Table of Contents

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, DC 20549

Form 10-K

(Mark One)

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

For the fiscal year ended December 31, 2021

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, 2021, 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 $5,150,459,010.

Number of shares of the registrant's common stock, par value $0.001 per share, outstanding on February 15, 2022: 59,203,486

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement for its 2022 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, 2021, are incorporated by reference into Part III of this Annual Report on Form 10-K.

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

TABLE OF CONTENTS

Unless otherwise stated, all references to "us," "our," "Blueprint," "Blueprint Medicines," "we," the "Company" and similar designations in this Annual Report on Form 10-K refer to Blueprint Medicines Corporation and its consolidated subsidiaries. Blueprint Medicines, AYVAKIT®, AYVAKYT®, 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 preclinical, clinical and commercial supply. This reliance on third parties increases the risk that we will not have sufficient quantities of our approved drugs or drug candidates or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

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

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

- Our business, results of operations and future growth prospects could be materially and adversely affected by the ongoing 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 variation or the negative of these words or other comparable terminology, although not all forward-looking statements contain these identifying words.

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

- the timing or likelihood of regulatory actions, filings and approvals for our current and future drug candidates, including our ability to obtain marketing approval for avapritinib and pralsetinib for additional indications or in additional geographies;
- our ability and plans in continuing to build out our commercial infrastructure and successfully launching, marketing and selling AYVAKIT (avapritinib) (marketed in Europe under the brand name AYVAKYT), GAVRETO (pralsetinib) and any current and future drug candidates for which we receive marketing approval;
- the rate and degree of market acceptance of AYVAKIT/AYVAKYT, GAVRETO and any current and future drug candidates for which we receive marketing approval;
- the pricing and reimbursement of AYVAKIT/AYVAKYT, GAVRETO and any current and future drug candidates for which we receive marketing approval;
- the initiation, timing, progress and results of our preclinical studies and clinical trials, including our ongoing clinical trials and any planned clinical trials for our current and future drug candidates and research and development programs;
- our ability to advance drug candidates into, and successfully complete, clinical trials;
- our ability to successfully develop manufacturing processes for any of our current and future drugs or drug candidates and to secure manufacturing, packaging and labeling arrangements for development activities and commercial production;
- the implementation of our business model and strategic plans for our business, drugs, drug candidates, platform and technology;
- the scope 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., our collaboration with CStone Pharmaceuticals to develop and commercialize avapritinib, pralsetinib and fisogatinib in Greater China, and our collaboration with Zai Lab to develop and commercialize BLU-701 and BLU-945 as inhibitors of epidermal growth factor receptor (EGFR), 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 ongoing 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/AYVAKYT, 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 life-changing medicines for people with cancer and blood disorders. Applying an approach that is both precise and agile, we create therapies that selectively target genetic drivers, with the goal of staying one step ahead across stages of disease. Since 2011, we have leveraged our research platform, including expertise in molecular targeting and world-class drug design capabilities, to rapidly and reproducibly translate science into a broad pipeline of precision therapies. Today, 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 systemic mastocytosis, or SM, lung cancer and other genomically defined cancers, and cancer immunotherapy.

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

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

Avapritinib

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

We are 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 April 2021, we presented registration-enabling data from the PATHFINDER trial at the virtual American Association for Cancer Research, or AACR, Annual Meeting.

In June 2021, the FDA approved avapritinib under the brand name AYVAKIT for the treatment of adult patients with advanced SM, including aggressive SM or ASM, SM with an associated hematologic neoplasm or SM-AHN, and mast cell leukemia or MCL. In January 2022, the Committee for Medicinal Products for Human Use, or CHMP, of the European Medicines Agency, or EMA, adopted a positive opinion recommending marketing authorization for avapritinib as a monotherapy for the treatment of adult patients with ASM, SM-AHN or MCL, after at least one systemic therapy. Pending the European Commission’s final decision on our Type 2 variation marketing authorisation application, or MAA, we anticipate obtaining regulatory approval from the EMA and launching avapritinib under the brand name AYVAKYT for advanced SM in Europe in the second quarter of 2022.

In addition, through our distribution agreement with Neopharm Israel Ltd., a marketing authorization application in Israel was submitted in June 2021 for avapritinib for patients with advanced SM and PDGFRA exon 18 mutant gastrointestinal stromal tumors, or GIST. In the future, we plan to pursue the regulatory approval and commercialization of avapritinib in additional global geographies, including through additional potential distribution agreements.

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 January 2022, we announced that the PIONEER trial was

fully enrolled. We plan to report top-line data for Part 2 of the PIONEER trial in mid-2022 and to submit a supplemental new drug application, or sNDA, to the FDA for avapritinib in non-advanced SM in the second half of 2022.

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

BLU-263

We are developing BLU-263, an investigational, orally available, potent and highly selective KIT inhibitor, 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 and potentially patients with other mast cell disorders.

In April 2021, we presented results from a Phase 1 trial of BLU-263 in healthy volunteers at the virtual AACR Annual Meeting, which showed that BLU-263 was well-tolerated at all doses tested. Based on these data, we initiated a Phase 2/3 trial of BLU-263 in patients with non-advanced SM, which we refer to as our HARBOR trial, in the second quarter of 2021. We anticipate presenting initial data from the HARBOR trial in the second half of 2022.

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

In November 2021, Roche announced that the European Commission granted conditional marketing authorization for GAVRETO as a monotherapy for the treatment of adults with RET fusion-positive advanced NSCLC not previously treated with a RET inhibitor. Roche submitted a Type II variation MAA to the EMA for pralsetinib for RET-altered thyroid cancers in December 2021, as well as marketing applications for pralsetinib for RET-altered NSCLC and thyroid cancers across multiple global geographies in 2021. Marketing applications are planned for pralsetinib for RET-altered NSCLC and thyroid cancers across additional global geographies in 2022.

In March 2021, China's National Medical Products Administration, or NMPA, approved GAVRETO for the treatment of RET fusion-positive NSCLC patients previously treated with platinum-based chemotherapy. In April 2021, China's NMPA accepted CStone's new drug application, or NDA, with Priority Review designation, for pralsetinib for the treatment of RET-mutant MTC and RET fusion-positive thyroid cancer.

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 the ARROW trial. In addition, Roche is conducting multiple ongoing studies, including a registration-enabling Phase 3 clinical trial in treatment-naïve patients with RET fusion-positive NSCLC, which is referred to as the ACCELERET-Lung trial; and, a registration-enabling Phase 3 clinical trial in patients with locally advanced or metastatic RET-mutated MTC who have not previously received a standard of care multi-kinase inhibitor therapy, which is referred to as the ACCELERET-MTC

trial. In June 2021, we reported updated data from the ARROW trial in metastatic RET fusion-positive NSCLC and other advanced solid tumors at the 2021 American Society of Clinical Oncology, or ASCO, Annual Meeting. The ARROW trial was fully enrolled in December 2021. Pursuant to our collaboration with Roche, we are co-developing 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 (ii) the treatment of patients with RET mutation-positive MTC that requires systemic treatment and for which there are no acceptable alternative treatments. In addition, the FDA has granted orphan drug designation to pralsetinib for the treatment of RET-rearranged NSCLC, JAK1/2-positive NSCLC or TRKC-positive NSCLC.

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

We are commercializing avapritinib for the treatment of patients with PDGFRA exon 18 mutant GIST, a rare disease that is a sarcoma, or tumor of bone or connective tissue, of the gastrointestinal tract. The FDA has granted breakthrough therapy designation for avapritinib for the treatment of unresectable or metastatic GIST harboring the PDGFRA D842V mutation. In addition, the FDA has granted orphan drug designation to avapritinib for the treatment of GIST, and the European Commission has granted orphan medicinal product designation to avapritinib for the treatment of GIST. Avapritinib is approved in the U.S. under the brand name AYVAKIT for the treatment of adults with unresectable or metastatic GIST harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations, and is approved in Europe with conditional marketing authorization under the brand name AYVAKYT as a monotherapy for the treatment of adult patients with unresectable or metastatic GIST harboring a PDGFRA D842V mutation.

In March 2021, CStone announced that China's NMPA approved AYVAKIT for the treatment of adults with unresectable or metastatic GIST harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations. AYVAKIT received accelerated approval in April 2021 from the Taiwan Food and Drug Administration, or TFDA, and approval in Hong Kong in December 2021, both for adults with unresectable or metastatic GIST harboring PDGFRA D842V mutations.

EGFR-Mutated NSCLC – BLU-701, BLU-945 and BLU-451

We are developing three investigational EGFR inhibitors, BLU-701, BLU-945 and BLU-451, which was formerly known as LNG-451, with the goal of addressing the nearly all activating mutations (>90 percent) in EGFR-driven NSCLC. The introduction of EGFR-targeted therapies, including osimertinib, has transformed the care of patients with EGFR-driven NSCLC; however, there is a significant need for new treatment options designed to prevent a broad range of resistance mechanisms before they emerge, with the goal of prolonging patient benefit. In addition, there are no approved targeted therapies for patients with disease progression following osimertinib, and limited treatment options for patients with EGFR exon 20 insertion-positive NSCLC.

BLU-701 and BLU-945 were specifically designed to provide comprehensive coverage of common activating and on-target resistance mutations, spare wild-type EGFR and other kinases to limit off-target toxicities, and treat or prevent CNS metastases, which occur frequently in patients with EGFR-driven NSCLC. We believe these profiles may enable BLU-701 and BLU-945 to become the backbones of a range of combination strategies with the potential to address important medical needs for patients with EGFR-driven NSCLC, including in early line treatment settings. We plan to develop BLU-701 and BLU-945 in combination with each other and other therapies, including osimertinib, as an initial treatment designed to prevent resistance from emerging. In addition, we plan to develop BLU-701 and BLU-945 as monotherapies in certain biomarker-selected patient populations.

In December 2021, we completed our acquisition of Lengo Therapeutics, Inc., along with its lead compound LNG-451, which we now refer to as BLU-451. BLU-451 is an oral precision therapy in development for the treatment of NSCLC in patients with EGFR exon 20 mutations.

EGFR-Positive NSCLC — BLU-701

BLU-701 is a selective and potent investigational inhibitor of 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. In preclinical data presented at the virtual AACR Annual Meeting in April 2021, BLU-701 showed strong and durable inhibition of tumor growth at doses that are EGFR wild-type sparing, and the potential to be used in both first- and second-line settings. BLU-701 indicated significant CNS penetration in preclinical models, with comparable exposure in the plasma and brain, which illustrates its potential to treat or prevent CNS metastases in patients with EGFR-driven tumors. Based on these preclinical data, we initiated a Phase 1/2 trial of BLU-701 in EGFR-mutant NSCLC, which we refer to as our HARMONY trial, in the fourth quarter of 2021. We plan to present initial clinical data from the HARMONY trial in the second half of 2022.

EGFR-Positive NSCLC — BLU-945

BLU-945 is a selective and potent investigational inhibitor of 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 mutations to first-generation EGFR inhibitors and osimertinib, respectively. In preclinical data presented at the virtual AACR Annual Meeting in April 2021, BLU-945 demonstrated potent antitumor activity in osimertinib-resistant tumor models, as well as activity in an intracranial patient-derived xenograft model. Both preclinical models harbored activating mutations combined with the T790M and C797S mutations. Based on these preclinical data, we initiated a Phase 1/2 trial of BLU-945 in patients with EGFR-driven NSCLC, which we refer to as our SYMPHONY trial, in the second quarter of 2021. We plan to present initial clinical data from the SYMPHONY trial in the second quarter of 2022.

EGFR-Positive NSCLC – Combinations with BLU-701 and/or BLU-945

Based on their differentiated selectivity profiles and potency against on-target EGFR activating and resistant mutants, we believe BLU-701 and BLU-945 have the potential to become backbone therapies for a range of combination strategies for EGFR-positive NSCLC across multiple treatment lines, potentially including combinations of BLU-701 or BLU-945 with other EGFR therapies or treatment modalities, as well as BLU-701 and BLU-945 together. In preclinical data presented at the virtual AACR Annual Meeting in April 2021, the combination of BLU-945 with either gefitinib or osimertinib showed enhanced antitumor activity when compared with either gefitinib or osimertinib alone. At the British Thoracic Oncology Group, or BTOG, Annual Conference in January 2022, we reported preclinical data supporting the development of BLU-701 and BLU-945 combination therapy in EGFR-driven NSCLC. Based on these results, we plan to develop BLU-701 and BLU-945 in combination with each other and other agents.

EGFR Exon 20 Insertion-Positive NSCLC — BLU-451

BLU-451 is a selective and potent investigational inhibitor under development for the treatment of EGFR exon 20 insertion-positive NSCLC. Based on preclinical data, BLU-451 potently inhibited all common EGFR exon 20 insertion variants with marked selectivity over wild-type EGFR and off-target kinases, and has shown significant CNS penetration. We recently received clearance for an investigational new drug, or IND, application for BLU-451 for EGFR exon 20 insertion-positive NSCLC. In the first quarter of 2022, we plan to initiate a Phase 1/2 trial of BLU-451 in EGFR exon 20 insertion-positive NSCLC, and we expect to present preclinical data for BLU-451 in the second quarter of 2022.

Cyclin E Aberrant Cancers – BLU-222

We are developing an investigational inhibitor, BLU-222, targeting CDK2 for the treatment of patients with cyclin E aberrant cancers. In subsets of patients across multiple cancer types, aberrant cyclin E, or CCNE1, hyperactivates CDK2, resulting in cell cycle dysregulation and tumor proliferation. Aberrant CCNE1 has been observed as a primary driver of disease, as well as a mechanism of resistance to CDK4/6 inhibitors and other therapies.

At the virtual AACR Annual Meeting in April 2021, we presented preclinical data showing that selective CDK2 inhibition arrested the cell cycle and blocked tumor proliferation in CCNE1-amplified cell lines, and demonstrated robust and sustained antitumor activity in vivo in models of CCNE1-amplified ovarian, breast and gastric cancer. A selective CDK2 inhibitor also showed improved tolerability compared to a pan-CDK inhibitor and chemotherapy, as measured by animal body weight.

We recently received FDA clearance for an IND application for BLU-222 for cyclin E aberrant cancers. We plan to initiate a Phase 1/2 trial of BLU-222 in cyclin E aberrant cancers, which we refer to as our VELA trial, in the first quarter of 2022, and to present preclinical data for BLU-222 in the second quarter of 2022. BLU-222 is being developed as a single agent and in combination with chemotherapy in gynecological cancers, and in combination with hormonal and the approved CDK-4/6 inhibitor ribociclib for hormone-receptor-positive, HER2-negative breast cancer.

Advanced Cancers – BLU-852

BLU-852 is a selective and potent investigational inhibitor of MAP4K1, a well-characterized immunokinase involved in the regulation of immune cells. Preclinical data presented at the virtual AACR Annual Meeting in April 2021 show that MAP4K1 inhibition enhanced intratumoral immune cell activation, overcame regulatory T cell, or Treg, mediated T cell suppression, and reduced tumor burden both as a monotherapy and in combination with checkpoint inhibition. These preclinical data support the continued development of BLU-852. Under our ongoing cancer immunotherapy collaboration, we expect Roche to initiate a Phase 1 trial of BLU-852, as a single agent and in combination with atezolizumab, in advanced cancers in 2023.

Fisogatinib — Hepatocellular Carcinoma

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 hepatocellular carcinoma, or HCC. Following a strategic evaluation of the evolving HCC treatment landscape and prioritization of resources across our broad precision therapy pipeline, we have decided to deprioritize our clinical development of fisogatinib for the treatment of advanced HCC. We have discontinued further enrollment of the Blueprint Medicines-sponsored clinical trial of fisogatinib as a monotherapy and in combination with sugemalimab, an anti-PD-L1 immunotherapy being developed by CStone. CStone continues to retain development and commercial rights to fisogatinib in the CStone territory, which encompasses Mainland China, Hong Kong, Macau and Taiwan.

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, we plan to expand our discovery platform by building capabilities, supported by external collaborations, for targeted protein degradation of both kinase and non-kinase targets in precision oncology, with the goal of advancing transformative therapies to patients and further broadening the significant productivity of our research engine. Beyond the discovery programs described above, we have multiple pre-development candidate programs for undisclosed kinase targets. In 2022, we plan to nominate two development candidates from our discovery programs. We also plan to share our vision for our expanded discovery platform at an R&D Day in the second half of 2022.

Under our immunotherapy collaboration with Roche, we are conducting activities for up to two discovery programs, including BLU-852. See "*—Collaborations and Licenses Summary*" below.

Collaborations and Licenses Summary

Roche—Immunotherapy Collaboration. In March 2016, we entered into a collaboration with Roche to discover, develop and commercialize small molecule therapeutics targeting kinases believed to be important in cancer immunotherapy (including the kinase target MAP4K1, 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 are also co-developing pralsetinib globally in RET-altered solid tumors, including NSCLC, MTC and other thyroid cancers, and expanding development of pralsetinib in multiple treatment settings.

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

Clementia. In October 2019, we entered into a license agreement with Clementia 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. Clementia initiated patient dosing in a Phase 2 clinical trial of BLU-782, now referred to as IPN60130, in the first quarter of 2022.

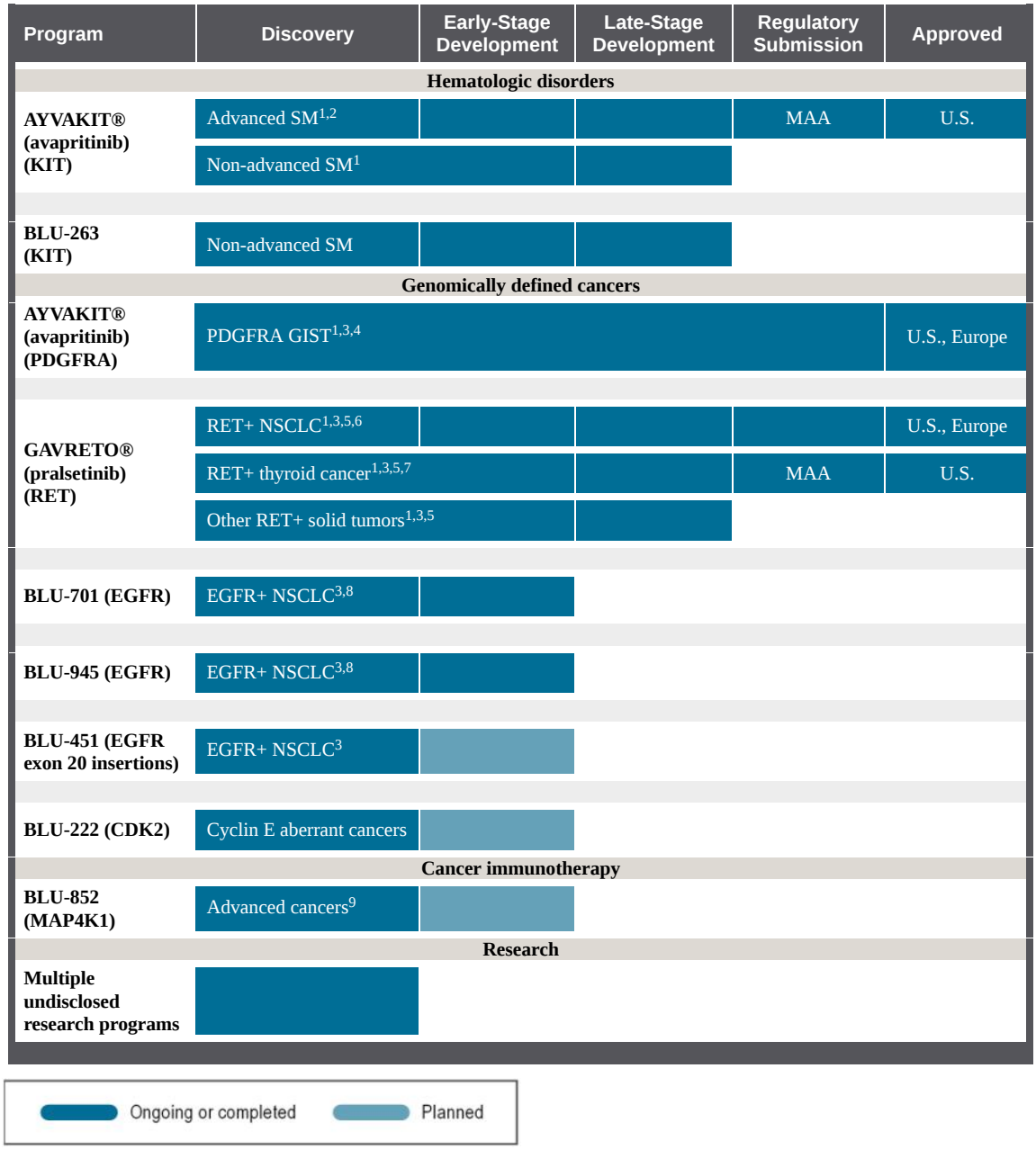
Zai Lab. In November 2021, we entered into a collaboration with Zai Lab to develop and commercialize BLU-701 and BLU-945 for the treatment of EGFR-driven NSCLC in Greater China, including Mainland China, Hong Kong, Macau and Taiwan. The collaboration aims to accelerate and expand global development of BLU-701 and BLU-945.

