trials under the research plan; (3) five option rights for licenses to develop, manufacture, and commercialize the collaboration targets; (4) participation on a joint research committee (JRC) and joint development committee (JDC); and (5) regulatory responsibilities under Phase 1 clinical trials. The Company determined that the license and research and development activities were not distinct from another, as the license has limited value without the performance of the research and

development activities. Participation on the JRC and JDC to oversee the research and development activities was determined to be quantitatively and qualitatively immaterial and therefore is excluded from performance obligations. The regulatory responsibilities related to filings and obtaining approvals related to the drugs that may result from each program do not represent separate performance obligations based on their dependence on the research and development efforts. As such, the Company determined that these promises should be combined into a single performance obligation.

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

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

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

Through December 31, 2020, the Company has achieved $19.5 million in milestone payments under this collaboration, and these amounts were added to the estimated transaction price and allocated to the existing performance obligation as it became probable that a significant reversal of cumulative revenue would not occur for each of the research milestones achieved.

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

During the year ended December 31, 2020, a reduction in the costs expected to be incurred in the future to satisfy the performance obligation under the collaboration became probable. Accordingly, the Company recorded a cumulative revenue catch-up of $7.9 million during the year ended December 31, 2020. For additional information, see Note 18, *Subsequent Events*.

A summary of revenue recognized under the Roche immunotherapy agreement during the years ended December 31, 2020, 2019 and 2018 is as follows (in thousands):

	Year Ended December 31,		
	2020	2019	2018
Roche collaboration research and development services revenue	$ 14,580	$ 8,165	$ 4,521

During the years ended December 31, 2020, 2019 and 2018, the Company recognized the following revenue due to the changes in the contract liability balances (in thousands):

	Year Ended December 31,		
	2020	2019	2018
Amounts included in the contract liability at the beginning of the period . .	$ 11,546	$ 4,578	$ 4,277

As of December 31, 2020, the Company had revenue deferred as a contract liability related to the Roche immunotherapy agreement of $34.7 million, of which $6.1 million was included in current liabilities, and the research and development services related to the performance obligation are expected to be performed over a remaining period of approximately 4.25 years. As of December 31, 2019, the Company had revenue deferred as a contract liability related to the Roche immunotherapy agreement of $46.1 million, of which $6.2 million was included in current liabilities.

11. Stockholder's Equity

On January 27, 2020, the Company closed a follow-on public offering of 4,710,144 shares of its common stock at a price to the public of $69.00 per share and received net proceeds of $308.4 million, after deducting underwriting discounts and commissions and offering expenses paid by the Company.

On July 30, 2020, the Company entered into the ATM Facility with 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 $250.0 million through Cowen as sales agent. During the year ended December 31, 2020, the Company issued and sold 1,784,926 shares of its common stock under the ATM Facility and received net proceeds of $194.7 million.

12. Stock-based Compensation

2015 Stock Option and Incentive Plan

In 2015, the Company's board of directors and stockholders approved the 2015 Stock Option and Incentive Plan (the 2015 Plan), which replaced the Company's 2011 Stock Option and Grant Plan, as amended (the 2011 Plan). The 2015 Plan includes incentive stock options, nonstatutory stock options, stock appreciation rights, restricted stock, restricted stock units, unrestricted stock, performance-based awards and cash-based awards. The Company initially reserved a total of 1,460,084 shares of common stock for the issuance of awards under the 2015 Plan. The 2015 Plan provides that the number of shares reserved and available for issuance under the 2015 Plan will be cumulatively increased on January 1 of each calendar year by 4% of the number of shares of common stock issued and outstanding on the immediately preceding December 31 or such lesser amount as specified by the compensation committee of the board of directors. For the calendar years beginning January 1, 2020 and 2021, the number of shares reserved for issuance under the 2015 Plan was increased by 1,970,888 and 2,311,741 shares, respectively. In addition, the total number of shares reserved for issuance is subject to adjustment in the event of a stock split, stock dividend or other change in the Company's capitalization. At December 31, 2020, there were 1,703,849 shares available for future grant under the 2015 Plan.

Stock-based Compensation Expense

The Company recognized stock-based compensation expense totaling $75.5 million, $54.7 million and $30.5 million for the year ended December 31, 2020, 2019 and 2018, respectively.