Mergers & Acquisitions Summary

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

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

Our Pipeline



(1) CStone has exclusive rights to develop and commercialize avapritinib, pralsetinib and fisogatinib in Mainland China, Hong Kong, Macau and Taiwan. For more information, see "—Collaborations and Licenses" below.
(2) Approved in the U.S. for the treatment of adults with advanced SM, including ASM, SM-AHN and MCL. Received a positive opinion from the EMA's CHMP for the treatment of adult patients with ASM, SM-AHN or MCL, after at least one systemic therapy.
(3) Unresectable or metastatic disease.
(4) 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.
(5) 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.
(6) 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. For more information, see "—Collaborations and Licenses" below.
(7) 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. Received conditional marketing authorization in Europe for the treatment of adults with advanced RET fusion-positive NSCLC not previously treated with a RET inhibitor.
(8) Received accelerated approval in the U.S. for the treatment of patients with advanced or metastatic RET-mutant MTC and RET fusion-positive thyroid cancer. Continued approval may be contingent on confirmatory trials.
(9) Zai Lab has exclusive rights to develop and commercialize BLU-701 and BLU-945 in Mainland China, Hong Kong, Macau and Taiwan. For more information, see "—Collaborations and Licenses" below.
(10) 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. 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 blood disorders as possible. To achieve this goal, key elements of our strategy are as follows:

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

- Deepen our strategic focus on SM and related mast cell disorders by seeking regulatory approval for avapritinib for the treatment of 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 seek international regulatory approvals under the Roche pralsetinib collaboration as a treatment for RET-altered cancers.

- Advance our innovative research programs, including BLU-701, BLU-945 and BLU-451, our selective and potent EGFR inhibitors for EGFR-driven NSCLC, BLU-222, our selective and potent CDK2 inhibitor for cyclin E aberrant cancers, 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 blood 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, and helping solve for intractable sites of progression, such as the brain.*** Most approved kinase inhibitors provide only temporary disease control. Patients may relapse due to the emergence of on-target resistance mutations or in cancer, tumors progress because therapies are unable to cross the blood-brain barrier to treat or prevent CNS metastases. Novel approaches, including innovative combinations, are needed to predict and inhibit resistant mutants and address common sites of progression including the brain, thus providing more durable clinical responses.

In addition, we plan to expand our discovery platform by building capabilities, supported by external collaborations, for targeted protein degradation of both kinase and non-kinase targets in precision oncology, with the goal of advancing transformative therapies to patients and further broadening the significant productivity of our research engine.

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 percent) 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: ASM, SM-AHN, and MCL. These advanced forms of SM have historically had a median overall survival of less than six months to 3.5 years and are characterized by prominent organopathy and dysfunction, as well as the debilitating symptoms of mast cell activation.

Advanced SM accounts for approximately 5-10 percent of the patients, or about 5,000 patients in the U.S., France, Germany, Italy, Spain, the United Kingdom and Japan, which we collectively refer to as the Major Markets. Non-advanced SM, including indolent SM and an intermediate form referred to as smoldering SM, account for the remaining 90-95 percent of patients, or about 70,000 patients in Major Markets. Population studies estimate the prevalence rate of all subtypes of SM is approximately 9.6 per 100,000 people.

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

For patients with 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 medical need for a significant portion of patients who have a heavy symptom burden that current therapies fail to address.

We are developing avapritinib for the treatment of SM 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 April 2021, we presented results from a Phase 1 trial of BLU-263 in healthy volunteers at the virtual AACR Annual Meeting, which showed that BLU-263 was well-tolerated at all doses tested. In January 2021, we announced positive topline results of BLU-263 in a Phase 1 healthy volunteer trial. Based on these data, we initiated the Phase 2/3 HARBOR trial of BLU-263 in patients with non-advanced SM in the second quarter of 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.

Data Presented at the Virtual American Association for Cancer Research Annual Meeting in April 2021

In a pre-specified interim analysis from the PATHFINDER trial, 32 patients who primarily received a starting avapritinib dose of 200 mg once daily were evaluable for response per the modified IWG-MRT-ECNM criteria, as of a data cutoff date of June 23, 2020. 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. Response assessments were completed per central review, and all reported clinical responses were confirmed.

Clinical Activity Data. Overall, the ORR was 75 percent (95% CI: 57%, 89%), and the CRh rate was 19 percent, with a median time to CRh of 5.6 months. These results show that responses deepened over time at a rate consistent with previously reported EXPLORER trial results. Avapritinib led to robust and durable benefits across a number of additional clinical activity measures. In new patient-reported outcomes data, avapritinib showed a statistically significant reduction in total symptom score after 40 weeks ($p<0.001$), as measured by the Advanced SM Symptom Assessment Form. Treatment with avapritinib resulted in robust improvements in patient-reported quality of life, based on the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire. Across multiple measures of mast cell burden, avapritinib showed profound reductions in serum tryptase, bone marrow mast cells, KIT D816V allele burden and spleen volume.

Safety Data. Avapritinib was generally well-tolerated in 62 patients enrolled in the PATHFINDER trial, and most adverse effects, or AEs, were reported as Grade 1 or 2. The most common treatment-emergent AEs reported by investigators greater than or equal to 15 percent were peripheral edema, periorbital edema, thrombocytopenia, anemia, neutropenia, diarrhea, nausea, vomiting and fatigue. Three patients, or 5 percent, discontinued avapritinib due to treatment-related AEs, and most patients, or 84 percent, have remained on treatment as of the data cutoff date.

Data Published in Nature Medicine in December 2021

Across the EXPLORER and PATHFINDER trials, 148 patients with advanced SM were enrolled as of a data cutoff date of May 27, 2020 for the EXPLORER trial and June 23, 2020 for the PATHFINDER trial. ORR was defined as CR/CRh, partial remission or clinical improvement. Response assessments were completed per central review, and all reported clinical responses were confirmed.

Clinical Activity Data. In the EXPLORER trial, 53 patients were response evaluable, and the ORR was 75 percent (95% CI: 62%, 86%). The median DOR was 38 months (95% CI: 22 months, not estimable). The estimated 24-month overall survival rate was 76 percent. Responses reported in the PATHFINDER pre-specified interim analysis of 32 evaluable patients were consistent with previously reported data. Across both studies, statistically significant improvements in patient-reported symptoms were observed, as measured by the Advanced SM Symptom Assessment Form Total Symptom Score. Avapritinib showed broad activity across all advanced SM subtypes, including SM-AHN. In the PATHFINDER trial, substantial reductions were observed in monocytosis in patients with SM and chronic myelomonocytic leukemia, and in eosinophilia in patients with SM and chronic eosinophilic leukemia, potentially reflecting the multi-lineage involvement of the KIT D816V mutation.

Safety Data. Avapritinib was generally well-tolerated, consistent with previously reported results. The most common treatment-emergent AEs included edema, thrombocytopenia, anemia, diarrhea, nausea, fatigue, vomiting,

neutropenia, headache, cognitive effects and abdominal pain. Overall, 10 percent of patients in the EXPLORER trial and 5 percent of patients in the PATHFINDER trial discontinued avapritinib due to treatment-related AEs.

Avapritinib—Phase 2 PIONEER Trial

PIONEER is a randomized, double-blind, placebo-controlled, registration-enabling trial evaluating avapritinib in patients with non-advanced 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 receive treatment with avapritinib in Part 3. Key trial endpoints include the change in patient-reported disease symptoms as measured by the Indolent SM Symptom Assessment Form Total Symptom Score, or ISM-SAF TSS, quantitative measures of mast cell burden and safety. In January 2022, we announced that the PIONEER trial was fully enrolled.

Previously reported data from Part 1 of the PIONEER trial show 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 24 weeks. We plan to report top-line data from the registration-enabling Part 2 of the PIONEER trial in mid-2022.

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 percent of patients), and RET fusions are implicated in several cancers, including papillary thyroid carcinoma (approximately 10- 20 percent of patients) and NSCLC (1-2 percent 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, or ORR, 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 are co-developing 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, Thyroid Cancers, and Other Solid Tumors

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 once daily. The dose-escalation portion of the

ARROW trial is complete, and as of December 2021, the expansion portion was fully enrolled at multiple sites in the United States, EU and Asia.

Data Presented at the American Society of Clinical Oncology Annual Meeting in June 2021

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. Response-evaluable populations comprised 216 patients with RET fusion-positive NSCLC who had measurable disease at baseline and received a starting pralsetinib dose of 400 mg once daily, and 19 patients with other RET fusion-positive solid tumors. All results were as of a data cutoff date of November 6, 2020, and all clinical responses were confirmed.

Clinical Activity Data. In 68 treatment-naïve patients with RET fusion-positive NSCLC, the ORR was 79 percent (95% CI: 68%, 88%) and the median DOR was not reached (95% CI: 9.0 months, not reached). For treatment-naïve patients, the initial study protocol limited enrollment to those determined by the investigator to be ineligible for standard platinum-based chemotherapy, which may be due to age, comorbidities or other poor prognostic factors. This eligibility restriction was removed in July 2019, with the goal of including a population more reflective of real-world practice. In an exploratory analysis of treatment-naïve patients enrolled after this expansion of inclusion criteria (n=25), the ORR was 88 percent (95% CI: 69%, 98%). In 126 patients with RET fusion-positive NSCLC who previously received platinum-based chemotherapy, the ORR was 62 percent (95% CI: 53%, 70%) and the median DOR was 22.3 months (95% CI: 15.1 months, not reached).

In a heavily pre-treated population of 19 patients with RET fusion-positive solid tumors beyond NSCLC and thyroid cancer, the ORR was 53 percent (95% CI: 29%, 76%) and the median DOR was 19.0 months (95% CI: 5.5 months, not estimable). Tumor reductions were shown in patients with the following cancers – pancreatic, cholangiocarcinoma, colon, lung except NSCLC, mesenchymal, salivary duct, sweat gland and thymus – as well as patients diagnosed with cancers of unknown primary origin. In the three patients with pancreatic cancer, a particularly difficult-to-treat tumor type, there was one complete response and two partial responses.

Safety Data. A total of 471 patients were enrolled with a pralsetinib dose starting at 400 mg once daily. Across tumor types, pralsetinib was generally well-tolerated with no new safety signals observed. The most common treatment-related AEs reported by investigators greater than or equal to 20 percent were neutropenia, increased aspartate aminotransferase, anemia, decreased white blood cell count, increased alanine aminotransferase, hypertension, constipation and asthenia. Overall, 6 percent of patients discontinued pralsetinib due to treatment-related AEs.

Data Published in The Lancet Oncology and The Lancet Diabetes and Endocrinology in June 2021

The Lancet Oncology published data from the ARROW trial in patients with RET fusion-positive NSCLC, which were consistent with results reported from an updated data cut at the 2021 ASCO Annual Meeting. *The Lancet Diabetes and Endocrinology* simultaneous published results from the ARROW trial in patients with RET-altered thyroid cancer. 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.

Clinical Activity Data. As of a data cutoff date of May 22, 2020, pralsetinib showed robust and durable antitumor activity in patients with RET-altered thyroid cancer who received a starting dose of 400 mg once daily. In 55 patients with RET-mutant MTC previously treated with cabozantinib or vandetanib, the ORR was 60 percent (95% CI: 46%, 73%) and the median DOR was not reached (95% CI: 15.1 months, not estimable). In 21 systemic treatment-naïve patients with RET-mutant MTC, the ORR was 71 percent (95% CI: 48%, 89%) and the median DOR was not reached (95% CI: not estimable, not estimable). In nine patients with RET fusion-positive thyroid cancer, the ORR was 89 percent (95% CI: 52%, 100%) and the median DOR was not reached (95% CI: not estimable, not estimable).

Safety Data. Pralsetinib was generally well-tolerated with safety results consistent with previously reported data. In 142 patients with RET-altered thyroid cancer, the most common treatment-related AEs were increased aspartate aminotransferase, decreased white blood cell count, hypertension, neutropenia, anemia, constipation, asthenia, increased alanine aminotransferase, hyperphosphatemia and lymphopenia. Four percent of patients with RET-altered thyroid cancer 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 unresectable or metastatic 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.

EGFR-Mutated NSCLC

Among the 80 to 85 percent of lung cancers classified as NSCLC, it is estimated that about 10-15 percent of cases in the U.S. and Europe, and about 40-50 percent 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, there is a significant need for new treatment options designed to prevent a broad range of resistance mechanisms before they emerge, with the goal of prolonging patient benefit. In addition, there are no approved targeted therapies for osimertinib-resistant EGFR-mutated NSCLC, and there are limited treatment options for patients with EGFR exon 20 insertion-positive NSCLC.

We are developing BLU-701 and BLU-945, in combination with each other and other agents, as well as monotherapies in certain biomarker-selected populations, for the treatment of patients with EGFR-mutated NSCLC. We initiated the Phase 1/2 HARMONY trial of BLU-701 in patients with EGFR-driven NSCLC in the fourth quarter of 2021, and initiated the Phase 1 SYMPHONY trial of BLU-945 in patients with EGFR-driven NSCLC in the second quarter of 2021.

We are developing BLU-451 for the treatment of NSCLC in patients with EGFR exon 20 insertion mutations, and we plan to initiate a Phase 1/2 trial for this patient population in the first quarter of 2022.

Cyclin E Aberrant Cancers

Cyclin dependent kinases and their cyclin partners regulate the cell cycle. In certain malignancies, CCNE1 is amplified or overexpressed, hyperactivating CDK2 and leading to cell cycle dysregulation and tumor proliferation. Data from the National Cancer Institute show that CCNE1 amplification is a primary disease driver in subsets of patients with ovarian cancer, endometrial cancer, gastric cancer and a broad range of other solid tumors. For example, approximately 20 percent of patients with ovarian serous cystadenocarcinoma harbor CCNE1 amplifications. In addition, aberrant CCNE1 is a known resistance mechanism in patients with estrogen-receptor-positive breast cancer treated with a CDK4/6 inhibitor. Studies have shown that ovarian and hormone-receptor-positive breast cancer patients with aberrant CCNE1 have poor outcomes. Collectively, these data highlight the broad potential of CDK2 as a therapeutic target.

Prior drug discovery efforts targeting CDK2 have been hindered by challenges in achieving selectivity over other CDK family members associated with toxicity. We are developing BLU-222, a selective and potent investigational

CDK2 inhibitor, for the treatment of patients with cyclin E aberrant cancers. We plan to initiate the Phase 1/2 VELA trial of BLU-222 in cyclin E aberrant cancers in the first quarter of 2022.

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 is 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 preclinical 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 the licensed product for which it retains global commercialization rights, and we and Roche will share post-Phase 1 development costs for the 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, 2021, we have achieved $23.5 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, 2021, we are eligible to receive up to approximately $319.3 million in contingent option fees and milestone payments related to specified research, preclinical, 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, 2021, we have received $105.0 million in specified regulatory and commercialization milestones. In addition to the upfront and milestone payments received through December 31, 2021, we are eligible to receive up to $822.0 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, as well as 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, 2021, we have received $23.0 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, 2021, we will be eligible to receive up to approximately $323.0 million in additional milestone payments, including $95.5 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 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, 2021, 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.

Zai Lab

On November 8, 2021, we entered into a license agreement, or the Zai Lab agreement, with Zai Lab. Under the Zai Lab agreement, we granted an exclusive license for the development and commercialization of BLU-701 and BLU-945 for the treatment of EGFR-driven NSCLC in Greater China, including Mainland China, Hong Kong, Macau and Taiwan.

We received an upfront cash payment of $25.0 million in the fourth quarter of 2021. Subject to the terms of the Zai Lab agreement, in addition to the upfront payment received, we will be eligible to receive up to $590.0 million in potential development, regulatory and sales-based milestone payments, and tiered royalties on a product-by-product basis ranging from the low-teens to mid-teens on annual net sales of BLU-701 and BLU-945 in Greater China, subject to adjustment in specified circumstances under the Zai Lab agreement.

Under the terms of the agreement, Zai Lab will be responsible for all the development costs for BLU-701 and BLU-945 occurring in Greater China.

Mergers & Acquisitions

Lengo Therapeutics, Inc.

On November 27, 2021, we entered into an Agreement and Plan of Merger, or the Merger Agreement, with Pavonis Merger Subsidiary, Inc., a Delaware corporation and our wholly-owned subsidiary, or Merger Sub, Lengo Therapeutics, Inc., a Delaware corporation, or Lengo, and Fortis Advisors LLC, a Delaware limited liability company, as the representative of the Lengo Securityholders (as defined below). On December 30, 2021, we completed the merger of Merger Sub with and into Lengo, with Lengo continuing as the surviving corporation and our wholly-owned subsidiary, or the Closing. Upon Closing we acquired Lengo's lead compound LNG-451, now known as BLU-451, which is in development for the treatment of EGFR exon 20 insertion-positive NSCLC, in addition to undisclosed preclinical precision oncology programs and research tools, including a catalog of covalent, highly brain penetrant kinase inhibitors that we plan to add

to our proprietary compound library to further enable future drug discovery efforts.

Upon Closing, we paid upfront merger consideration of $250.0 million in cash, or the Upfront Merger Consideration, to Lengo stockholders and option holders, or collectively, the Lengo Securityholders. The Merger Agreement also provided that we shall pay future contingent cash milestone payments of up to $215.0 million in the aggregate to the Lengo Securityholders upon the achievement of specified regulatory approval and sales milestones. The Upfront Merger Consideration is subject to customary net indebtedness, transaction expenses, and other adjustments, as set forth in the Merger Agreement.