Stock-based compensation expense by award type included within the consolidated statements of operations and comprehensive income (loss) was as follows (in thousands):

	Year Ended December 31,		
	2020	2019	2018
Stock options	$ 57,237	$ 47,726	$ 30,095
Restricted stock units	18,407	6,445	167
Employee stock purchase plan	958	482	272
Subtotal	76,602	54,653	30,534
Capitalized stock-based compensation costs	(1,076)	—	—
Stock-based compensation expense included in total cost and operating expenses	$ 75,526	$ 54,653	$ 30,534

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

	Year Ended December 31,		
	2020	2019	2018
Research and development	$ 33,642	$ 28,596	$ 17,019
Selling, general and administrative	41,884	26,057	13,515
Total stock-based compensation expense	$ 75,526	$ 54,653	$ 30,534

At December 31, 2020, there was $173.7 million of total unrecognized compensation cost related to non-vested stock awards, which is expected to be recognized over a weighted-average period of 2.7 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,		
	2020	2019	2018
Risk-free interest rate	1.02 %	2.21 %	2.77 %
Expected dividend yield	— %	— %	— %
Expected term (years)	6.0	6.0	6.0
Expected stock price volatility	60.48 %	63.83 %	69.08 %

The following table summarizes the stock option activity for the year ended December 31, 2020:

	Shares	Weighted-Average Exercise Price	Remaining Contractual Life (in Years)	Aggregate Intrinsic Value(1) (in thousands)
Outstanding at December 31, 2019	5,795,710	$ 58.82	7.69	$ 134,409
Granted	1,502,403	62.55		
Exercised	(842,649)	39.50		
Canceled	(424,823)	75.44		
Outstanding at December 31, 2020	6,030,641	$ 61.28	7.41	$ 306,810
Exercisable at December 31, 2020	3,181,167	$ 51.60	6.36	$ 192,611

(1) Intrinsic value represents the amount by which the fair market value as of December 31, 2020 of the underlying common stock exceeds the exercise price of the option.

The weighted-average grant date fair value of options granted in the years ended December 31, 2020, 2019 and 2018 was $34.77, $48.96 and $49.40, respectively. The total intrinsic value of options exercised in the years ended December 31, 2020, 2019, and 2018 was $43.3 million, $33.8 million, and $29.4 million, respectively.

At December 31, 2020, the total unrecognized compensation expense related to unvested stock option awards was $112.4 million, which is expected to be recognized over a weighted-average period of approximately 2.5 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 years ended December 31, 2020:

	Shares	Weighted-Average Grant Date Fair Value
Unvested shares at December 31, 2019	419,755	$ 82.50
Granted	961,283	60.01
Vested	(109,556)	83.64
Forfeited	(99,796)	65.72
Unvested shares at December 31, 2020	1,171,686	$ 65.37

The Company started to grant restricted stock units to employees in June 2018. The total fair value of restricted stock units vested during the years ended December 31, 2020 and 2019 was $7.4 million and $0.7 million, respectively. There were no restricted stock units vested during the year ended December 31, 2018. At December 31, 2020, the total unrecognized compensation expense related to unvested restricted stock units was $61.3 million, which is expected to be recognized over a weighted-average period of approximately 3.0 years.

2020 Inducement Plan

In March 2020, the Company's board of directors adopted the 2020 Inducement Plan (the Inducement Plan), pursuant to which the Company may grant, subject to the terms of the Inducement Plan and Nasdaq rules, nonstatutory stock options, stock appreciation rights, restricted stock awards, restricted stock units, and other stock-based awards. The Company initially reserved a total of 1,000,000 shares of common stock for the issuance of awards under the Inducement Plan. The number of shares reserved and available for issuance under the Inducement Plan can be increased at any time with the approval of the Company's board of directors. The Inducement Plan permits the board of directors or a committee thereof to use the stock-based awards available under the Inducement Plan to attract key employees for the growth of the Company. As of December 31, 2020, there were 324,485 shares issued under the Inducement Plan.

2015 Employee Stock Purchase Plan

In 2015, the Company's board of directors and stockholders approved the 2015 ESPP, which became effective upon the closing of the IPO in May 2015. The Company initially reserved a total of 243,347 shares of common stock for issuance under the 2015 ESPP. The 2015 ESPP provides that the number of shares reserved and available for issuance under the 2015 ESPP will be cumulatively increased on January 1 of each calendar years 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, 2020 and 2021, the number of shares reserved for issuance under the 2015 ESPP was increased by 492,722 and 577,935 shares, respectively. The Company issued 38,516, 20,724, and 13,878 shares under the ESPP during the years ended December 31, 2020, 2019, and 2018 respectively.