The Merger Agreement also provided that approximately $25.0 million of the Upfront Merger Consideration was placed into a third party escrow account, or the Indemnification Escrow, to secure the Lengo Securityholders' obligations to indemnify us for certain matters, including breaches of representations and warranties, covenants included in the Merger Agreement, payments made by us to dissenting stockholders, specified tax claims, excess parachute claims, purchase price adjustments, and other customary matters, subject to certain specified limitations, including, among other things, limitations on the period during which we may make certain claims for indemnification and limitations on the amounts for which the Lengo Securityholders may be liable.

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 our marketed drugs 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 formulations, solid state forms, manufacturing processes, patient selection markers and diagnostic discoveries that may be useful with our drugs 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, 2022, we own or have licensed 37 issued U.S. patents, 18 pending U.S. non-provisional patent applications, 21 pending U.S. provisional applications, 62 issued foreign patents, 147 foreign pending patent applications, and 12 pending Patent Cooperation Treaty, or PCT, international patent applications related to our most advanced programs and platform technology. The foreign issued patents and pending 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, Macao, Mexico, New Zealand, Philippines, Russia, Singapore, South Africa, and Taiwan. Our issued patents and pending patent applications pertain to our marketed drugs AYVAKIT® and GAVRETO® and drug candidates, including fisogatinib, BLU-263, BLU-945, BLU-701, BLU-451, and BLU-222 as well as novel recurrent fusions.

We file trademarks to protect our products. Typically, we file trademark applications in the U.S., Europe, and elsewhere in the world as appropriate. In addition to multiple pending trademark applications in the U.S. and other major countries, we have registered trademarks, including but not limited to AYVAKIT and GAVRETO in the U.S. and to AYVAKYT in the EU.

The intellectual property portfolios for our approved drugs and most advanced programs as of January 31, 2022 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. In addition to patents and trademarks for our drug products, we seek to obtain all available regulatory exclusivities for our marketed products, including data and orphan exclusivities in the relevant jurisdictions.

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 solid forms, methods of use and manufacture. As of January 31, 2022, the portfolio contains 12 issued U.S. patents, 16 issued foreign patents, including one European patent validated in 38 countries, four pending U.S. non-provisional patent applications, three pending U.S. provisional applications, four pending PCT international patent applications and 51 pending foreign patent applications. The patents that have issued or will issue covering our KIT and PDGFRA program will have a statutory expiration date between 2034 and 2042. Patent term adjustments, patent term extensions, and supplementary protection certificates 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 thereof, compositions of matter for RET inhibitors with different compound families, as well as solid forms, formulations, methods of use and manufacture. As of January 31, 2022, the portfolio contains seven issued U.S. patents, five pending U.S. non-provisional patent applications, two U.S. provisional patent applications, three pending PCT international applications, 58 pending foreign patent applications and nine issued foreign patents. The patents that have issued or will issue covering our RET program will have a statutory expiration date between 2036 and 2042. Patent term adjustments, patent term extensions, and supplementary protection certificates 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, 2022, the patent portfolio for our FGFR4 program, including fisogatinib contains nine issued U.S. patents, two pending U.S. non-provisional patent applications, one pending PCT international application, 21 pending foreign patent applications and 29 issued foreign patents. 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, patent term extensions, and supplementary protection certificates could result in later expiration dates.

EGFR Program

The intellectual property portfolio for our EGFR program contains patent applications directed to compositions of matter for BLU-945, BLU-701, BLU-451 and analogs thereof, compositions of matter for EGFR inhibitors with different compound families, as well as solid forms, formulations, methods of use and manufacture. As of January 31, 2022, we owned one issued U.S. patent, one pending U.S. non-provisional patent application, 13 pending U.S. provisional applications, four pending PCT international patent applications and 14 pending foreign patent applications and two issued foreign patents, including one European patent validated in 6 countries directed to our EGFR program, including BLU-945, BLU-701, and BLU-451. The patents that have issued or will issue covering our EGFR program will have a statutory expiration date between 2034 and 2042. Patent term adjustments, patent term extensions, and supplementary protection certificates could result in later expiration dates.

CDK2 Program

The intellectual property portfolio for our CDK2 program contains patent applications directed to compositions of matter for CDK2 inhibitors for BLU-222 and analogs thereof, compositions of matter for CDK2 inhibitors with different compound families, as well as methods of use. As of January 31, 2022, we owned three pending U.S. provisional applications. The patents that will issue covering our CDK2 program will have a statutory expiration date of 2042. Patent term adjustments, patent term extensions, and supplementary protection certificates 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, 2022, the patent portfolio directed to our platform contains eight issued U.S. patents, six pending U.S. non-provisional patent applications, three pending European Union patent applications and six issued European patents. 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.

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

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

AYVAKIT/AYVAKYT faces competition for advanced SM from Novartis AG's midostaurin and imatinib, and may face competition from drug candidates in development, including that being developed by Cogent Biosciences, Inc. We are developing avapritinib for non-advanced SM, and we are developing BLU-263 for the treatment of non-advanced SM and other mast cell disorders. If avapritinib and BLU-263 are approved for non-advanced SM, they may face competition from drug candidates in development, 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.

EGFR-Mutated NSCLC

We are developing BLU-701 and BLU-945 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, BLU-701 and BLU-945 may face competition from drug candidates in development for EGFR-mutated NSCLC, including those being developed by Allist Pharmaceuticals, Arrivent Biopharma, Inc., Betta Pharmaceuticals, Black Diamond Therapeutics, Inc., Boehringer Ingelheim RCV GmbH & Co KG, Bridge Biotherapeutics, Inc., Centessa Pharmaceuticals plc, C4 Therapeutics, Inc., Chia Tai Tianqing Pharmaceutical Group, Daiichi Sankyo Company, Limited, Janssen Pharmaceuticals, Inc., Kanaph Therapeutics and Theseus Pharmaceuticals, Inc.

We are developing BLU-451 for EGFR exon 20 insertion-positive NSCLC, which, if approved, will face competition from Janssen Pharmaceuticals, Inc. and Takeda Pharmaceuticals. In addition, BLU-451 may face competition from drug candidates in development for EGFR exon 20 insertion-positive NSCLC, including those being developed by Abbisko Therapeutics Co., Ltd., Bayer AG, Black Diamond Therapeutics, Inc., Centessa Pharmaceuticals plc, Cullinan Oncology, Inc., Daiichi Sankyo Company, Limited, Dizal Pharmaceutical Co. Ltd., Shenzhen Forward Pharmaceutical Co., Ltd., Shanghai Junshi Biosciences Co., Ltd., Oric Pharmaceuticals, Inc. and Scorpion Therapeutics, Inc.

Cyclin E Aberrant Cancers

We are developing BLU-222 for cyclin E aberrant cancers, which, if approved, will face competition from indication-specific therapies such as Genentech's bevacizumab, AstraZeneca and Merck's olaparib, Clovis Oncology's rucaparib, GSK's niraparib, Merck's pembrolizumab, and Eisai's lenvatinib. In addition, BLU-222 may face competition from drug candidates in development for cyclin E aberrant cancers, including those being developed by ARC Therapeutics, Inc., Cedilla Therapeutics, Inc., Cyclacel Pharmaceuticals Inc., Monte Rosa Therapeutics, Inc., Nuvation Bio, Inc., Regor Therapeutics Inc., Pfizer Inc., AstraZeneca plc, Zentalis Pharmaceuticals, Inc. and Repare Therapeutics, Inc.

Advanced Cancers

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

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 blood 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 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 blood 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 preclinical 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, BLU-945, BLU-701, BLU-222 and BLU-451 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, including for avapritinib in order to identify GIST patients with the PDGFRA D842V mutation and pralsetinib in order to identify NSCLC patients with RET fusions. We 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 preclinical laboratory tests, animal studies and formulation studies performed in accordance with applicable regulations, including the FDA's good laboratory practice, or GLP, regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin and must be actively maintained, including by submitting 15- or 7-day safety reports and annual safety reports;
- performance of adequate and well-controlled human clinical trials in accordance with applicable IND and other clinical trial-related regulations, sometimes referred to as good clinical practices, or GCPs, to establish the safety and efficacy of the proposed drug for its proposed indication;
- submission to the FDA of an NDA for a new drug;
- a determination by the FDA within 60 days of its receipt of an NDA to file the NDA for review;
- review of the drug candidate by an FDA advisory committee, where appropriate or if applicable;
- payment of user fees for FDA review of the NDA (unless a fee waiver applies);
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the API and finished drug product are produced to assess compliance with the FDA's current good manufacturing practice, or cGMP, requirements, where appropriate or if applicable;
- potential FDA audit of the preclinical study sites and/or clinical trial sites that generated the data in support of the NDA; and
- FDA review and approval of the NDA prior to any commercial marketing or sale of the drug in the U.S.

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

The clinical stage of development involves the administration of the drug candidate to healthy volunteers and/or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial

sponsor's control, in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety and assess efficacy. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Further, each clinical trial must be reviewed and approved by an independent institutional review board, or IRB, at or servicing each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of trial participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed. There are also requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries. Failure to timely register a clinical trial or to submit study results to such public registries can give rise to civil monetary penalties and also prevent a non-compliant party from receiving future grant funds from the federal government.

Clinical trials are generally conducted in three sequential phases that may overlap or be combined, known as Phase 1, Phase 2 and Phase 3 clinical trials. Phase 1 clinical trials 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 AEs and safety risks and preliminary evaluation of efficacy. Phase 3 clinical trials generally involve large numbers of patients (from several hundred to several thousand subjects) at multiple sites, in multiple countries and are designed to provide the data necessary to demonstrate the efficacy of the drug for its intended use, 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 preclinical studies and clinical trials are then submitted to the FDA as part of an NDA, along with proposed labeling for the drug and information about the manufacturing process and facilities that will be used to ensure drug quality, results of analytical testing conducted on the chemistry of the drug, and other relevant information. The NDA is a request for approval to market the drug and must contain adequate evidence of safety and efficacy, which is demonstrated by extensive preclinical and clinical testing. The application includes both negative or ambiguous results of preclinical studies and clinical trials as well as positive findings. Data may come from company-sponsored clinical trials intended to test the safety and efficacy of a use of a drug, or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of the investigational drug product to the satisfaction of the FDA. FDA approval of an NDA must be obtained before a drug may be offered for sale in the U.S.

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

Under the Prescription Drug User Fee Act, or PDUFA, as amended, each NDA must be accompanied by a user fee. 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, preclinical studies or manufacturing. If a Complete Response Letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, withdraw the application or request a hearing. Even if such data and information is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. 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 preclinical or preliminary clinical data demonstrates the potential to address an unmet medical need. The FDA will determine that a product will fill an unmet medical need if it will provide a therapy where none exists or provide a therapy that may be potentially superior to existing therapy based on efficacy or safety factors.

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

In addition, drugs studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval and may be approved on the basis of adequate and well-controlled clinical trials establishing that the drug has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require a sponsor of a drug receiving accelerated approval to perform post-marketing studies to verify and describe the predicted effect on

irreversible morbidity or mortality or other clinical endpoint, and 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 preclinical studies, early phase clinical trials, and/or other clinical development programs.

Post-Marketing Requirements

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

In the U.S., once a drug is approved, its manufacture is subject to comprehensive and continuing regulation by the FDA. The FDA regulations require that drugs be manufactured in specific approved facilities and in accordance with cGMP. We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our drugs in accordance with cGMP regulations. cGMP regulations require among other things, quality control and quality assurance as well as the corresponding maintenance of records and documentation and the obligation to investigate and correct any deviations from cGMP. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs 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 preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness. Orphan drug exclusivity, as described below, may offer a seven-year period of marketing exclusivity, except in certain circumstances. Pediatric exclusivity is another type of regulatory market exclusivity in the U.S. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods 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 EU, 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 EU 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 when, without incentives, it is unlikely that sales of the drug in the EU would be sufficient to justify the necessary investment in developing the drug or biological product.

In 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 EU, orphan medicinal product designation also entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity is granted following 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, including for avapritinib in order to identify GIST patients with the PDGFRA D842V mutation and pralsetinib in order to identify NSCLC patients with RET fusions. 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, preclinical 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, preclinical, 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 Member States of the EU plus Norway, Iceland and Liechtenstein), *in vitro* diagnostic medical devices are currently required to conform with the general safety and performance requirements of the E.U. Directive on *in vitro* diagnostic medical devices (Directive No 98/79/EC, as amended), however the new in-vitro diagnostics Regulation (Regulation (EU) 2017/746) will apply from 26 May 2022. Until then, manufacturers can opt to place in-vitro diagnostic devices on the market under Directive 98/79/EC or under the new Regulation if they fully comply with it. To demonstrate compliance with the general safety and performance 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 EU 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 EU.

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.

Clinical Trial Approval

In April 2014, the EU adopted a new Clinical Trials Regulation (EU) No 536/2014, or the Clinical Trials Regulation, which replaced the current Clinical Trials Directive 2001/20/EC on 31 January 2022. The Clinical Trials Regulation is directly applicable in all EU Member States meaning no national implementing legislation in each EU Member State is required. It overhauls the current system of approvals for clinical trials in the EU. Specifically, the new legislation 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 UK and the EU, medicinal products can only be commercialized after obtaining a marketing authorization, or MA. There are two types of marketing authorizations:

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

drugs that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.

National MAs, which are issued by the competent authorities of the Member States of the EU and only cover their respective territory, are available for products not falling within the mandatory scope of the centralized procedure. Where a product has already been authorized for marketing in a Member State of the EU, this national MA can be recognized in another Member State through the mutual recognition procedure. If the product has not received a national MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the decentralized procedure. Under the decentralized procedure an identical dossier is submitted to the competent authorities of each of the Member States in which the MA is sought, one of which is selected by the applicant as the reference member state, or RMS.

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

Now that the UK (which comprises Great Britain and Northern Ireland) has left the EU, Great Britain will no longer be covered by centralized MAs (under the Northern Ireland Protocol, centralized MAs will continue to be recognized in Northern Ireland). All medicinal products with a current centralized MA were automatically converted to Great Britain MAs on January 1, 2021. For a period of two years from January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or MHRA, the UK medicines regulator, may rely on a decision taken by the European Commission on the approval of a new marketing authorization in the centralized procedure, in order to more quickly grant a new Great Britain MA. A separate application will, however, still be required.

European Pediatric Investigation Plan

In the EU, 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 Data and Market Exclusivity

In the EU, 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 EU from referencing the innovator's data to assess a biosimilar or generic application for eight years, after which a biosimilar or generic marketing authorization can be submitted, and the innovator's data may be referenced, but not marketed 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.

European Orphan Drug Designation and Exclusivity

Regulation (EC) No. 141/2000, as implemented by Regulation (EC) No. 847/2000 provides that a drug can be designated as an orphan drug by the European Commission if its sponsor can establish: that (1) the product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (2) either (a) such

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

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

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

Regulatory Requirements After a Marketing Authorization has been Obtained

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

- Compliance with the EU's stringent pharmacovigilance or safety reporting rules must be ensured. These rules can impose post-authorization studies and additional monitoring obligations.
- The manufacturing of authorized medicinal products, for which a separate manufacturer's license is mandatory, must also be conducted in strict compliance with the applicable EU laws, regulations and guidance, including Directive 2001/83/EC, Directive 2003/94/EC, Regulation (EC) No 726/2004 and the European Commission Guidelines for Good Manufacturing Practice. These requirements include compliance with EU cGMP standards when manufacturing medicinal products and active pharmaceutical ingredients, including the manufacture of active pharmaceutical ingredients outside of the EU with the intention to import the active pharmaceutical ingredients into the EU.
- The marketing and promotion of authorized drugs, including industry-sponsored continuing medical education and advertising directed toward the prescribers of drugs and/or the general public, are strictly regulated in the EU. Direct-to-consumer advertising of prescription medicines is prohibited across the EU.

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

Brexit and the Regulatory Framework in the United Kingdom

On June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the EU, commonly referred to as Brexit, and the UK formally left the EU on January 31, 2020. There was a transition period during which EU pharmaceutical laws continued to apply to the UK, which expired on December 31, 2020. However, the EU and the UK have concluded a trade and cooperation agreement, or TCA, which was provisionally applicable since January 1, 2021 and has been formally applicable since May 1, 2021. The TCA includes specific provisions concerning pharmaceuticals, which include the mutual recognition of GMP, inspections of manufacturing facilities for medicinal products and GMP documents issued, but does not foresee wholesale mutual recognition of UK and EU pharmaceutical regulations. At present, Great Britain has implemented EU legislation on the marketing, promotion and sale of medicinal products through the Human Medicines Regulations 2012 (as amended) (under the Northern Ireland Protocol, the EU regulatory framework will continue to apply in Northern Ireland). The regulatory regime in Great Britain therefore currently aligns with EU regulations, however it is possible that these regimes will diverge in future now that Great Britain's regulatory

system is independent from the EU and the TCA does not provide for mutual recognition of UK and EU pharmaceutical legislation.

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.

In addition to federal regulation, many states have begun to focus on efforts to regulate privacy and data security. For example, in California the California Consumer Protection Act, or CCPA, which went into effect on January 1, 2020, 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 CCPA, other personal information that we process may be subject to the CCPA and possible changes to the CCPA may broaden its scope.

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

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 and drug candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue. Factors payors consider in determining reimbursement are based on whether the product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

Further, due to the ongoing 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, included aggregate reductions of Medicare payments to providers of 2% per fiscal year. These reductions went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022 due to the COVID-19 pandemic. Following the temporary suspension, a 1% payment reduction will occur beginning April 1, 2022 through June 30, 2022, and the 2% payment reduction will resume on July 1, 2022.

In March 2010, the Affordable Care Act became law in the United States. The goal of the Affordable Care Act is to reduce the cost of healthcare and substantially change the way healthcare is financed by both governmental and private insurers. The Affordable Care Act, among other things, increases minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extends the rebate program to individuals enrolled in Medicaid managed care organizations, establishes annual fees and taxes on manufacturers of certain branded prescription drugs and biologic products, and creates a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (increased to 70%, effective January 1, 2019, by the Bipartisan Budget Act of 2018) 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 judicial, Congressional and executive challenges to certain aspects of the Affordable Care Act. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the Affordable Care Act brought by several states without specifically ruling on the constitutionality of the Affordable Care Act. Prior to the Supreme Court's decision, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the Affordable Care Act marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the Affordable Care Act. It is unclear how other healthcare reform measures of the Biden administration or other efforts, if any, to challenge, repeal or replace the Affordable Care Act will impact our business.

Prior to the Biden administration, on October 13, 2017, former President Trump signed an Executive Order terminating the cost-sharing subsidies that reimburse insurers under the Affordable Care Act. The former Trump administration concluded that cost-sharing reduction, or CSR, payments to insurance companies required under the Affordable Care Act have not received necessary appropriations from Congress and announced that it will discontinue

these payments immediately until those appropriations are made. 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, other legislative and regulatory changes have been proposed and adopted in the United States since the ACA was enacted:

- On April 13, 2017, CMS published a final rule that gives states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces.

- On May 30, 2018, the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a pharmaceutical manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.

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

- On December 20, 2019, former President Trump signed into law the Further Consolidated Appropriations Act (H.R. 1865), which repealed the Cadillac tax, the health insurance provider tax, and the medical device excise tax. It is impossible to determine whether similar taxes could be instated in the future.