13. Net income per share

Basic net income (loss) per share (earnings per share, EPS) is calculated by dividing net income (loss) by the weighted average shares of common stock outstanding during the period, without consideration for common stock equivalents. Diluted net income (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 income (loss) per share calculation, the effect of stock options, unvested restricted stock units and ESPP shares on weighted average number of shares is calculated using the treasury stock method. In periods with reported net operating losses, all

common stock equivalents are deemed anti-dilutive such that basic net loss per share and diluted net loss per share are equal.

The calculation of net income (loss) and the number of shares used to compute basic and diluted net income (loss) per share for the years ended December 31, 2020, 2019 and 2018 are as follows (in thousands, except per share data):

	Year Ended December 31,		
	2020	2019	2018
Net income (loss) - basic and diluted	$ 313,882	$ (347,694)	$ (236,642)
Weighted average shares outstanding - basic	54,534	47,829	43,867
Effect of dilutive securities:			
Stock options	1,303	—	—
Restricted stock units	331	—	—
Weighted average shares outstanding - diluted	56,168	47,829	43,867
Net income (loss) per share - basic	$ 5.76	$ (7.27)	$ (5.39)
Net income (loss) per share - diluted	5.59	(7.27)	(5.39)

For the years ended December 31, 2020, 2019 and 2018, the following dilutive securities were not included in the computation of net income (loss) per share because the effect would be anti-dilutive (in thousands):

	Year Ended December 31,		
	2020	2019	2018
Stock options	4,480	5,796	4,558
Restricted stock units	13	420	37
ESPP shares	19	14	10
Total	4,512	6,230	4,605

14. Income Taxes

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, 2020, 2019 and 2018

	Year Ended December 31,		
	2020	2019	2018
Federal income tax (benefit) at statutory rate	21.00 %	21.00 %	21.00 %
Permanent differences	(0.47)	1.11	1.71
Federal research and development credits	(0.96)	0.77	1.79
Federal orphan drug credits	(10.35)	6.90	18.06
State income tax, net of federal benefit	0.08	7.46	7.08
Other	1.50	2.13	0.04
Foreign rate differential	0.37	(0.03)	—
Deferred rate change	2.60	(0.08)	—
Change in valuation allowance	(13.42)	(39.26)	(49.68)
Effective income tax rate	0.35 %	— %	— %

The Company's deferred tax assets and liabilities consist of the following (in thousands):

	Year Ended December 31,		
	2020	2019	2018
Deferred tax assets:			
Net operating loss carryforwards	$ 140,769	$ 219,935	$ 127,421
Research and development credit carryforwards	23,679	19,240	13,714
Orphan drug credit carryforwards	125,153	92,538	68,536
Accrued expenses and other	32,206	25,842	12,248
Deferred revenue	7,317	10,971	10,320
Deferred lease incentive	—	—	3,993
Deferred rent	19,308	26,196	1,436
Total gross deferred tax asset	348,432	394,722	237,668
Deferred tax liability			
Depreciation	(5,451)	(4,474)	(4,162)
Right of use assets	(14,539)	(19,869)	—
Debt discount	—	—	—
Valuation allowance	(328,442)	(370,379)	(233,506)
Net deferred tax asset	$ —	$ —	$ —

Coronavirus Aid, Relief and Economic Security Act

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

In addition, the CARES Act raises the corporate charitable deduction limit to 25% of taxable income and makes qualified improvement property generally eligible for 15-year cost-recovery and 100% bonus depreciation. The enactment of the CARES Act resulted in $3.7 million of bonus depreciation to the Company's income tax provision for the year ended December 31, 2020. Additionally, the Company was able to offset 100% of its current year Federal taxable income with NOLs carried forward from previous years.

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 $328.4 million, $370.4 million and $233.5 million has been established at December 31, 2020, 2019 and 2018, respectively. The change in the valuation allowance was ($42.0) million, $136.9 million and $119.0 million for the years ended December 31, 2020, 2019 and 2018, respectively. The decrease in the deferred tax asset between December 31,2020 and 2019 was mostly due to the utilization of federal and state net operating losses to offset current year taxable income.

The Company has incurred net operating losses (NOL) since inception. As of December 31, 2020, the Company had federal and state NOL carryforwards of $435.7 million and $776.0 million, respectively, which begin to expire in 2030, and of which $414 million of the Company's federal NOL carryforwards have an unlimited carryforward. As of December 31, 2020, the Company had federal and state research and development tax credit carryforwards of $14.2 million and $11.2 million, respectively, which begin to expire in 2030. As of December 31, 2020, the Company had federal orphan drug credits of $125.2 million, which begin to expire in 2035 and state investment tax credits of $0.8 million, which begin to expire in 2021. The Company has analyzed and validated its research and development tax credits as well as its orphan drug credits for 2011-2019. The Company generated research credits in 2020 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, 2020 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 net operating losses 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 analyzed shifts in the stock ownership to determine if its net operating losses and tax credit carryforwards may be subject to limitation under Sections 382 and 383. Based on this analysis, it was determined that it is more likely than not that an ownership change occurred on the following dates: March 24, 2011; April 5, 2011; November 10, 2014; and February 7, 2017. As a consequence of these ownership changes, the Company's net operating loss carryforwards and tax credit carryforwards allocable to the periods preceding each ownership change are subject to limitations under Section 382. Approximately $2 million of the Company's NOL carryforwards may be available for utilization within their applicable carryforward periods. 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 loss. As of December 31, 2020 and 2019, the Company has no unrecognized tax benefits or accrued interest related to unrecognized tax benefits. As of December 31, 2020, 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.

15. Leases

38 Sidney Street

On February 12, 2015, the Company entered into a lease for approximately 38,500 rentable square feet of office and laboratory space at 38 Sidney Street in Cambridge, Massachusetts, which the Company gained control over on June 15, 2015, and occupancy commenced in October 2015. The initial term of the lease agreement will expire on October 31, 2022, unless terminated sooner. The Company has an option to extend the lease for five additional years. The lease has a total commitment of $17.8 million over the initial seven-year term. The Company has agreed to pay an initial annual base rent of approximately $2.3 million, which rises periodically until it reaches approximately $2.8 million. The lease provided the Company with an allowance for leasehold improvements of $4.3 million. During the year ended December 31, 2018, prior to the adoption of ASC 842, the Company recorded rent expense on a straight-line basis and the leasehold improvement incentives as a reduction to rent expense ratably over the lease term. The lease agreement required the Company to pay an intital security deposit of $1.3 million, of which a total of $0.4 million was released subsequently, and the remaining $0.9 million is recorded in restricted cash on the Company's consolidated balance sheet as of December 31, 2020. In the first quarter of 2018, the Company subleased the space to a third party and the term of the sublease will expire on February 28, 2021.

45 Sidney Street

On April 28, 2017, the Company entered into a lease agreement for approximately 99,833 rentable square feet of office and laboratory space located at 45 Sidney Street in Cambridge, Massachusetts. The initial term of the lease agreement commenced on October 1, 2017 and will expire on November 30, 2029, unless terminated sooner. The lease agreement also provides the Company with an option to extend the lease agreement for two consecutive five-year periods at the then fair market annual rent, as defined in the lease agreement.

During the initial term of the lease agreement, the Company has agreed to pay an initial annual base rent of approximately $7.7 million, which increases annually until it reaches approximately $10.6 million in the last year of the initial term. The lease provided the Company with a tenant improvement allowance of approximately $14.2 million for improvements to be made to the premises. During the year ended December 31, 2018, prior to the adoption of ASC 842, the Company recorded rent expense on a straight-line basis and the leasehold improvement incentives as a reduction to rent expense ratably over the lease term. The lease agreement required the Company to pay an initial security deposit of $3.5 million, of which $3.0 million is recorded in restricted cash on the Company's consolidated balance sheet as of

December 31, 2019, and $0.5 million was recorded in prepaid and other current assets, which was subsequently released in January 2020.

On September 19, 2018, the Company entered into an amendment to the lease agreement for its office and laboratory space located at 45 Sidney Street in Cambridge, Massachusetts to expand the rentable square footage from approximately 99,833 square feet to approximately 139,216 square feet. The initial term of the lease with respect to the expansion premises commenced on March 1, 2019 and will expire on November 30, 2029, unless terminated sooner. Pursuant to the lease amendment, the rent commencement date for the expansion premises was July 1, 2019.