Additionally, there has been increasing legislative and enforcement interest in the United States with respect to drug pricing practices. Specifically, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, and review the relationship between pricing and manufacturer patient programs. At a federal level, President Biden signed an Executive Order on July 9, 2021 affirming the administration's policy to (i) support legislative reforms that would lower the prices of prescription drug and biologics, including by allowing Medicare to negotiate drug prices, by imposing inflation caps, and, by supporting the development and market entry of lower-cost generic drugs and biosimilars; and (ii) support the enactment of a public health insurance option. Among other things, the Executive Order also directs HHS to provide a report on actions to combat excessive pricing of prescription drugs, enhance the domestic drug supply chain, reduce the price that the Federal government pays for drugs, and address price gouging in the industry; and directs the FDA to work with states and Indian Tribes that propose to develop section 804 Importation Programs in accordance with the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, and the FDA's implementing regulations. FDA released such implementing regulations on September 24, 2020, which went into effect on November 30, 2020, providing guidance for states to build and submit importation plans for drugs from Canada. On September 25, 2020, CMS stated drugs imported by states under this rule will not be eligible for federal rebates under Section 1927 of the Social Security Act and manufacturers would not report these drugs for "best price" or Average Manufacturer Price purposes. Since these drugs are not considered covered outpatient drugs, CMS further stated it will not publish a

National Average Drug Acquisition Cost for these drugs. If implemented, importation of drugs from Canada may materially and adversely affect the price we receive for any of our product candidates. Further, on November 20, 2020 CMS issued an Interim Final Rule implementing the Most Favored Nation, or MFN, Model under which Medicare Part B reimbursement rates would have been be calculated for certain drugs and biologicals based on the lowest price drug manufacturers receive in Organization for Economic Cooperation and Development countries with a similar gross domestic product per capita. However, on December 29, 2021 CMS rescinded the Most Favored Nations rule. Additionally, on November 30, 2020, HHS published a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. Pursuant to court order, the removal and addition of the aforementioned safe harbors were delayed and recent legislation imposed a moratorium on implementation of the rule until January 1, 2026. Although a number of these and other proposed measures may require authorization through additional legislation to become effective, and the Biden administration may reverse or otherwise change these measures, both the Biden administration and Congress have indicated that they will continue to seek new legislative measures to control drug costs.

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

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

In addition, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the EU provides options for its member states to restrict the range of medicinal drugs for which their national health insurance systems provide reimbursement and to control the prices of medicinal drugs for human use. A member state may approve a specific price for the medicinal drug or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal drug on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical drugs will allow favorable reimbursement and pricing arrangements for any of our drugs. Historically, drugs launched in the 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.

We may be subject to federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers.

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.

Additionally, we may be subject to analogous state and foreign laws and regulations, such as state anti-kickback, false claims laws, consumer protection, and unfair competition laws, which may apply to pharmaceutical

business practices, including but not limited to, research, distribution, sales, and marketing arrangements as well as submitting claims involving healthcare items or services reimbursed by any third-party payor, including commercial insurers. Such laws are enforced by various state agencies and through private actions. Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant federal government compliance guidance that otherwise restricts payments that may be made to healthcare providers and other potential referral sources, require drug manufacturers to report information related to pricing and marketing information, such as the tracking and reporting of gifts, compensations, and other remuneration and items of value provided to physicians and other healthcare providers and entities, require the registration of pharmaceutical sales representatives, and restrict marketing practices or require disclosure of marketing expenditures. State and foreign laws also govern the privacy and security of health information in certain circumstances. Such data privacy and security laws may differ from one another in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

In the U.S., to help patients afford our approved product, we may utilize programs to assist them, including patient assistance programs and co-pay coupon programs for eligible patients. PAPs are regulated by and subject to guidance from CMS OIG. In addition, at least one insurer has directed its network pharmacies to no longer accept co-pay coupons for certain specialty drugs the insurer identified. Our co-pay coupon programs could become the target of similar insurer actions. In September 2014, the OIG of the HHS issued a Special Advisory Bulletin warning manufacturers that they may be subject to sanctions under the federal anti-kickback statute and/or civil monetary penalty laws if they do not take appropriate steps to exclude Part D beneficiaries from using co-pay coupons. Accordingly, companies exclude these Part D beneficiaries from using co-pay coupons. Further, on December 31, 2020, CMS published a new rule, effective January 1, 2023, requiring manufacturers to ensure the full value of co-pay assistance is passed on to the patient or these dollars will count toward the Average Manufacturer Price and Best Price calculation of the drug. On May 21, 2021, PhRMA sued the HHS in the U.S. District Court for the District of Columbia, to stop the implementation of the rule claiming that the rule contradicts federal law surrounding Medicaid rebates. It is unclear how the outcome of this litigation will affect the rule.

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal and state enforcement bodies have recently increased their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of investigations, prosecutions, convictions, and settlements in the healthcare industry. In November 2020, the OIG issued a Fraud Alert highlighting its view that pharmaceutical promotional speaker programs can pose a high risk of fraud and abuse. It is possible that governmental authorities will conclude that our business practices may 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 are found to be in violation of any of these laws or any other related governmental regulations that may apply to us, we may be subject to significant civil, criminal, and administrative penalties, damages, fines, individual imprisonment, disgorgement, exclusion of drugs from government funded healthcare programs, such as Medicare and Medicaid, contractual damages, reputational harm, diminished profits and future earnings, and the curtailment or restructuring of our operations, as well as additional oversight, and reporting obligations if we become subject to a corporate integrity agreement or similar settlement to resolve allegations of non-compliance with these laws. If any of the physicians or other healthcare 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, which may also adversely affect our business. Ensuring business arrangements comply with applicable healthcare laws, as well as responding to possible investigations by government authorities, can be time- and resource-consuming and can divert a company's attention from the business. Additionally, we may be subject to analogous state and foreign laws and regulations, such as state anti-kickback, false claims laws, consumer protection, and unfair competition laws, which may apply to pharmaceutical business practices, including but not limited to, research, distribution, sales, and marketing arrangements as well as submitting claims involving healthcare items or services reimbursed by any third-party payor, including commercial insurers. Such laws are enforced by various state agencies and through private actions. Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant federal government compliance guidance that otherwise restricts payments that may be made to healthcare providers and other potential referral sources, require drug manufacturers to report information related to pricing and marketing information, such as the tracking and reporting of gifts, compensations, and other remuneration and items of value provided to physicians and other healthcare providers and entities, require the registration of pharmaceutical sales representatives, and restrict marketing practices or require disclosure of marketing expenditures. State and foreign laws also govern the privacy and security of health information in certain circumstances. Such data

privacy and security laws may differ from one another in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

In the U.S., to help patients afford our approved product, we may utilize programs to assist them, including patient assistance programs and co-pay coupon programs for eligible patients. PAPs are regulated by and subject to guidance from CMS OIG. In addition, at least one insurer has directed its network pharmacies to no longer accept co-pay coupons for certain specialty drugs the insurer identified. Our co-pay coupon programs could become the target of similar insurer actions. In September 2014, the OIG of the HHS issued a Special Advisory Bulletin warning manufacturers that they may be subject to sanctions under the federal anti-kickback statute and/or civil monetary penalty laws if they do not take appropriate steps to exclude Part D beneficiaries from using co-pay coupons. Accordingly, companies exclude these Part D beneficiaries from using co-pay coupons. Further, on December 31, 2020, CMS published a new rule, effective January 1, 2023, requiring manufacturers to ensure the full value of co-pay assistance is passed on to the patient or these dollars will count toward the Average Manufacturer Price and Best Price calculation of the drug. On May 21, 2021, PhRMA sued the HHS in the U.S. District Court for the District of Columbia, to stop the implementation of the rule claiming that the rule contradicts federal law surrounding Medicaid rebates. It is unclear how the outcome of this litigation will affect the rule.

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal and state enforcement bodies have recently increased their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of investigations, prosecutions, convictions, and settlements in the healthcare industry. In November 2020, the OIG issued a Fraud Alert highlighting its view that pharmaceutical promotional speaker programs can pose a high risk of fraud and abuse. It is possible that governmental authorities will conclude that our business practices may 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 are found to be in violation of any of these laws or any other related governmental regulations that may apply to us, we may be subject to significant civil, criminal, and administrative penalties, damages, fines, individual imprisonment, disgorgement, exclusion of drugs from government funded healthcare programs, such as Medicare and Medicaid, contractual damages, reputational harm, diminished profits and future earnings, and the curtailment or restructuring of our operations, as well as additional oversight, and reporting obligations if we become subject to a corporate integrity agreement or similar settlement to resolve allegations of non-compliance with these laws. If any of the physicians or other healthcare 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, which may also adversely affect our business. Ensuring business arrangements comply with applicable healthcare laws, as well as responding to possible investigations by government authorities, can be time- and resource-consuming and can divert a company's attention from the business.

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, 2022, we had 495 full- and part-time employees globally, approximately 461 of whom are employed in the U.S. and approximately 34 are employed in foreign countries. Of those employees, 278 are engaged in research and development activities and 219 hold Doctorate or Master’s degrees. To allow us flexibility in meeting varying workflow demands, we also engage consultants and temporary workers when needed.

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

None of our U.S. employees are represented by a labor union or covered by a collective bargaining agreement. Outside the U.S., our employees in France, Germany and Italy, respectively, are covered by a collective 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, the identification of new variants of the COVID-19 virus 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. We believe the risks described below include risks that are material to us as well as other risks that may adversely affect our business, financial condition, results of operations and growth prospects. Please see review the discussion regarding some of the forward-looking statements that are qualified by these risk factors contained elsewhere in this Annual Report on Form 10-K. If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected.

Risks Related to Commercialization

We 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 been commercializing 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 are currently under review or planned in the U.S. or globally. To execute our business plan, in addition to successfully marketing and selling our approved drugs, we will need to successfully:

- establish and maintain our relationships with healthcare providers who will be treating patients who may receive our drugs and any future drugs;
- obtain and maintain adequate pricing and reimbursement for AYVAKIT/AYVAKYT, GAVRETO and any future drugs;
- gain regulatory acceptance for the development and commercialization of current or future drug candidates in our pipeline, including for additional indications or in additional geographies for marketed drugs in our portfolio;
- maintain our existing collaborations with 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.

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

Accordingly, the 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.

AYVAKIT/AYVAKYT faces competition for advanced SM from Novartis AG's midostaurin and imatinib, and may face competition from drug candidates in development, including that being developed by Cogent Biosciences, Inc. If avapritinib and BLU-263 are approved for non-advanced SM, they may face competition from drug candidates in development, 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., 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 BLU-701 and BLU-945 for treatment-resistant EGFR-mutated NSCLC, which, if approved, will face competition from AstraZeneca plc's osimertinib and aumolertinib, which is under collaboration between Jiangsu Hansoh Pharmaceutical Group Co., Ltd. and EQRX, Inc. and approved in China. In addition, BLU-701 and BLU-945 may face competition from drug candidates in development for EGFR-mutated NSCLC, including those being developed by Allist Pharmaceuticals, Arrivent Biopharma, Inc., Betta Pharmaceuticals, Black Diamond Therapeutics, Inc., Boehringer Ingelheim RCV GmbH & Co KG, Bridge Biotherapeutics, Inc., Centessa Pharmaceuticals plc, C4 Therapeutics, Inc., Daiichi Sankyo Company, Limited, Janssen Pharmaceuticals, Inc., Kanaph Therapeutics, Theseus Pharmaceuticals, Inc.

We are developing BLU-451 for EGFR exon 20 insertion-positive NSCLC, which, if approved, will face competition from Janssen Pharmaceuticals, Inc. and Takeda Pharmaceuticals. In addition, BLU-451 may face competition from drug candidates in development for EGFR exon 20 insertion-positive NSCLC, including those being developed by Abbisko Therapeutics Co., Ltd., Bayer AG, Black Diamond Therapeutics, Inc., Centessa Pharmaceuticals plc, Cullinan Oncology, Inc., Daiichi Sankyo Company, Limited, Dizal Pharmaceutical Co. Ltd., Shenzhen Forward Pharmaceutical Co., Ltd., Shanghai Junshi Biosciences Co., Ltd., Oric Pharmaceuticals, Inc., and Scorpion Therapeutics, Inc.

We are developing BLU-222 for cyclin E aberrant cancers, which, if approved, will face competition from indication-specific therapies such as Genentech's bevacizumab, AstraZeneca and Merck's olaparib, Clovis Oncology's rucaparib, GSK's niraparib, Merck's pembrolizumab, and Eisai's lenvatinib. In addition, BLU-222 may face competition from drug candidates in development for cyclin E aberrant cancers, including those being developed by ARC Therapeutics, Inc., Cedilla Therapeutics, Inc., Cyclacel Pharmaceuticals Inc., Monte Rosa Therapeutics, Inc., Nuvation Bio, Inc., Regor Therapeutics Inc., Pfizer Inc., AstraZeneca plc, Zentalis Pharmaceuticals, Inc. and Repare Therapeutics, Inc.

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

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

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

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

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

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

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

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

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

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

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

clinical trials required for regulatory approval and successful commercialization of our drug candidates, which could prompt adverse publicity or other disruptions related to current or potential participants in such programs.

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

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

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

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

- the development of our approved drugs and drug candidates may be adversely affected if we are unable to appropriately select patients for enrollment in our clinical trials;
- our drug candidates may not receive marketing approval if safe and effective use of a therapeutic drug candidate depends on an in vitro diagnostic;
- regulatory authorities may impose post-marketing requirements regarding the development and commercialization of companion diagnostic tests for our drugs and drug candidates; and

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

As a result, our business may be materially harmed.

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

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

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

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

- successful enrollment in, and initiation and completion of, clinical trials, including our ongoing and planned clinical trials for our drugs and drug candidates;
- successful initiation and completion of preclinical studies for our other drug candidates;
- successful development of any companion diagnostic tests for use with our drugs and drug candidates;
- receipt of regulatory approvals from applicable regulatory authorities and transitioning any conditional marketing authorizations to full approvals;
- in-house commercial manufacturing capabilities or arrangements with third-parties for clinical supply and commercial manufacturing, packaging and labeling and the receipt by such third-party manufacturers of requisite approvals to supply commercial inventories of our approved drugs and drug candidates;
- obtaining and maintaining patent and trade secret protection or regulatory exclusivity for our drugs and drug candidates;
- successful commercialization of our approved drugs and drug candidates, if and when approved, whether alone or in collaboration with others;
- acceptance of our approved drugs and drug candidates, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies;
- obtaining and maintaining healthcare coverage and adequate reimbursement;
- enforcing and defending intellectual property rights and claims; and
- maintaining a continued acceptable safety profile of our drugs and drug candidates following approval.

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

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

We may not be able to initiate or continue clinical trials for our drug candidates, 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 agreements with third parties to develop companion diagnostic tests for use in some of our other current or future clinical trials in order to help identify eligible patients, we may experience delays in reaching, or fail to reach, agreement on acceptable terms to develop such companion diagnostic tests. Any third parties whom we engage to develop companion diagnostic tests may experience delays or may not be successful in developing such companion diagnostic tests, furthering the difficulty in identifying patients for our clinical trials. In addition, current commercially available diagnostic tests to identify appropriate patients for our clinical trials or any approved drug candidates may become unavailable in the future.

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

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

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

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

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

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

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

- 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 ongoing COVID-19 pandemic.

As of May 26, 2021, the FDA noted it is continuing to ensure timely reviews of applications for medical products during the ongoing COVID-19 pandemic in line with its user fee performance goals and conducting mission critical domestic and foreign inspections to ensure compliance of manufacturing facilities with FDA quality standards. 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 ongoing COVID-19 pandemic and travel restrictions FDA is unable to complete such required inspections during the review period. In 2020 and 2021, a number of 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 preclinical studies or could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other regulatory authorities. As is the case with all oncology drugs, it is likely that there may be side effects associated with the use of our drugs and drug candidates. Results of our trials could reveal a high and unacceptable severity and prevalence of these or other side effects. In such an event, our trials could be suspended or terminated, and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our drugs or drug candidates for any or all targeted indications. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete clinical trials or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

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

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

- regulatory authorities may withdraw or limit their approval of such drug;
- regulatory authorities may require the addition of labeling statements, such as a “boxed” warning or a contraindication;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;

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

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

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 the treatment of moderate to severe indolent SM. In addition, the FDA previously granted breakthrough designation to our drugs, AYVAKIT and GAVRETO, for the treatment of certain patients with GIST, advanced SM 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. On May 26. 2021, 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, including due to the inability for the FDA to complete any inspections of manufacturing facilities or clinical sites that may be required for an approval.

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 EU, the European Commission grants orphan 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 five (5) in ten thousand (10,000) persons in the EU 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 EU would be sufficient to justify the necessary investment in developing the drug. In the EU, orphan medicinal product designation entitles a party to financial incentives such as reduction of fees or fee waivers.

Generally, if a drug with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the drug is entitled to a period of marketing exclusivity, which precludes the 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 EU. The EU 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. The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted. In addition, a designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. Moreover, orphan drug exclusive marketing rights in the U.S. may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process. While we intend to continue seek orphan drug designation for our drug candidates, we may never receive such designations. Even if we receive orphan drug designation for any of our drug candidates, there is no guarantee that we will enjoy the benefits of those designations.

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

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

A key element of our strategy is to use our novel target discovery engine to identify kinases that are drivers of diseases in genomically defined patient populations with high unmet medical need in order to build a pipeline of drug candidates. Although our research and development efforts to date have resulted in a pipeline of drug candidates, we may not be able to continue to identify novel kinase drivers and develop drug candidates. We may also pursue opportunities to acquire or in-license additional businesses, technologies or drugs, form strategic alliances or create joint ventures with third parties to complement or augment our existing business. 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 preclinical or clinical drug candidates or programs does not have sufficient potential to warrant the allocation of resources toward such program or drug candidate. Accordingly, we may choose not to develop a potential drug candidate or elect to suspend, deprioritize or terminate one or more of our discovery programs or preclinical or clinical drug candidates or programs. If we suspend, deprioritize or terminate a program or drug candidate in which we have invested significant resources, we will have expended resources on a program that will not provide a full return on our investment and may have missed the opportunity to have allocated those resources to potentially more productive uses, including existing or future programs or drug candidates.

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 additional products will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and other third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. In the United States, the principal decisions about reimbursement for new medicines are typically made by the Centers for Medicare & Medicaid Services, 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 other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular drugs. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for drugs. We cannot be sure that coverage will be available for any drug candidate that we commercialize and, if coverage is available, the level of reimbursement. Reimbursement may impact the demand for, or the price of, any drug candidate for which we obtain marketing approval. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any drug candidate for which we obtain marketing approval. Further, due to the ongoing COVID-19 pandemic, many individuals have lost or will be losing employer-based insurance coverage, which may adversely affect our ability to commercialize our products. It is unclear what effect, if any, American Rescue Plan and other government efforts to expand coverage will have on the number of covered individuals. See section entitled "*Business – Coverage and Reimbursement*."

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

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

The United States has enacted or proposed legislative and regulatory changes affecting the healthcare system that could prevent or delay marketing approval of our current drug candidates or any future drug candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product for which we obtain marketing approval. Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of our products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business. In the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs. For example, in March 2010, the ACA was passed, which substantially changes the way healthcare is financed by both governmental and private

insurers, and significantly impacts the U.S. pharmaceutical industry. See section entitled "*Business – Coverage and Reimbursement*."

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

We may face competition in the U.S. for our development candidates and investigational medicines, if approved, from therapies sourced from foreign countries that have placed price controls on pharmaceutical products. Proponents of drug reimportation may attempt to pass legislation that would directly allow reimportation under certain circumstances. Legislation or regulations allowing the reimportation of drugs, if enacted, could decrease the price we receive for any products that we may develop and adversely affect our future revenues and prospects for profitability.

The Creating and Restoring Equal Access to Equivalent Samples Act, or the CREATES Act, was enacted in 2019 requiring sponsors of approved new drug applications and biologics license applications to provide sufficient quantities of product samples on commercially reasonable, market-based terms to entities developing generic drugs and biosimilar biological products. The law establishes a private right of action allowing developers to sue application holders that refuse to sell them product samples needed to support their applications. If we are required to provide product samples or allocate additional resources to responding to such requests or any legal challenges under this law, our business could be adversely impacted.

Other legislative measures have also been enacted that may impose additional pricing and product development pressures on our business, and we expect that additional foreign, federal and state healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in limited coverage and reimbursement and reduced demand for our drugs and drug candidates, if approved, or additional pricing pressures.

We are currently unable to predict what additional legislation or regulation, if any, relating to the health care industry may be enacted in the future or what effect recently enacted federal legislation or any such additional legislation or regulation would have on our business. The pendency or approval of such proposals or reforms could result in a decrease in our stock price or limit our ability to raise capital or to enter into collaboration agreements for the further development and commercialization of our approved drugs and drug candidates.

Our relationships with customers and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, exclusion from government healthcare programs, contractual damages, reputational harm and diminished profits and future earnings.

Our arrangements with third-party payors and customers expose us to broadly applicable fraud and abuse and other healthcare laws and regulations, including but not limited to, the federal healthcare Anti-Kickback Statute, the False Claims Act, the federal Health Insurance Portability and Accountability Act of 1996, 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. See section entitled "*Business – Other Healthcare Laws*."

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

harm our reputation, divert the attention of management, increase our expenses and reduce the availability of assistance to our patients.

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

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

Our future profitability may depend, in part, on our ability to commercialize current or future drug candidates in foreign markets for which we may rely on collaboration with third parties. We are not permitted to market or promote any of our drug candidates before we receive regulatory approval from the applicable regulatory authority in that foreign market. To obtain separate regulatory approval in many other countries we must comply with numerous and varying regulatory requirements of such countries regarding safety and efficacy and governing, among other things, clinical trials, manufacturing, commercial sales, pricing and distribution of our drug candidates, and we cannot predict success in these jurisdictions. If we seek to develop our drug candidates or obtain approval of our drug candidates and ultimately commercialize our drug candidates in foreign markets, we would be subject to additional risks and uncertainties, including:

- our customers' ability to obtain reimbursement for our drug candidates in foreign markets;
- our inability to directly control commercial activities because we are relying on third parties;
- the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements, including the European General Data Protection Regulation 2016/679, commonly referred to as GDPR;
- different medical practices and customs in foreign countries affecting acceptance in the marketplace;
- import or export licensing requirements;
- longer accounts receivable collection times;
- longer lead times for shipping;
- language barriers for technical training;
- reduced protection of intellectual property rights in some foreign countries;
- the existence of additional potentially relevant third-party intellectual property rights;
- foreign currency exchange rate fluctuations; and
- the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute.

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

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

In some countries, particularly countries in the EU, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a drug. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our drug candidate to other available therapies. If reimbursement of our drugs is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be materially harmed.

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

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

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

Risks Related to Our Financial Position and Need for Additional Capital

We are a precision therapy company 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 preclinical studies and clinical development for our drug candidates, commencing pre-commercial activities and the commercial launches for AYVAKIT/AYVAKYT and GAVRETO, and producing the active pharmaceutical ingredient, or API, drug substance and drug product material for use in preclinical studies and clinical trials for our drug candidates and commercial sale of our approved drugs.

To date, we have financed our operations primarily through public offerings of our common stock, private placements of our convertible preferred and common stock, collaborations and a license agreement. Through December 31, 2021, we have received an aggregate of $3.0 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, $996.3 million in upfront payments and milestone payments under our collaborations with Roche, CStone and Zai, our license agreement with Clementia and our former collaboration with Alexion. In addition, since January 2020, we also have generated revenue through sales of our drug products.

Since inception, we have incurred significant operating losses, with the exception of the year ended December 31, 2020. Our net loss was $644.1 million for the year ended December 31, 2021. 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 our net loss was $347.7 million for the year ended December 31, 2019. As of December 31, 2021, we had an accumulated deficit of $1,275.4 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 substantial 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 preclinical studies, clinical trials, our compassionate use program and for use as commercial supply , as applicable;
- the scope, progress, results and costs of drug discovery, preclinical development, laboratory testing and clinical trials for our approved drugs and drug candidates;
- the costs, timing and outcome of regulatory review of marketing applications for our drug candidates, including seeking marketing approval for avapritinib and pralsetinib for additional indications or in additional geographies;
- the success of our collaborations with Roche, CStone and Zai Lab 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, CStone and Zai Lab 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, Zai Lab 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, Zai Lab 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 and sponsor the clinical trials for our approved drugs and drug candidates, CROs will conduct all of our clinical trials. As a result, many important aspects of our development programs, including their conduct and timing, will be outside of our direct control. Our reliance on third parties to conduct current or future clinical trials will also result in less direct control over the management of data developed through clinical trials than would be the case if we were relying entirely upon our own staff. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. Outside parties may:

- have staffing difficulties;
- fail to comply with contractual obligations;
- experience regulatory compliance issues;
- undergo changes in priorities or become financially distressed; or
- form relationships with other entities, some of which may be our competitors.

Some of these factors may be beyond our control. 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 preclinical, clinical and commercial supply. This reliance on third parties increases the risk that we will not have sufficient quantities of our approved drugs or drug candidates or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not currently own or operate, nor do we have any plans to establish in the future, any manufacturing facilities or personnel. We rely, and expect to continue to rely, primarily on third parties for the manufacture of our drug candidates for preclinical development and clinical testing, as well as for the commercial manufacture of our current and future drugs. This reliance on third parties increases the risk that we will not have sufficient quantities of our drugs or drug candidates or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

The facilities used by our contract 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. Manufacturers and manufacturers' facilities are required to comply with extensive FDA, and comparable foreign regulatory authority requirements, including ensuring that quality control and manufacturing procedures conform to cGMP regulations and applicable product tracking and tracing requirements. If our 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 ongoing 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, and could require comparability studies for the setup of manufacturing operations at alternative facilities. 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.

Since March 2020 when foreign and domestic inspections were largely placed on hold, the FDA has been working to resume routine surveillance, bioresearch monitoring and pre-approval inspections on a prioritized basis. Since April 2021, the FDA has conducted limited inspections and employed remote interactive evaluations, using risk management methods, to meet user fee commitments and goal dates. Ongoing travel restrictions and other uncertainties continue to impact oversight operations both domestic and abroad and it is unclear when standard operational levels will resume. The FDA is continuing to complete mission-critical work, prioritize other higher-tiered inspectional needs (e.g., for-cause inspections), and carry out surveillance inspections using risk-based approaches for evaluating public health. Should FDA determine that an inspection is necessary for approval and an inspection cannot be completed during the review cycle due to restrictions on travel, and the FDA does not determine a remote interactive evaluation to be adequate, the agency has stated that it generally intends to issue, depending on the circumstances, a complete response letter or defer action on the application until an inspection can be completed. During the COVID-19 public health emergency, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. 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 CARES Act in response to the U.S. COVID-19 pandemic. Throughout the ongoing COVID-19 pandemic, 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 ongoing 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 ongoing 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 ongoing 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 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, as well as the use of these compounds in the treatment of diseases, formulations, solid state forms, and manufacturing processes and other technologies, inventions and improvements that

are important to the development and implementation of our business. We also rely on copyright, trade secrets, know-how and continuing technological innovation to develop and maintain our proprietary and intellectual property position.

We own or license patents and patent applications that relate to our approved drugs AYVAKIT® (avapritinib) and GAVRETO® (pralsetinib) and our drug candidates fisogatinib, BLU-263, BLU-945, BLU-701, BLU-451 and BLU-222. We also own or license patents and patent applications relating to other compounds that are inhibitors of KIT and PDGFRA, FGFR4, RET, EGFR and CDK2, as well as methods of use, formulations, solid state forms, and manufacturing processes. The issued U.S. patent directed to AYVAKIT® composition of matter has a statutory expiration date in 2034, the issued U.S. patent directed to GAVRETO® composition of matter has a statutory expiration date in 2036.

As of January 31, 2022, the patent portfolio for our KIT and PDGFRA program, including AYVAKIT® and BLU-263 contains 12 issued U.S. patents, 16 issued foreign patents, including one European patent validated in 38 countries, four pending U.S. non-provisional patent applications, three pending U.S. provisional applications, four pending PCT international patent applications and 51 pending foreign patent applications. The patents that have issued or will issue covering our KIT and PDGFRA program will have a statutory expiration date between 2034 and 2042. Patent term adjustments, patent term extensions, and supplementary protection certificates could result in later expiration dates.

As of January 31, 2022, the patent portfolio for our RET program, including GAVRETO® contains seven issued U.S. patents, five pending U.S. non-provisional patent applications, two U.S. provisional patent applications, three pending PCT international applications, 58 pending foreign patent applications and nine issued foreign patents. The patents that have issued or will issue covering our RET program will have a statutory expiration date between 2036 and 2042. Patent term adjustments, patent term extensions, and supplementary protection certificates could result in later expiration dates.

As of January 31, 2022, the patent portfolio for our FGFR4 program, including fisogatinib contains nine issued U.S. patents, two pending U.S. non-provisional patent applications, one pending PCT international application, 21 pending foreign patent applications and 29 issued foreign patents. 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, patent term extensions, and supplementary protection certificates could result in later expiration dates.

As of January 31, 2022, the patent portfolio for our EGFR program, including BLU-945, BLU-701, and BLU-451 contains one issued U.S. patent, one pending U.S. non-provisional patent application, 13 pending U.S. provisional applications, four pending PCT international patent applications and 14 pending foreign patent applications and two issued foreign patents, including one European patent validated in 6 countries directed to our EGFR program, including BLU-945, BLU-701, and BLU-451. The patents that have issued or will issue covering our EGFR program will have a statutory expiration date between 2034 and 2042. Patent term adjustments, patent term extensions, and supplementary protection certificates could result in later expiration dates.

As of January 31, 2022, the patent portfolio for our CDK2 program, including BLU-222 contains three pending U.S. provisional applications. The patents that will issue covering our CDK2 program will have a statutory expiration date of 2042. Patent term adjustments, patent term extensions, and supplementary protection certificates could result in later expiration dates.

The intellectual property portfolio directed to our platform includes patents and 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, 2022, the patent portfolio directed to our platform contains eight issued U.S. patents, six pending U.S. non-provisional patent applications, three pending European Union patent applications and six issued European patents. 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 and licensed patent portfolio may not provide us with adequate and continuing patent protection sufficient to exclude others from commercializing drugs similar or identical to our drugs and drug candidates, including generic versions of such drugs or drug candidates.

Other parties have developed technologies that may be related or competitive to our own, and such parties may have filed or may file patent applications, or may have received or may receive patents, claiming inventions that may overlap or conflict with those claimed in our own patent applications or issued patents, with respect to either the same methods or formulations or the same subject matter, in either case, that we may rely upon to dominate our patent position in the market. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the U.S. and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we were the first-to-file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights cannot be predicted with any certainty. For example, we are aware of 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 small molecule therapeutics. Some of these patent applications have already been allowed or issued, and others may issue in the future. For example, we are aware of 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 ongoing COVID-19 pandemic.

Due to the continued evolution and uncertain global impacts of the ongoing COVID-19 pandemic and the identification of new variants of COVID-19, we cannot precisely determine or quantify the impact this pandemic will have on our business, operations and financial performance. The extent to which the ongoing COVID-19 pandemic 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 ongoing 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 ongoing 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, commercial, business development, financial and legal expertise of our executive officers, as well as the other principal members of our management, scientific and clinical team. Although we have entered into employment agreements with our executive officers, each of our executive officers may terminate their employment with us at any time. In addition, insurance coverage is increasingly expensive, including with respect to directors and officers liability insurance, or D&O insurance. We may

not be able to maintain D&O insurance at a reasonable cost or in an amount adequate to satisfy any liability that may arise. An inability to secure and maintain D&O insurance may make it difficult for us to retain and attract talented and skilled directors and officers to serve our company, which could adversely affect our business. We do not maintain "key person" insurance for any of our executives or other employees.

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

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

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

As of January 31, 2022, we had 495 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 ongoing 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, as the UK regulatory system is now independent from the EU, Brexit could result in the UK significantly altering its regulations affecting the clearance or approval of our drug or drug candidates that are developed in the UK. Any new regulations could add time and expense to the conduct of our business, as well as the process by which our drug candidates receive regulatory approval in the UK, as compared to the European Union and elsewhere.

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. Notably, for example, on May 25, 2018, the European General Data Protection Regulation 2016/679, which is commonly referred to as GDPR, took effect. The GDPR applies to any company established in the EEA as well as any company outside the EEA that collects or otherwise processes personal data in connection with the offering goods or services to individuals in the EEA or the monitoring of their behavior. The GDPR enhances data protection obligations for processors and controllers of personal data, including, for example, expanded disclosures about how personal information is to be used, 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 EEA.

Further, European data protection laws also prohibit the transfer of personal data from the EEA and Switzerland to third countries that are not considered to provide adequate protections are provided for personal data, including the U.S. With regard to transfers of personal data from the EEA, transfers to third countries that have not been approved as "adequate" are prohibited unless an appropriate safeguard specified by the GDPR is implemented, such as the Standard Contractual Clauses, or SCCs, approved by the European Commission or binding corporate rules, or a derogation applies. In 2020, the Court of Justice of the European Union, or the CJEU, deemed that transfers made pursuant to the EU SCCs and other alternative transfer mechanisms, including binding corporate rules, need to be analyzed on a case-by-case basis to ensure EU standards of data protection are met in the jurisdiction where the data importer is based, and there continue to be concerns about whether these transfer mechanisms will face additional challenges. European regulators have issued recent guidance following the CJEU case that imposes significant new diligence requirements on transferring data outside the European Union, including under an approved transfer mechanism. This guidance requires an "essential equivalency" assessment of the laws of the destination country transferred. If essentially equivalent protections are not available in the destination country, the exporting entity must then assess if supplemental measures can be put in place that, in combination with the chosen transfer mechanism, would address the deficiency in the laws and ensure that essentially equivalent protection can be given to the data.

On June 4, 2021, the European Commission issued new SCCs that account for the CJEU's decision and other developments, which need to be put in place for new contracts involving the transfer of personal data from the European Economic Area to a third country as of September 27, 2021, and incorporated into existing contracts by December 27, 2022. Complying with these obligations and applicable guidance regarding cross-border data transfers could be expensive and time consuming, may require us to modify our data handling policies and procedures and may ultimately prevent or restrict us from transferring personal data outside the European Economic Area which could cause significant business disruption.

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

In addition, we are subject to Swiss data protection laws, including the Federal Act on Data Protection, or the FADP. While the FADP provides broad protections to personal data, on September 25, 2020, the Swiss federal Parliament enacted a revised version of the FADP, which is anticipated to become effective in 2022 or the beginning of 2023. The new version of the FADP aligns Swiss data protection law with the GDPR.

Further, in addition to existing European data protection law, the European Union also is considering another draft data protection regulation. The proposed regulation, known as the Regulation on Privacy and Electronic Communications, or ePrivacy Regulation, would replace the current ePrivacy Directive. The Draft Regulation is still the subject of negotiations between the Council of the European Union and the European Parliament. An update is expected in 2022. The aim is for the Draft Regulation to be in force some time in 2023. New rules related to the ePrivacy Regulation are likely to include enhanced consent requirements in order to use communications content and communications metadata, as well as obligations and restrictions on the processing of data from an end-user's terminal equipment, which may negatively impact our product offerings and our relationships with our customers.

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

As another prominent example, we are also subject to data protection regulation in the UK. Following the UK's withdrawal from the EU on January 31, 2020 and the end of the transitional arrangements agreed between the UK and EU as of January 1, 2021, the GDPR has been incorporated into UK domestic law by virtue of section 3 of the European Union (Withdrawal) Act 2018 and amended by the Data Protection, Privacy and Electronic Communications (Amendments etc.) (EU Exit) Regulations 2019, or the UK GDPR. United Kingdom-based organizations doing business in the European Union will need to continue to comply with the GDPR. Although the UK is regarded as a third country under the EU's GDPR, the European Commission has now issued a decision recognizing the UK as providing adequate protection under the EU GDPR and, therefore, transfers of personal data originating in the EU to the UK remain unrestricted. Like the EU GDPR, the UK GDPR restricts personal data transfers outside the UK to countries not regarded by the UK as providing adequate protection. The UK government has confirmed that personal data transfers from the UK to the EEA remain free flowing. The UK data protection authority has issued draft guidance on a mechanism governing transfers of personal data from UK to third countries, which incorporates the EU SCCs through an addendum. The aim is for the guidance to be finalised in the first half of 2022. Non-compliance with the UK GDPR may result in monetary penalties of up to £17.5 million or 4% of worldwide revenue, whichever is higher. Although the UK is regarded as a third country under the EU's GDPR, the European Commission has now issued a decision recognizing the UK as providing adequate protection under the EU GDPR and, therefore, transfers of personal data originating in the EU to the UK remain unrestricted. Like the EU GDPR, the UK GDPR restricts personal data transfers outside the UK to countries not regarded by the UK as providing adequate protection. The UK government has confirmed that personal data transfers from the UK to the EEA remain free flowing.

In addition to European data protection requirements, we are subject to the California Consumer Privacy Act, or CCPA, which took effect on January 1, 2020 and imposes sweeping privacy and security obligations on many companies doing business in California and provides for substantial fines for non-compliance and, in some cases, a private right of action to consumers who are victims of data breaches involving their unredacted or unencrypted personal information. While there is currently an exception for protected health information that is subject to HIPAA and clinical trial regulations, as currently written, the CCPA may impact our business activities. The CCPA became enforceable as of July 1, 2020, but there continues to be uncertainty about how the law will be interpreted and enforced.

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

Also, on March 2, 2021, Virginia enacted the Consumer Data Protection Act, or CDPA. The CDPA will become effective January 1, 2023. The CDPA will regulate how businesses, which the CDPA refers to as "controllers", collect and share personal information. The law applies to companies that conduct business in Virginia or product products or services that are targeted to residents of Virginia and either: (1) annually control or process personal data of at least 100,000 Virginia residents; or (2) control or process the personal data of at least 25,000 Virginia residents and derive over 50% of gross revenue from the sale of personal data. While the CDPA incorporates many similar concepts of the CCPA and CPRA, there are also several key differences in the scope, application, and enforcement of the law that will change the operational practices of controllers. The new law will impact how controllers collect and process personal sensitive data, conduct data protection assessments, transfer personal data to affiliates, and respond to consumer rights requests. In addition, on July 8, 2021, Colorado's governor signed the Colorado Privacy Act, or CPA, into law. The CPA is rather similar to the Virginia's CPDA but also contains additional requirements. The new measure applies to companies conducting business in Colorado or who produce or deliver commercial products or services intentionally targeted to its residents of the state and that either: (1) control or process the personal data of at least 100,000 Colorado residents during a calendar year; or (2) derive revenue or receive a discount on the price of goods or services from the sale of personal data and process or control the personal data of at least 25,000 Colorado residents.