The Company has agreed to pay an initial annual base rent of approximately $3.2 million for the expansion premises, which increases annually until it reaches approximately $4.2 million in the last year of the initial term for the expansion premises. Pursuant to the lease amendment, the landlord has also agreed to provide the Company with a tenant improvement allowance of approximately $3.2 million for improvements to be made to the expansion premises. The lease amendment required the Company to pay an additional security deposit of $0.8 million to the landlord for the expansion premises, which is recorded in restricted cash on the Company's consolidated balance sheet as of December 31, 2020.

The lease agreements do not contain residual value guarantees and the components of lease cost for the years ended December 31, 2020 and 2019 were as follows (in thousands):

	Year Ended December 31,	
Operating leases:	2020	2019
Lease cost	$ 17,600	$ 16,162
Sublease income	(2,919)	(2,834)
Net lease cost	$ 14,681	$ 13,328

For the year ended December 31, 2018, rent expense under ASC 840, net of sublease income, was $7.3 million.

The Company has not entered into any material short-term leases or financing leases as of December 31, 2020.

Supplemental cash flow information related to leases for the years ended December 31, 2020 and 2019 was as follows (in thousands):

	Year Ended December 31,	
	2020	2019
Cash paid for amounts included in the measurement of lease liabilities:	$ 14,444	$ 12,247
Lease liabilities arising from obtaining right-of-use assets:		
Operating leases	$ 479	$ 23,300

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

	Operating leases
Weighted average remaining lease term in years	8.4
Weighted average discount rate	8.2%

Future minimum lease payments under non-cancellable leases as of December 31, 2020 were as follows (in thousands):

2021	14,879
2022	14,836
2023	12,864
2024	13,241
2025	13,517
Thereafter	56,842
Total future minimum lease payments	126,179
Less imputed interest	(36,575)
Total	$ 89,604

16. 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 employees or 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. Expense related to the 401(k) Plan for the years ended December 31, 2020, 2019 and 2018 were not material.

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. As of December 31, 2020, the Swiss Plan had an unfunded status of $6.4 million, which resulted from fair value of plan assets of $7.7 million and projected benefit obligation of $14.1 million. The accumulated benefit obligation at December 31, 2020 was $11.8 million. The Company's net periodic benefit cost as well as contributions to the Swiss Plan for the years ended December 31, 2020 and 2019 were not material.

17. Commitments

In connection with the commercialization of AYVAKIT/AYVAKYT and GAVRETO, the Company has negotiated manufacturing agreements with certain vendors that require the Company to meet minimum purchase obligations on an annual basis. The aggregate amount of future minimum purchase obligations under these manufacturing agreements over the period of next five years is approximately $30.9 million as of December 31, 2020.

18. Subsequent Events

On January 8, 2021, the Company entered into a ninth amendment to its collaboration and license agreement, as amended, with Roche related to the discovery, development and commercialization of small molecule therapeutics targeting kinases in cancer immunotherapy. Pursuant to the amendment, the Company and Roche agreed to modify certain time periods related to Roche's option rights for one of the collaboration programs and agreed to terminate two of the other collaboration programs, including certain mechanics related to the wind-down of activities for such terminated targets.

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Leadership

Jeff Albers
Chief Executive Officer and President

Debbie Durso-Bumpus
Chief People Officer

Kate Haviland
Chief Operating Officer

Becker Hewes
Chief Medical Officer

Mike Landsittel
Chief Financial Officer

Tracey L. McCain, Esq.
Executive Vice President,
Chief Legal and Compliance Officer

Christopher K. Murray, Ph.D.
Senior Vice President,
Technical Operations

Fouad Namouni
President, Research and Development

Christina Rossi
Chief Commercial Officer

Board of Directors

Jeff Albers
Chief Executive Officer, President and Board Member, Blueprint Medicines

Alexis Borisy
Chairman and Chief Executive Officer, EQRx, Inc.

Lonnel Coats
Chief Executive Officer, President and Board Member, Lexicon Pharmaceuticals, Inc.

George D. Demetri, M.D.
Professor of Medicine at Harvard Medical School, Director of the Center for Sarcoma and Bone Oncology and Physician at the Dana-Farber Cancer Institute

Mark Goldberg, M.D.
Associate Professor of Medicine, Harvard Medical School

Nicholas Lydon, Ph.D.
Co-founder and Chairman, Recludix Pharma Inc.