With the CPA, Colorado became the third state to enact a comprehensive privacy law but it is quite possible that other states will follow suit and bills have been proposed in many states. We expect anticipate that more states to may enact legislation similar to the CCPA and the other recent consumer privacy laws. Such proposed legislation, if enacted, may add additional complexity, variation in requirements, restrictions and potential legal risk, require additional investment of resources in compliance programs, impact strategies and the availability of previously useful data and could result in increased compliance costs and/or changes in business practices and policies. The existence of comprehensive privacy laws in different states in the country will make our compliance obligations more complex and costly and may increase the likelihood that we may be subject to enforcement actions or otherwise incur liability for noncompliance.

The increasing number and complexity of regional, country and U.S. state data protection laws, and other changes in laws or regulations across the globe, especially those associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could lead to government enforcement actions and significant penalties against us and could have a material adverse effect on our business, financial condition or results of operations.

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

We are exposed to the risk that our employees, principal investigators, CROs and consultants may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violate the regulations of the FDA and other regulatory authorities, including those laws requiring the reporting of true, complete and accurate information to such authorities; healthcare fraud and abuse laws and regulations in the U.S. and abroad; or laws that require the reporting of financial information or data accurately. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Activities subject to these laws also involve the improper use of information obtained in the course of clinical trials or creating fraudulent data in our preclinical studies or clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of conduct applicable to all of our employees, but it is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from

governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. In addition, we are subject to the risk that a person could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

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

We may acquire or in-license additional businesses, technologies or platforms, approved drugs, drug candidates or discovery-stage programs, or form strategic alliances, collaborations or partnerships that we believe will complement or augment our existing business. If we acquire businesses with promising markets or technologies, we may not be able to realize the benefit of acquiring such businesses if we are unable to successfully integrate them with our existing operations and company culture. We may encounter numerous difficulties in developing, manufacturing and marketing any new drugs or drug candidates resulting from a strategic alliance, collaboration, partnership or acquisition that delay or prevent us from realizing their expected benefits or enhancing our business. In addition, we cannot assure you that, following any such transaction, we will achieve the expected synergies to justify the transaction.

We may be subject to adverse legislative or regulatory tax changes that could negatively impact our financial condition.

The rules dealing with U.S. federal, state and local income taxation are constantly under review by persons involved in the legislative process and by the IRS and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect our stockholders or us. We assess the impact of various tax reform proposals and modifications to existing tax treaties in all jurisdictions where we have operations to determine the potential effect on our business and any assumptions we have made about our future taxable income. We cannot predict whether any specific proposals will be enacted, the terms of any such proposals or what effect, if any, such proposals would have on our business if they were to be enacted. For tax years beginning after December 31, 2021, the Tax Cuts and Jobs Act of 2017 eliminates the once available option to deduct research and development expenditures currently and requires taxpayers to amortize them over five years. The U.S. Congress is considering legislation that would defer the amortization requirement to future periods; however, we have no assurance that the provision will be repealed or otherwise modified. If the requirement is not repealed or modified, it will have a material impact on our cash flows beginning in 2022.

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, 2022. 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 year 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. We did not sell any shares of common stock under the sales agreement during the year ended December 31, 2021. 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 substantial costs as a result of operating as a public company, and our management is required to devote substantial time to new compliance initiatives and corporate governance practices.

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

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, 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 (the Code), if a corporation undergoes an "ownership change" (generally defined as a greater than 50% change (by value) in the ownership of its equity over a three-year period), the corporation's ability to use its pre-change net operating loss carryforwards and certain other pre-change tax attributes to offset its post-change income may be limited. We may have experienced such ownership changes in the past, and we may experience ownership changes in the future as a result of shifts in our stock ownership, some of which are outside our control. As of December 31, 2021, we had federal net operating loss carryforwards of approximately $872.6 million, and our ability to utilize those net operating loss carryforwards could be limited by an "ownership change" as described above, which could result in increased tax liability to us. In addition, pursuant to the TCJA, we may not use net operating loss carry-forwards generated in taxable years beginning after December 31, 2017 to reduce our taxable income in any year beginning after December 31, 2020 by more than 80%, and we may not carry back any net operating losses to prior years. These rules apply regardless of the occurrence of an ownership change.

With respect to the net operating losses and research and development tax credit carryforwards acquired from the acquisition of Lengo, the Company has not completed a study to assess whether an ownership change under Section 382 of the Code has occurred, or whether there have been multiple ownership changes since Lengo's formation. Accordingly, the Company's ability to utilize the aforementioned carryforwards may be limited and in turn, may not be able to take full advantage of these carryforwards for U.S. federal or state income tax purposes.

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 139,216 rentable square feet of office and laboratory space under a lease that will expire on November 30, 2029, unless terminated sooner.

We also lease approximately 39,000 rentable square feet at our former corporate headquarters at 38 Sidney Street in Cambridge, Massachusetts under a lease that was extended on December 15, 2021. The extended lease will expire on November 30, 2029. Since the first quarter of 2018, we have subleased these premises, and the term of the existing subleases will expire on February 28, 2022 and September 30, 2022.

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, 2022, 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.

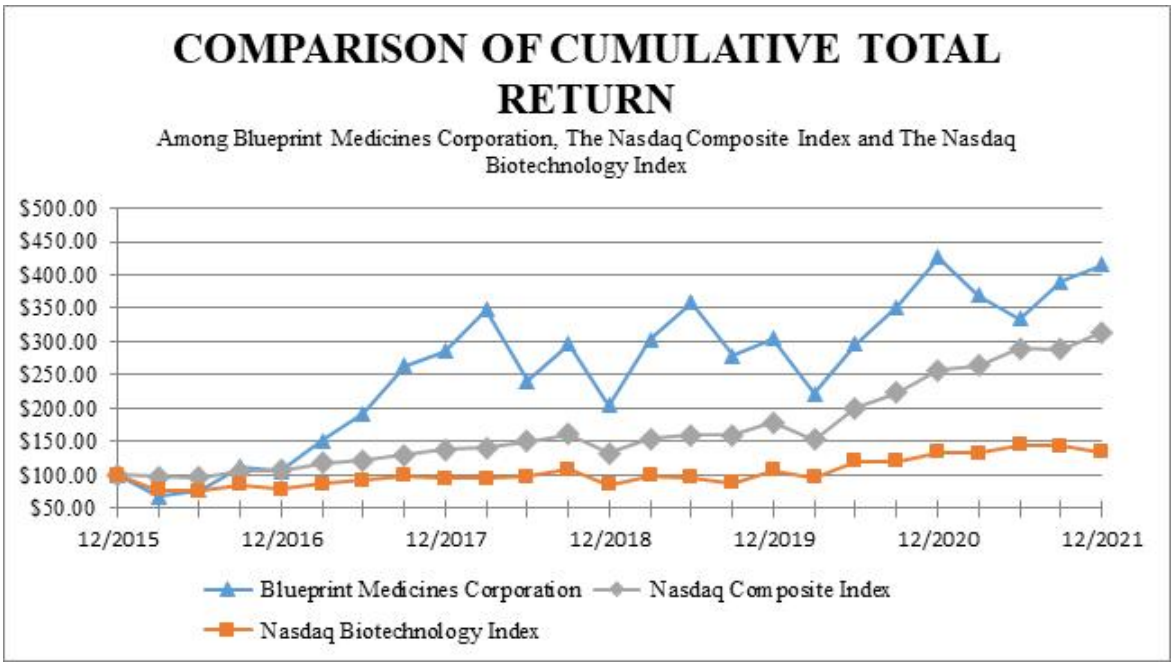
Dividends

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, 2021. The comparison assumes $100 was invested in our common stock and in each of the foregoing indices after the market closed on December 31, 2015, and it assumes reinvestment of dividends, if any. The stock price performance included in this graph is not necessarily indicative of, nor is it intended to forecast, future stock price performance.



Securities Authorized for Issuance under Equity Compensation Plans

Information about our equity compensation plans will be included in our definitive proxy statement to be filed with the SEC with respect to our 2022 Annual Meeting of Stockholders and is incorporated herein by reference.

Unregistered Sales of Equity Securities and Use of Proceeds

None.

Recent Sales of Unregistered Equity Securities

None.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

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

Item 6. Reserved

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

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

Information pertaining to fiscal year 2019 was included in the Company's Annual Report on Form 10-K for the year ended December 31, 2020 on pages 86 through 107 under Part II, Item 7, "Management's Discussion and Analysis

of Financial Position and Results of Operations," which was filed with the Securities and Exchange Commission (the "SEC") on February 17, 2021.

Overview

We are a global precision therapy company that is inventing life-changing medicines for people with cancer and blood disorders. Applying an approach that is both precise and agile, we create therapies that selectively target genetic drivers, with the goal of staying one step ahead across stages of disease. Since 2011, we have leveraged our research platform, including expertise in molecular targeting and world-class drug design capabilities, to rapidly and reproducibly translate science into a broad pipeline of precision therapies. Today, 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 SM, lung cancer and other genomically defined cancers, and cancer immunotherapy.

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

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

Avapritinib

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

In June 2021, the FDA approved avapritinib under the brand name AYVAKIT for the treatment of adult patients with advanced SM, including ASM, SM-AHN, and MCL. In January 2022, the CHMP of the EMA adopted a positive opinion recommending marketing authorization for avapritinib as a monotherapy for the treatment of adult patients with ASM, SM-AHN or MCL, after at least one systemic therapy. Pending the European Commission's final decision on our MAA, we anticipate obtaining regulatory approval from the EMA and launching avapritinib under the brand name AYVAKYT for advanced SM in Europe in the second quarter of 2022.

In addition, through our distribution agreement with Neopharm Israel Ltd., a marketing authorization application in Israel was submitted in June 2021 for avapritinib for patients with advanced SM and PDGFRA exon 18 mutant GIST. In the future, we plan to pursue the regulatory approval and commercialization of avapritinib in additional global geographies, including through additional potential distribution agreements.

We are 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 April 2021, we presented registration-enabling data from the PATHFINDER trial at the virtual AACR Annual Meeting.

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 January 2022, we announced that the PIONEER trial was fully enrolled. We plan to report top-line data for Part 2 of the PIONEER trial in mid-2022 and to submit an sNDA to the FDA for avapritinib in non-advanced SM in the second half of 2022.

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

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

BLU-263

We are developing BLU-263, an investigational, orally available, potent and highly selective KIT inhibitor, 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 CNS penetration 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 and potentially patients with other mast cell disorders.

In April 2021, we presented results from a Phase 1 trial of BLU-263 in healthy volunteers at the virtual AACR Annual Meeting, which showed that BLU-263 was well-tolerated at all doses tested. Based on these data, we initiated the Phase 2/3 HARBOR trial of BLU-263 in patients with non-advanced SM in the second quarter of 2021. We anticipate presenting initial data from the HARBOR trial in the second half of 2022.

RET-Altered Cancers — GAVRETO® (pralsetinib)

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

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

In November 2021, Roche announced that the European Commission granted conditional marketing authorization for GAVRETO as a monotherapy for the treatment of adults with RET fusion-positive advanced NSCLC not previously treated with a RET inhibitor. Roche submitted a Type II variation MAA to the EMA for pralsetinib for RET-altered thyroid cancers in December 2021, as well as marketing applications for pralsetinib for RET-altered NSCLC and thyroid cancers across multiple global geographies in 2021. Marketing applications are planned for pralsetinib for RET-altered NSCLC and thyroid cancers across additional global geographies in 2022.

In March 2021, China's NMPA approved GAVRETO for the treatment of RET fusion-positive NSCLC patients previously treated with platinum-based chemotherapy. In April 2021, China's NMPA accepted CStone's new drug application, or NDA, with Priority Review designation, for pralsetinib for the treatment of RET-mutant MTC and RET fusion-positive thyroid cancer.

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 the ARROW trial. In addition, Roche is conducting multiple ongoing studies, including a registration-enabling Phase 3 clinical trial in treatment-naïve patients with RET fusion-positive NSCLC, which is referred to as the ACCELERET-Lung trial; and a registration-enabling Phase 3 clinical trial in patients with locally advanced or metastatic RET-mutated MTC who have not previously received a standard of care multi-kinase inhibitor therapy, which is referred to as the ACCELERET-MTC trial. In June 2021, we reported updated data from the ARROW trial in metastatic RET fusion-positive NSCLC and other advanced solid tumors at the 2021 ASCO Annual Meeting. The ARROW trial was fully enrolled in December 2021. Pursuant to our collaboration with Roche, we are co-developing 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 (ii) the treatment of patients

with RET mutation-positive MTC that requires systemic treatment and for which there are no acceptable alternative treatments. In addition, the FDA has granted orphan drug designation to pralsetinib for the treatment of RET-rearranged NSCLC, JAK1/2-positive NSCLC or TRKC-positive NSCLC.

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

We are commercializing avapritinib for the treatment of patients with PDGFRA exon 18 GIST, a rare disease that is a sarcoma, or tumor of bone or connective tissue, of the gastrointestinal tract. Avapritinib is approved in the U.S. under the brand name AYVAKIT for the treatment of adults with unresectable or metastatic GIST harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations, and is approved in Europe with conditional marketing authorization under the brand name AYVAKYT as a monotherapy for the treatment of adult patients with unresectable or metastatic GIST harboring a PDGFRA D842V mutation.

In March 2021, CStone announced that China's NMPA approved AYVAKIT for the treatment of adults with unresectable or metastatic GIST harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations. AYVAKIT received accelerated approval in April 2021 from the TFDA and approval in Hong Kong in December 2021, both for adults with unresectable or metastatic GIST harboring PDGFRA D842V mutations.

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

EGFR-Mutated NSCLC — BLU-701, BLU-945 and BLU-451

We are developing three investigational EGFR inhibitors, BLU-701, BLU-945 and BLU-451, which was formerly known as LNG-451, with the goal of addressing the nearly all activating mutations (>90 percent) in EGFR-driven NSCLC. The introduction of EGFR-targeted therapies, including osimertinib, has transformed the care of patients with EGFR-driven NSCLC; however, there remains a significant need for new treatment options designed to prevent a broad range of resistance mechanisms before they emerge, with the goal of prolonging patient benefit. In addition, there are no approved targeted therapies for patients with disease progression following osimertinib, and limited treatment options for patients with EGFR exon 20 insertion-positive NSCLC.

BLU-701 and BLU-945 were specifically designed to provide comprehensive coverage of common activating and on-target resistance mutations, spare wild-type EGFR and other kinases to limit off-target toxicities, and treat or prevent CNS metastases, which occur frequently in patients with EGFR-driven NSCLC. We believe these profiles may enable BLU-701 and BLU-945 to become the backbones of a range of combination strategies with the potential to address important medical needs for patients with EGFR-driven NSCLC, including in early line treatment settings. We plan to develop BLU-701 and BLU-945 in combination with each other and other therapies, including osimertinib, as an initial treatment designed to prevent resistance from emerging. In addition, we plan to develop BLU-701 and BLU-945 as monotherapies in certain biomarker-selected patient populations.

In December 2021, we completed our acquisition of Lengo Therapeutics, Inc., along with its lead compound LNG-451, which we now refer to as BLU-451. BLU-451 is an oral precision therapy in development for the treatment of NSCLC in patients with EGFR exon 20 mutations.

EGFR-Positive NSCLC — BLU-701

BLU-701 is a selective and potent investigational inhibitor of 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. In preclinical data presented at the virtual AACR Annual Meeting in April 2021, BLU-701 showed strong and durable inhibition of tumor growth at doses that are EGFR wild-type sparing, and the potential to be used in both first- and second-line settings. BLU-701 indicated significant CNS penetration in preclinical models, with comparable exposure in the plasma and brain, which illustrates its potential to treat or prevent CNS metastases in patients with EGFR-driven tumors. Based on these preclinical data, we initiated a Phase 1/2 trial of BLU-701 in EGFR-

mutant NSCLC, which we refer to as our HARMONY trial, in the fourth quarter of 2021. We plan to present initial clinical data from the HARMONY trial in the second half of 2022.

EGFR-Positive NSCLC — BLU-945

BLU-945 is a selective and potent investigational inhibitor of 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 mutations to first-generation EGFR inhibitors and osimertinib, respectively. In preclinical data presented at the virtual AACR Annual Meeting in April 2021, BLU-945 demonstrated potent antitumor activity in osimertinib-resistant tumor models, as well as activity in an intracranial patient-derived xenograft model. Both preclinical models harbored activating mutations combined with the T790M and C797S mutations. Based on these preclinical data, we initiated a Phase 1/2 trial of BLU-945 in patients with EGFR-driven NSCLC, which we refer to as our SYMPHONY trial, in the second quarter of 2021. We plan to present initial clinical data from the SYMPHONY trial in the second quarter of 2022.

EGFR-Positive NSCLC — Combinations with BLU-701 and/or BLU-945

Based on their differentiated selectivity profiles and potency against on-target EGFR activating and resistant mutants, we believe BLU-701 and BLU-945 have the potential to become backbone therapies for a range of combination strategies for EGFR-positive NSCLC across multiple treatment lines, potentially including combinations of BLU-701 or BLU-945 with other EGFR therapies or treatment modalities, as well as BLU-701 and BLU-945 together. In preclinical data presented at the virtual AACR Annual Meeting in April 2021, the combination of BLU-945 with either gefitinib or osimertinib showed enhanced antitumor activity when compared with either gefitinib or osimertinib alone. At the BTOG Annual Conference in January 2022, we reported preclinical data supporting the development of BLU-701 and BLU-945 combination therapy in EGFR-driven NSCLC. Based on these results, we plan to develop BLU-701 and BLU-945 in combination with each other and other agents.

EGFR Exon 20 Insertion-Positive NSCLC — BLU-451

BLU-451 is a selective and potent investigational inhibitor under development for the treatment of EGFR exon 20 insertion-positive NSCLC. Based on preclinical data, BLU-451 potently inhibited all common EGFR exon 20 insertion variants with marked selectivity over wild-type EGFR and off-target kinases, and has shown significant CNS penetration. We recently received clearance for an IND application for BLU-451 for EGFR exon 20 insertion-positive NSCLC. In the first quarter of 2022, we plan to initiate a Phase 1/2 trial of BLU-451 in EGFR exon 20 insertion-positive NSCLC, and we expect to present preclinical data for BLU-451 in the second quarter of 2022.

Cyclin E Aberrant Cancers — BLU-222

We are developing an investigational inhibitor, BLU-222, targeting CDK2 for the treatment of patients with cyclin E aberrant cancers. In subsets of patients across multiple cancer types, aberrant CCNE1 hyperactivates CDK2, resulting in cell cycle dysregulation and tumor proliferation. Aberrant CCNE1 has been observed as a primary driver of disease, as well as a mechanism of resistance to CDK4/6 inhibitors and other therapies

At the virtual AACR Annual Meeting in April 2021, we presented preclinical data showing that selective CDK2 inhibition arrested the cell cycle and blocked tumor proliferation in CCNE1-amplified cell lines, and demonstrated robust and sustained antitumor activity in vivo in models of CCNE1-amplified ovarian, breast and gastric cancer. A selective CDK2 inhibitor also showed improved tolerability compared to a pan-CDK inhibitor and chemotherapy, as measured by animal body weight.

We recently received FDA clearance for an IND application for BLU-222 for cyclin E aberrant cancers. We plan to initiate a Phase 1/2 trial of BLU-222 in cyclin E aberrant cancers, which we refer to as our VELA trial, in the first quarter of 2022, and to present preclinical data for BLU-222 in the second quarter of 2022. BLU-222 is being developed as a single agent and in combination with chemotherapy in gyneocological cancers, and in combination with hormonal and the approved CDK 4/6-inhibitor ribociclib for hormone-receptor-positive, HER2-negative breast cancer.