Daniel Lynch
Chairman, Blueprint Medicines

Charles A. Rowland, Jr.
Former Chief Executive Officer, Aurinia Pharmaceuticals Inc.

Lynn Seely, M.D.
Former Chief Executive Officer, President and Board Member, Myovant Sciences, Ltd.

Annual Meeting of Stockholders
The 2021 annual meeting of stockholders will be held on Wednesday, June 2, 2021 at 4 p.m. ET online at http://www.virtualshareholdermeeting.com/BPMC2021.

Stock Listing
NASDAQ: BPMC

Independent Auditors
Ernst & Young LLP

SEC Form 10-K
A copy of Blueprint Medicines' Form 10-K filed with the Securities and Exchange Commission is available free of charge from the company's Investor Relations Department by calling (617) 714-6674, emailing ir@blueprintmedicines.com or sending a written request to: Investor Relations, Blueprint Medicines Corporation, 45 Sidney Street, Cambridge, MA 02139

Transfer Agent
The transfer agent is responsible, among other things, for handling stockholder questions regarding lost stock certificates, address changes, including duplicate mailings, and changes in ownership or name in which shares are held. These requests may be directed to the transfer agent at the following address: Computershare Trust Company, N.A., Meidinger Tower, 462 South 4th Street, Louisville, KY 40202, www-us.computershare.com/contactus

Cautionary Note Regarding Forward-Looking Statements

This annual report contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, statements regarding plans, strategies, timelines and expectations for Blueprint Medicines' current or future approved drugs and drug candidates, including timelines for marketing applications and approvals, the initiation of clinical trials or the results of ongoing and planned clinical trials; Blueprint Medicines' plans, strategies and timelines to nominate development candidates; plans and timelines for additional marketing applications for avapritinib and pralsetinib and, if approved, commercializing avapritinib and pralsetinib in additional geographies or for additional indications; the potential benefits of any of Blueprint Medicines' current or future approved drugs or drug candidates in treating patients; the potential benefits of Blueprint Medicines' collaboration with Roche and Genentech for pralsetinib; and Blueprint Medicines' strategy, goals and anticipated milestones, business plans and focus. The words "aim," "may," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "project," "potential," "continue," "target" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements in this annual report are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this annual report, including, without limitation,risks and uncertainties related to the impact of the COVID-19 pandemic to Blueprint Medicines' business, operations, strategy, goals and anticipated milestones, including Blueprint Medicines' ongoing and planned research and discovery activities, ability to conduct ongoing and planned clinical trials, clinical supply of current or future drug candidates, commercial supply of current or future approved products, and launching, marketing and selling current or future approved products; Blueprint Medicines' ability and plans in continuing to establish and expand a commercial infrastructure, and successfully launching, marketing and selling current or future approved products; Blueprint Medicines' ability to successfully expand the approved indications for AYVAKIT/AYVAKYT and GAVRETO or obtain marketing approval for AYVAKIT/AYVAKYT in additional geographies in the future; the delay of any current or planned clinical trials or the development of Blueprint Medicines' current or future drug candidates; Blueprint Medicines' advancement of multiple early-stage efforts; Blueprint Medicines' ability to successfully demonstrate the safety and efficacy of its drug candidates and gain approval of its drug candidates on a timely basis, if at all; the preclinical and clinical results for Blueprint Medicines' drug candidates, which may not support further development of such drug candidates; actions of regulatory agencies, which may affect the initiation, timing and progress of clinical trials; Blueprint Medicines' ability to obtain, maintain and enforce patent and other intellectual property protection for AYVAKIT/AYVAKYT, GAVRETO or any drug candidates it is developing; Blueprint Medicines' ability to develop and commercialize companion diagnostic tests for AYVAKIT/AYVAKYT, GAVRETO or any of its current and future drug candidates; and the success of Blueprint Medicines' current and future collaborations, partnerships or licensing arrangements. These and other risks and uncertainties are described in greater detail in the section entitled "Risk Factors" in Blueprint Medicines' filings with the Securities and Exchange Commission (SEC), including Blueprint Medicines' Annual Report on Form 10-K for the year ended December 31, 2020, as filed with the SEC on February 17, 2021, and any other filings that Blueprint Medicines has made or may make with the SEC in the future. Any forward-looking statements contained in this annual report represent Blueprint Medicines' views only as of April 21, 2021 and should not be relied upon as representing its views as of any subsequent date. Except as required by law, Blueprint Medicines assumes no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

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