Advanced Cancers — BLU-852

BLU-852 is a selective and potent investigational inhibitor of MAP4K1, a well-characterized immunokinase involved in the regulation of immune cells. Preclinical data presented at the virtual AACR Annual Meeting in April 2021 show that MAP4K1 inhibition enhanced intratumoral immune cell activation, overcame Treg mediated T cell suppression, and reduced tumor burden both as a monotherapy and in combination with checkpoint inhibition. These preclinical data support the continued development of BLU-852. Under our ongoing cancer immunotherapy collaboration, we expect Roche to initiate a Phase 1 trial of BLU-852, as a single agent and in combination with atezolizumab, in advanced cancers in 2023.

Fisogatinib — Hepatocellular Carcinoma

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. Following a strategic evaluation of the evolving HCC treatment landscape and prioritization of resources across our broad precision therapy pipeline, we have decided to deprioritize our clinical development of fisogatinib for the treatment of advanced HCC. We have discontinued further enrollment the Blueprint Medicines-sponsored clinical trial of fisogatinib as a monotherapy and in combination with sugemalimab, an anti-PD-L1 immunotherapy being developed by CStone. CStone continues to retain development and commercial rights to fisogatinib in the CStone territory.

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, we plan to expand our discovery platform by building capabilities, supported by external collaborations, for targeted protein degradation of both kinase and non-kinase targets in precision oncology, with the goal of advancing transformative therapies to patients and further broadening the significant productivity of our research engine. Beyond the discovery programs described above, we have multiple pre-development candidate programs for undisclosed kinase targets. In 2022, we plan to nominate two development candidates from our discovery programs. We also plan to share our vision for our expanded discovery platform at an R&D Day in the second half of 2022.

Under our immunotherapy collaboration with Roche, we are conducting activities for up to two discovery programs, including BLU-852. See "*—Collaborations and Licenses Summary*" below.

Collaborations and Licenses

Roche—Immunotherapy Collaboration. In March 2016, we entered into a collaboration with Roche to discover, develop and commercialize small molecule therapeutics targeting kinases believed to be important in cancer immunotherapy (including the kinase target MAP4K1, 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 are also co-developing pralsetinib globally in RET-altered solid tumors, including NSCLC, MTC and other thyroid cancers, and expanding development of pralsetinib in multiple treatment settings.

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

Clementia. In October 2019, we entered into a license agreement with Clementia 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 ALK2 in development for the treatment of FOP. The FDA has granted a rare pediatric disease designation, orphan drug

designation and fast track designation to BLU-782, each for the treatment of FOP. Clementia initiated patient dosing in a Phase 2 clinical trial of BLU-782, now referred to as IPN60130, in the first quarter of 2022.

Zai Lab. In November 2021, we entered into a collaboration with Zai Lab to develop and commercialize BLU-701 and BLU-945 for the treatment of EGFR-driven NSCLC in Greater China, including Mainland China, Hong Kong, Macau and Taiwan. The collaboration aims to accelerate and expand global development of BLU-701 and BLU-945.

Mergers & Acquisitions Summary

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

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

Note on the COVID-19 Pandemic

Due to the continued evolution and uncertain global impacts of the ongoing COVID-19 pandemic, and the identification of new variants of COVID-19, 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. Since we implemented this policy in 2020, we have continued to evaluate and update this policy from time to time 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. We currently offer our office-based employees a certain degree of flexibility of in their work location and we intend to maintain this policy for the foreseeable future. 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 ongoing 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. COVID-19 may also impact and has impacted our commercial activities for AYVAKIT/AYVAKYT and GAVRETO, including patient access to testing and identification. 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 in-person interactions are not feasible. We will continue to assess the duration, scope and severity of the COVID-19 pandemic as it evolves 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, 2021, we have received an aggregate of $3.0 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, $996.3 million in upfront and milestone payments under our collaborations with Roche, CStone and Zai Lab, our license agreement with Clementia and our former collaboration with Alexion Pharma Holding, or Alexion. In addition, since January 2020, we have also generated revenue through the sales of our approved drug products.

Since inception, we have incurred significant operating losses, with the exception of the year ended December 31, 2020. Our net loss was $644.1 million for the year ended December 31, 2021. 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. As of December 31, 2021, we had an accumulated deficit of $1,275.4 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 our drug and any current or future drug candidates for which we may obtain marketing approval;
- seek marketing approval for our drug candidates, including avapritinib and pralsetinib in additional indications or avapritinib 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 BLU-701, BLU-945, BLU-451 and BLU-222;
- continue to manufacture increasing quantities of drug substance and drug product material for use in preclinical 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, CStone and Zai Lab;
- maintain, expand and protect our intellectual property portfolio;
- acquire or in-license additional businesses, technologies, drugs or drug candidates, form strategic alliances or create joint ventures with third parties; and
- hire additional research, clinical, quality, manufacturing, regulatory, commercial and general and administrative personnel.

Revenue

In January 2020, the FDA granted approval of avapritinib under the brand name AYVAKIT for the treatment of adults with unresectable or metastatic GIST harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations. In September 2020, the European Commission granted conditional marketing authorization to AYVAKYT as a monotherapy for the treatment of adult patients with unresectable or metastatic GIST harboring the PDGFRA D842V mutation. In June 2021, the FDA granted a subsequent approval for AYVAKIT, expanding the labeled indications to include adult patients with advanced SM, including aggressive SM, SM with an associated hematological neoplasm and mast cell leukemia.

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. In

December 2020, the FDA granted a subsequent accelerated approval for GAVRETO, expanding the labeled indications to include adult and pediatric patients 12 years of age and older with advanced or metastatic RET-mutant 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, 2021, our revenue mainly consisted of product sales of our drugs as well as collaboration revenue under our collaborations with Roche, CStone and Zai Lab. We recorded net product revenue from the U.S. product sales of GAVRETO through June 30, 2021, and on July 1, 2021, we transferred certain responsibilities associated with product sales to customers, pricing and distribution matters related to U.S. product sales of GAVRETO to Roche and did not record any net product revenue from product sales of GAVRETO during the second half of 2021. Products sales of GAVRETO were reflected as part of collaboration loss sharing in the consolidated financial statements. For additional information, see Note 11, *Collaboration and License Agreements*, to our consolidated financial statements included in this Form 10-K. Collaboration revenue for the year ended December 31, 2021 primarily includes amounts that were recognized related to milestone and upfront payments, amounts due to us for supply of inventory (under our collaboration agreements) and research and development services, and royalties on drug sales.

In the future, we expect to generate revenue from a combination of sources, including sales of our current drug product and any current or future drug candidates for which we receive marketing approval, royalties on drug sales, upfront, milestone, profit sharing and other payments, if any, under any current or future 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 as well as the sales of drug substance and drug product to our collaboration partners during the respective period, including salary related expenses and stock-based compensation expense for employees involved with production and distribution, freight, and indirect overhead costs. In addition, shipping and handling costs for product shipments are recorded in cost of sales as incurred.

Prior to receiving the initial FDA approval for AYVAKIT and GAVRETO in January 2020 and September 2020, respectively, and subsequent approval for AYVAKIT in June 2021, we manufactured inventory to be sold upon commercialization and recorded approximately $37.7 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 years ended December 31, 2021 and 2020. We estimate our cost of goods sold related to product revenue as a percentage of net product revenue will continue to be positively impacted as we sell through certain inventory that was previously expensed prior to FDA approval. We expect to utilize low cost inventory for an extended period of time. Cost of goods sold related to sales of drug products to our collaboration partners are at lower margins and will partially offset the positive impact of the previously expensed inventory.

Expenses

Collaboration Loss Sharing

On July 1, 2021, Roche took over certain responsibilities associated with product sales to customers, pricing and distribution matters related to GAVRETO in the U.S. and became the principal for recording product sales to customers in the U.S. Collaboration loss sharing consists of our share of the losses incurred from sales of GAVRETO to customers in the U.S. under our collaboration for pralsetinib with Roche. For additional information, see Note 11,

Collaboration and License Agreements, to our consolidated financial statements included in this Form 10-K. We expect collaboration loss sharing will fluctuate from quarter to quarter as a result of the timing and amount of GAVRETO sales.

Research and Development Expenses

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

- expenses incurred to acquire in-process research and development asset with no alternative future use;
- employee-related expenses including salaries, benefits, and stock-based compensation expense;
- expenses incurred under agreements with third parties that conduct research and development, preclinical activities, clinical activities and manufacturing on our behalf;
- expenses incurred under agreements with third parties for the development and commercialization of companion diagnostic tests;
- expenses incurred in connection with research and development activities under our immunotherapy collaboration with Roche, and development activities under our collaboration for pralsetinib with Roche;
- the cost of consultants in connection with our research and development activities;
- the cost associated with regulatory quality assurance and quality control operations;
- the cost of lab supplies and acquiring, developing and manufacturing preclinical study materials, clinical trial materials and commercial supply materials; and
- facilities, depreciation, and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance, and other operating costs in support of research and development activities.

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

The successful development of our drug candidates is highly uncertain. As such, at this time, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the remainder of the development of these drug candidates. We are also unable to predict when, 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, 2021 and 2020. Other development and pre-development candidate expenses, unallocated expenses and internal research and development expenses have been classified separately.

	Year Ended December 31,	
	2021	2020
	(in thousands)	
Avapritinib external expenses	$ 59,355	$ 77,074
Pralsetinib external expenses	29,118	63,066
Fisogatinib external expenses	2,985	4,190
BLU-263 external expenses	22,219	14,138
BLU-701/945 external expenses	47,325	14,549
BLU-222 external expenses	14,353	3,192
BLU-451 external expenses	259,957	—
Other development and pre-development candidate expenses and unallocated expenses	59,609	52,217
Internal research and development expenses	106,112	98,434
Total research and development expenses	$ 601,033	$ 326,860

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

We expect that our research and development expenses will increase in future periods as we expand our operations and incur additional costs in connection with our clinical trials and preparing regulatory filings. These increases will likely include the costs related to the implementation and expansion of clinical trial sites and related

patient enrollment, monitoring, program management and manufacturing expenses for active pharmaceutical ingredient, or API, drug product and drug substance for current and future clinical trials and commercial inventory. In addition, we expect that our research and development expenses will increase in future periods as we incur additional costs in connection with research and development activities under our immunotherapy collaboration with Roche, development activities under our collaboration for pralsetinib with Roche and development activities for companion diagnostic tests for any 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.

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 our product sales in the state jurisdictions where we conduct business and foreign withholding income taxes incurred.

Critical Accounting Policies and Estimates

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

Critical accounting estimates are those estimates that, in accordance with generally accepted accounting principles, involve a significant level of estimation uncertainty and have had or are reasonably likely to have a material impact on our consolidated financial statements. Management has determined that our most critical accounting estimates are those relating to revenue recognition, accrued research and development expenses and acquisitions. We have

reviewed our critical accounting estimates with our audit committee. For further discussion about our general accounting policies, see Note 2 *Summary of Significant Accounting Policies and Recent Accounting Pronouncements*, to our consolidated financial statements included in the Form 10-K.

Revenue Recognition

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

Product Revenue

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

Collaboration Revenue

Revenue recognized from collaborations and other arrangements will include royalties on drug 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 under these types of contracts.

Accrued Research and Development Expenses

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

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

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

Acquisitions

To determine whether acquisitions or licensing transactions should be accounted for as a business combination or as an asset acquisition, we make certain judgments, which include assessing whether the acquired set of activities and assets would meet the definition of a business under the relevant accounting rules.

If the acquired set of activities and assets meets the definition of a business, assets acquired and liabilities assumed are required to be recorded at their respective fair values as of the acquisition date. The excess of the purchase price over the fair value of the acquired net assets, where applicable, is recorded as goodwill. If the acquired set of activities and assets does not meet the definition of a business, the transaction is recorded as an acquisition of assets and, therefore, any acquired in-process research and development assets that does not have an alternative future use is charged to research and development expense at the acquisition date, and goodwill is not recorded.

The judgments made in determining estimated the fair values of the identifiable intangible assets acquired, the assigned to assets acquired and liabilities assumed in a business combination, as well as estimated asset lives, can materially affect our consolidated results of operations. The fair values of intangible assets, including acquired in-process research and development assets, are determined using information available near the acquisition date based on estimates and assumptions that are deemed reasonable by management. Significant estimates and assumptions include, but are not limited to, probability of technical success, revenue growth and discount rate. When significant identifiable intangible assets are acquired, we generally engage an independent third-party valuation firm to assist in determining the fair values of these assets.

Results of Operations

Comparison of Years Ended December 31, 2021 and 2020

The following table summarizes our results of operations for the years ended December 31, 2021 and 2020, together with the changes in those items in dollars and as a percentage.

	Year Ended December 31,			
	2021	2020	Dollar Change	% Change
	(in thousands)			
Revenues:				
Product revenue, net	$ 57,687	$ 22,134	$ 35,553	161 %
Collaboration revenue	122,393	771,601	(649,208)	(84)
Total revenue	180,080	793,735	(613,655)	(77)
Cost and operating expenses:				
Cost of sales	17,934	425	17,509	4,120
Collaboration loss sharing	7,801	—	7,801	100
Research and development	601,033	326,860	274,173	84
Selling, general and administrative	195,293	157,743	37,550	24
Total cost and operating expenses	822,061	485,028	337,033	69
Other income (expense):				
Interest income, net	2,386	6,599	(4,213)	(64)
Other expense, net	(1,489)	(366)	1,123	307
Total other income (expense)	897	6,233	(5,336)	(86)
Income (loss) before income taxes	(641,084)	314,940	(956,024)	(304)
Income tax expense	3,001	1,058	1,943	184
Net income (loss)	$ (644,085)	$ 313,882	$ (957,967)	(305)%

Product Revenue, Net

Product revenue, net increased by $35.6 million from $22.1 million for the year ended December 31, 2020 to $57.7 million for the year ended December 31, 2021.

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. In June 2021, the FDA granted a subsequent approval for AYVAKIT, expanding the labeled indications to include adult patients with advanced SM, including aggressive SM, SM with an associated hematological neoplasm and mast cell leukemia.

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 thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate). We recorded net product revenue from the U.S. product sales of GAVRETO through June 30, 2021, and on July 1, 2021, we transferred certain responsibilities associated with product sales to customers, pricing and distribution matters related to U.S. product sales of GAVRETO to our collaboration partner and did not record any net product revenue from product sales of GAVRETO during the second half of 2021. Products sales of GAVRETO were reflected as part of collaboration loss sharing in the consolidated financial statements. For additional information, see Note 11, *Collaboration and License Agreements*, to our consolidated financial statements included in the Form 10-K.

The following table summarizes revenue recognized from sales of AYVAKIT/AYVAKIT and GAVRETO during the years ended December 31, 2021, and 2020 (in thousands):

	Year Ended December 31,					
	2021			2020		
	United States	Rest of World	Total	United States	Rest of World	Total
AYVAKIT/AYVAKYT	$ 44,959	$ 8,022	$ 52,981	$ 20,522	$ 740	$ 21,262
GAVRETO	4,706	—	4,706	872	—	872
Total product revenue, net	$ 49,665	$ 8,022	$ 57,687	$ 21,394	$ 740	$ 22,134

Collaboration Revenue

Collaboration revenue decreased by $649.2 million from $771.6 million for the year ended December 31, 2020 to $122.4 million for the year ended December 31, 2021. The following table summarizes the revenue recognized from our collaboration and license agreements during the years ended December 31, 2021 and 2020 (in thousands):

	Year Ended December 31,	
	2021	2020
Collaboration with Roche for pralsetinib	$ 56,022	$ 753,100
CStone collaboration	33,395	3,630
Zai Lab collaboration	25,000	—
Cancer immunotherapy with Roche	7,636	14,580
Other	340	291
Total collaboration and license revenue	$ 122,393	$ 771,601

Revenue recognized under our collaboration with Roche for pralsetinib for the year ended December 31, 2021 consisted of $50.0 million in specified regulatory milestone payments and $6.0 million associated with services related to Roche territory-specific activities. Revenue recognized under our CStone collaboration for the year ended December 31, 2021 primarily consisted of $24.4 million associated with royalties on drug sales and the manufacturing services related to CStone territory-specific activities during the year, including supply of drug products to CStone for sale in their territory, and $9.0 million in milestone revenue related to development milestones that were achieved during the year. Revenue recognized under our Zai Lab collaboration for the year ended December 31, 2021 consisted of a $25.0 million upfront cash payment. We recognized $7.6 million in revenue under our cancer immunotherapy collaboration with Roche for the year ended December 31, 2021, which was primarily related to the amortization of the total $68.5 million of upfront and milestone payments received as of such period.

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. 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 and regulatory milestones that were achieved during the year and $1.6 million associated with drug supply related to CStone 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 during such period.

Cost of Product Sales

Cost of sales increased by $17.5 million from $0.4 million for the year ended December 31, 2020 to $17.9 million for the year ended December 31, 2021 and was related to manufacturing costs associated with our product sales

as well as costs associated with the sale of drug product to our collaboration partners. The following table summarizes the cost of sales by type during the years ended December 31, 2021 and 2020 (in thousands):

	Year Ended December 31,	
	2021	2020
Cost of product sales	$ 3,958	$ 425
Cost of collaboration sales	13,976	—
Total cost of sales	$ 17,934	$ 425

The increase in costs of product sales was primarily driven by the lower margin product sales to our collaboration partners. Costs associated with product revenue, net remain at higher margins as costs associated with the manufacture of our drugs prior to FDA approval were recorded as research and development expenses and, therefore, were not included in cost of sales during such period.

Collaboration Loss Sharing

Our loss sharing under the collaboration with Roche for pralsetinib was $7.8 million for the year ended December 31, 2021.

Research and Development Expense

Research and development expense increased by $274.2 million from $326.9 million for the year ended December 31, 2020 to $601.0 million for the year ended December 31, 2021. The increase in research and development expense was primarily related to $260.0 million incurred to acquire in-process research and development compounds through the acquisition of Lengo, an increase of approximately $8.6 million in costs related to early discovery efforts, a decrease of $9.3 million in reimbursement from the global development cost sharing arrangement under our collaboration with Roche for pralsetinib, as well as increased costs and personnel expenses, including an increase of $6.0 million in stock-based compensation expense. These increases in research and development expense were primarily offset by a decrease of $8.8 million in expenses associated with the manufacturing of clinical supply.

Selling, general and Administrative Expense

Selling, general and administrative expense increased by $37.6 million from $157.7 million for the year ended December 31, 2020 to $195.3 million for the year ended December 31, 2021. The increase in selling, general and administrative expense was primarily related to increased costs and personnel expenses, including an increase of $10.1 million in stock-based compensation expense, as well as an increase of $17.1 million in commercial expenses to expand our commercial infrastructure for commercialization of AYVAKIT/AYVAKYT and GAVRETO. The increase in selling, general and administrative expense was partially offset by $8.1 million increase in reimbursement in connection with the commercialization of GAVRETO in the U.S. under our collaboration with Roche for pralsetinib.

Interest Income, Net

Interest income, net decreased by $4.2 million from $6.6 million for the year ended December 31, 2020 to $2.4 million for the year ended December 31, 2021. The decrease was primarily due to a combination of lower cash, cash equivalents and marketable securities balance and lower rate of return on investments in the capital markets.

Other Expense, Net

Other expense, net increased by $1.1 million from $0.4 million for the year ended December 31, 2020 to $1.5 million for the year ended December 31, 2021. The increase was primarily related to changes in foreign currency exchange rates.

Income Tax Expense

Income tax expense increased by $1.9 million from $1.1 million for the year ended December 31, 2020 to $3.0 million for the year ended December 31, 2021. The increase was primarily related to an increase in foreign withholding income tax, which is partially offset by a decrease in state income taxes in 2021.

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, 2021, we have received an aggregate of $3.0 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, $996.3 million in upfront payments and milestone payments under our collaborations with Roche and CStone, Zai Lab and 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, 2021, we had cash, cash equivalents and marketable securities of $1,034.6 million.

Cash Flows

The following table provides information regarding our cash flows for the years ended December 31, 2021, 2020 and 2019:

	Year Ended December 31,	
(in thousands)	**2021**	**2020**
Net cash provided by (used in) operating activities	$ (298,653)	$ 387,035
Net cash used in investing activities	(225,860)	(434,249)
Net cash provided by financing activities	50,716	617,759
Net increase (decrease) in cash and cash equivalents	$ (473,797)	$ 570,545

Net Cash Provided by (Used in) Operating Activities. For the year ended December 31, 2021, compared to the same period in 2020, the $685.7 million decrease in net cash provided by operating activities was primarily due to a $958.0 million decrease in net income. During the year ended December 31, 2020, the Company had a net income of $313.9 million which was driven by the $753.1 million collaboration revenue recognized under our collaboration agreement with Roche for pralsetinib.

Net Cash Used in Investing Activities. For the year ended December 31, 2021, compared to the same period in 2020, the $208.4 million decrease in net cash used in investing activities was primarily due to a $466.5 million decrease in net purchases of available-for-sale investments offset by $258.1 million of cash used to acquire an in-process research and development asset.

Net Cash Provided by Financing Activities. For the year ended December 31, 2021, compared to the same period in 2020, the $567.0 million decrease in net cash provided by financing activities was primarily due to the $503.2 million in proceeds received from our common stock offerings net of issuance costs and the $79.3 million received from the issuance of common stock related to the collaboration agreement with Roche for Pralsetinib in 2020, partially offset by a $15.5 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 avapritinib in additional geographies, to the extent these expenses are not the responsibility of our collaborators. In addition, we expect to incur additional significant commercialization expenses for AYVAKIT/AYVAKYT, GAVRETO and other drug candidates, if approved, related to drug sales, marketing, manufacturing and distribution to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of potential collaborators or licensors. We will also incur additional significant costs if we choose to pursue additional indications or geographies for any of our approved drugs or drug candidates or otherwise expand more rapidly than we presently anticipate. Accordingly, we may seek to obtain additional funding from time to time in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we may be forced to delay, reduce or eliminate certain of our research and development programs or future commercialization efforts.

As of December 31, 2021, we had cash, cash equivalents and marketable securities of $1,034.6 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 and any of our current or future drug candidates for which we receive marketing approval;
- the costs of securing manufacturing, packaging and labeling arrangements for development activities and commercial production, including API, drug substance and drug product material for use in preclinical studies, clinical trials, our compassionate use program and for use as commercial supply, as applicable;
- the scope, progress, results and costs of drug discovery, preclinical development, laboratory testing and clinical trials for our approved drugs and drug candidates;
- the costs, timing and outcome of regulatory review of marketing applications for our drug candidates, including seeking marketing approval for avapritinib and pralsetinib for additional indications or avapritinib in additional geographies;
- the success of our collaborations with Roche, CStone and Zai Lab 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 preclinical development and testing and clinical trials and, for any drug candidates that receive marketing approval, establishing and maintaining commercial infrastructure is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain additional marketing approvals, including for avapritinib and pralsetinib in additional indications or avapritinib 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 avapritinib 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, CStone and Zai Lab 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

We have entered into arrangements that contractually obligate us to make payments that will affect our liquidity and cash flows in future periods. Our contractual obligations primarily consist of our obligations under non-cancellable operating leases and unconditional purchase obligations related to certain commercial manufacturing agreements. The aggregate amount of future minimum purchase obligations under these manufacturing agreements over the period of next five years is approximately $34.2 million as of December 31, 2021, of which $16.7 million are expected to be paid within one year. The aggregate amount of future operating lease obligations over the term of our leases, excluding net sublease receivables, is $148.3 million as of December 31, 2021. For additional information on our leases and timing of future payments, see Note 16, *Leases*, to the consolidated financial statements included in this Form 10-K.

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 preclinical research studies, synthetic chemistry and other services and products for operating purposes. We have not included these payments in the 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 contractual obligations above because the achievement and timing of these milestones is not fixed and determinable.

Recently Issued and Adopted Accounting Pronouncements

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

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, 2021 and 2020, we had cash, cash equivalents and marketable securities of $1,034.6 million and $1,549.7 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, 2021 and 2020, 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, 2021 and 2020.

Item 8. Financial Statements and Supplementary Data.

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

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

None.

Item 9A. Controls and Procedures

Management's Evaluation of our Disclosure Controls and Procedures

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

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer (our principal executive officer and principal financial officer, respectively), evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2021. Based upon such evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that, as of December 31, 2021, 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, 2021 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, 2021.

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, 2021, 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, 2021, 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, 2021 and 2020, 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, 2021, and the related notes and our report dated February 17, 2022 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, 2022

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, 2021 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

At-the-Market Offering Agreement

On February 17, 2022, we entered into a sales agreement with Cowen and Company, LLC, or Cowen, pursuant to which we may offer and sell, from time to time at our sole discretion, shares of our common stock, par value $0.001 per share, having an aggregate offering price of up to $300.0 million through Cowen as sales agent. 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. Cowen will use commercially reasonable efforts to sell the shares from time to time, based upon instructions from us (including any price, time or size limits or other customary parameters or conditions we may impose). We will pay Cowen a commission of up to 3.0% of the gross sales proceeds of any common stock sold through Cowen under the sales agreement, and we have also provided Cowen with customary indemnification rights. We are not obligated to make any sales of our common stock under the sales agreement. The offering of shares of our common stock pursuant to the sales agreement will terminate upon the earlier of (i) the sale of all common stock subject to the sales agreement or (ii) the termination of the sales agreement in accordance with its terms.

The foregoing description of the sales agreement is qualified in its entirety by reference to the complete text of such agreement, a copy of which is attached hereto as Exhibit 1.1 to this Annual Report on Form 10-K and incorporated herein by reference. The legal opinion of Goodwin Procter LLP relating to the shares of our common stock being offered pursuant to the sales agreement is filed as Exhibit 5.1 to this Annual Report on Form 10-K.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this Item 10 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2022 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 2022 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 2022 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 2022 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 2022 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 February 17, 2022, by and between Blueprint Medicines Corporation and Cowen and Company, LLC				*
2.1~††	Agreement and Plan of Merger by and among the Company, Pavonis Merger Subsidiary, Inc., Lengo Therapeutics, Inc. and Fortis Advisors, LLC, dated November 27, 2021	8-K	001-37359	2.1	December 30, 2021
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
5.1	Opinion of Goodwin Procter LLP				*
10.1#	2011 Stock Option and Grant Plan, as amended, and forms of award agreements thereunder	S-1	333-202938	10.1	March 23, 2015
10.2#	2015 Stock Option and Incentive Plan and forms of award agreements thereunder	10-K	001-37359	10.2	February 13, 2020
10.3#	2015 Employee Stock Purchase Plan	10-K	001-37359	10.3	February 13, 2020

10.4#	2020 Inducement Plan and form of award agreements thereunder	S-8	333-238039	99.1	May 6, 2020
10.5	Lease Agreement, dated February 11, 2015, by and between the Registrant and 38 Sidney Street Limited Partnership	S-1	333-202938	10.4	March 23, 2015
10.6	First Amendment to Lease Agreement, dated January 26, 2018, by and between the Registrant and 38 Sidney Street Limited Partnership	10-K	001-37359	10.5	February 26, 2019
10.7	Second Amendment to Lease Agreement, dated April 6, 2021, by and between Blueprint Medicines Corporation and BRE-BMR 38 SIDNEY LLC	10-Q	001-37359	10.1	April 29,2021
10.8	Third Amendment to Lease Agreement, dated December 15, 2021, by and between Blueprint Medicines Corporation and BRE-BMR 38 SIDNEY LLC				*
10.9	Lease Agreement, dated April 28, 2017, by and between the Registrant and UP 45/75 Sidney Street, LLC	10-Q	001-37359	10.1	May 3, 2017
10.10	First Amendment of Lease, dated September 19, 2018, between Blueprint Medicines Corporation and UP 45/75 Sidney Street, LLC	8-K	001-37359	10.1	September 25, 2018
10.11#	Employment Agreement, dated November 6, 2015, by and between the Registrant and Jeffrey W. Albers	10-Q	001-37359	10.2	November 9, 2015
10.12#	First Amendment to Employment Agreement, dated December 22, 2021, by and between the Registrant and Jeffrey W. Albers	8-K	001-37359	10.1	December 23, 2021
10.13#	Amended and Restated Employment Agreement, dated January 4, 2022 and effective as of April 4, 2022, by and between the Registrant and Jeffrey W. Albers	8-K	001-37359	10.1	January 5, 2022
10.14#	Employment Agreement, dated November 6, 2015, by and between the Registrant and Anthony L. Boral	10-Q	001-37359	10.4	November 9, 2015
10.15#	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
10.16#	Employment Agreement, dated March 10, 2016, by and between the Registrant and Kathryn Haviland	10-K	001-37359	10.9	March 11, 2016
10.17#	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
10.18#	Second Amendment to Employment Agreement, dated December 22, 2021, by and between the Registrant and Kathryn Haviland	8-K	001-37359	10.4	December 23, 2021

10.19#	Amended and Restated Employment Agreement, dated January 4, 2022 and effective as of April 4, 2022, by and between the Registrant and Kathryn Haviland	8-K	001-37359	10.2	January 5, 2022
10.20#	Employment Agreement, dated September 6, 2016, by and between the Registrant and Tracey L. McCain	10-Q	001-37359	10.3	November 10, 2016
10.21#	First Amendment to Employment Agreement, dated December 22, 2021, by and between the Registrant and Tracey L. McCain	8-K	001-37359	10.5	December 23, 2021
10.22#	Employment Agreement, dated November 9, 2016, by and between the Registrant and Marion Dorsch	8-K	001-37359	10.1	November 14, 2016
10.23#	Employment Agreement, dated October 10, 2017, by and between the Registrant and Christopher Murray	10-Q	001-37359	10.1	October 31, 2017
10.24#	First Amendment to Employment Agreement, dated December 22, 2021, by and between the Registrant and Christopher Murray	8-K	001-37359	10.8	December 23, 2021
10.25#	Employment Agreement, dated November 22, 2017, by and between the Registrant and Michael Landsittel	8-K	001-37359	10.1	November 22, 2017
10.26#	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
10.27#	Second Amendment to Employment Agreement, dated December 22, 2021, by and between the Registrant and Michael Landsittel	8-K	001-37359	10.2	December 23, 2021
10.28#	Employment Agreement, dated October 29, 2018, by and between the Registrant and Christina Rossi	8-K	001-37359	10.1	October 29, 2018
10.29#	First Amendment to Employment Agreement, dated December 22, 2021, by and between the Registrant and Christina Rossi	8-K	001-37359	10.6	December 23, 2021
10.30#	Amended and Restated Employment Agreement, dated January 4, 2022 and effective as of April 4, 2022, by and between the Registrant and Christina Rossi	8-K	001-37359	10.3	January 5, 2022
10.31#	Employment Agreement, dated March 6, 2019, by and between the Registrant and Ariel Hurley	8-K	001-37359	10.1	March 8, 2019
10.32#	First Amendment to Employment Agreement, dated December 22, 2021, by and between the Registrant and Ariel Hurley	8-K	001-37359	10.11	December 23, 2021
10.33#	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

10.34#	Second Amendment to Employment Agreement, dated December 22, 2021, by and between the Registrant and Debra Durso-Bumpus	8-K	001-37359	10.10	December 23, 2021
10.35#	Employment Agreement, effective September 1, 2020, by and between the Registrant and Fouad Namouni, M.D.	8-K	001-37359	10.1	September 1, 2020
10.36#	First Amendment to Employment Agreement, dated December 22, 2021, by and between the Registrant and Fouad Namouni	8-K	001-37359	10.3	December 23, 2021
10.37#	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
10.38#	First Amendment to Amended and Restated Employment Agreement, dated December 22, 2021, by and between the Registrant and Becker Hewes	8K	001-37359	10.7	December 23, 2021
10.39#††	Employment Agreement, effective as of May 19, 2021, by and between the Registrant and Percy Carter	10-Q	001-37359	10.1	July 29, 2021
10.40#	First Amendment to Employment Agreement, dated December 22, 2021, by and between the Registrant and Percy H. Carter	8-K	001-37359	10.9	December 23, 2021
10.41#	Amended and Restated Employment Agreement, dated January 19, 2022 and effective as of April 4, 2022, by and between the Registrant and Philina Lee	8K	001-37359	10.1	January 20, 2022
10.42†	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
10.43†	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
10.44	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
10.45†	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
10.46††	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

10.47††	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
10.48††	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
10.49††	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
10.50††	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-K	001-37359	10.32	February 17, 2021
10.51††	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
10.52†	License and Collaboration Agreement, dated June 1, 2018, between the Registrant and CStone Pharmaceuticals	10-Q	001-37359	10.1	August 1, 2018
10.53††	License Agreement, effective October 15, 2019, by and between the Registrant and Clementia Pharmaceuticals, Inc.	10-Q	001-37359	10.1	November 5, 2019
10.54~††	Collaboration and License Agreement, dated November 8, 2021, by and between the Registrant and Zai Lab (Shanghai) Co. Ltd				*
10.55	Form of Indemnification Agreement entered into between the Registrant and its directors	S-1	333-202938	10.11	March 23, 2015
10.56	Form of Indemnification Agreement entered into between the Registrant and its officers	S-1	333-202938	10.12	March 23, 2015
10.57	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				*
23.2	Consent of Goodwin Procter LLP (contained in its opinion filed as Exhibit 5.1 and incorporated herein by reference)				*
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.

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

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

††Certain portions of the exhibit have been omitted pursuant to Regulation S-K Item 601(b) because it is both (i) not material to investors and (ii) likely to cause competitive harm to the Company if publicly disclosed.

* Filed herewith.

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

Item 16. Form 10-K Summary.

Not applicable.

SIGNATURES

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

BLUEPRINT MEDICINES CORPORATION

Date: February 17, 2022

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 Chairman of the Board *(Principal Executive Officer)*	February 17, 2022
/s/ Michael Landsittel Michael Landsittel	Chief Financial Officer *(Principal Financial Officer)*	February 17, 2022
/s/ Ariel Hurley Ariel Hurley	Vice President, Finance and Controller *(Principal Accounting Officer)*	February 17, 2022
/s/ Nicholas Lydon Nicholas Lydon, Ph.D.	Director	February 17, 2022
/s/ Alexis Borisy Alexis Borisy	Director	February 17, 2022
/s/ Mark Goldberg Mark Goldberg, M.D.	Director	February 17, 2022
/s/ Charles A. Rowland, Jr. Charles A. Rowland, Jr.	Director	February 17, 2022
/s/ George Demetri George Demetri, M.D.	Director	February 17, 2022
/s/ Lonnel Coats Lonnel Coats	Director	February 17, 2022
/s/ Lynn Seely Lynn Seely, M.D.	Director	February 17, 2022
/s/ Daniella Beckman Daniella Beckman	Director	February 17, 2022

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, 2021 and 2020, 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, 2021, 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, 2021 and 2020, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2021, 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, 2021, 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, 2022 expressed an unqualified opinion thereon.

Basis for Opinion

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

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

Critical Audit Matters

The critical audit 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.

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.

Collaboration Agreement with Zai Lab

Description of the Matter

As discussed in Note 11 to the consolidated financial statements, the Company recognized $25.0 million in revenue under the collaboration agreement with Zai Lab (Shanghai) Co., Ltd., ("Zai Lab").

The Company determined that agreement contained two material components: (i) licenses granted to Zai Lab to exploit and develop each licensed product in the Zai Lab territory and related activities in the Zai Lab territory, including manufacturing, and (ii) the parties' participation in the global development of the licensed products. The Company accounts for the licenses and related activities pursuant to ASC 606, Revenue from Contracts with Customers, and the global development activities under ASC 808, Collaborative Arrangements.

The Company evaluated the Zai Lab territory specific licenses and related activities under ASC 606 as these transactions are considered transactions with a customer and identified three material promises at the outset of the Zai Lab agreement, which consists of the following for each licensed product: (1) the exclusive license, (2) the initial know-how transfer and (3) manufacturing activities related to development and commercial supply of the licensed product in the Zai Lab territory.

Auditing management's identification of the material promises were challenging as the contract includes implicit and explicit goods and services. Significant judgment was required in the evaluation of the identification of the promises.

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 material promises in its contracts.

To test the identification of material promises , we assessed, among other things, the stated terms of the Company's arrangement with Zai Lab. We also conducted meetings with personnel at the Company responsible for negotiating the contract and overseeing the delivery of the components in order to understand the nature as well as understand whether they were capable of being distinct in the context of the contract. Finally, we assessed the Company's analyses to support their conclusion of the amount of revenue to recognize in 2021.

Lengo Therapeutics Inc. Acquisition

Description of the Matter

As described in Note 3 to the Company's consolidated financial statements, the Company completed the acquisition of all the outstanding shares of Lengo Therapeutics Inc. ("Lengo")

for upfront consideration of $250.0 million, subject to customary net indebtedness, transaction expenses, and other adjustments and future contingent cash milestone payments of up to $215.0 million, upon achievement of specified regulatory approval and sales milestones. The acquisition was accounted for as an acquisition of assets that did not meet the definition of a business. The asset acquisition did not constitute a business as substantially all of the fair value of the gross assets acquired was concentrated in Lengo's lead compound LNG-451, now known as BLU-451. The acquired assets and liabilities were recorded at their relative fair values and the Company immediately expensed the acquired intellectual property in the consolidated statement of operations and comprehensive loss in the amount of $260.0 million as the acquired assets represent in-process research and development with no alternative future use.

Auditing management's conclusion that substantially all of the fair value of the gross assets acquired is concentrated in a single identifiable asset or group of similar identifiable assets and therefore the Lengo acquisition should be accounted for as an asset acquisition required significant auditor judgment.

How We Addressed the Matter in Our Audit

We obtained an understanding, evaluated the design and tested the operating effectiveness of management's controls over the identification and aggregation of the Lengo assets acquired and the application of the qualitative and quantitative considerations in applying the accounting guidance.

To test the Lengo asset acquisition conclusion, our audit procedures included, among others, reviewing the agreement between the Company and Lengo and other information to determine the completeness of identified assets acquired. We assessed the reasonableness of the qualitative and quantitative considerations utilized when determining if substantially all of the fair value of the gross assets acquired is concentrated in a single identifiable asset or group of similar identifiable assets by comparing it to evidence obtained about Lengo and its legacy operations. As part of our testing of the assessment made by management, we evaluated the reasonableness of the significant assumptions used in the Company's estimate of the gross fair value of the assets acquired. We involved our valuation professionals to assist with our evaluation of the methodology used by the Company and significant assumptions included in the fair value estimates.

/s/ Ernst & Young LLP

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

Boston, Massachusetts
February 17, 2022

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

	December 31,	
	2021	2020
Assets		
Current assets:		
Cash and cash equivalents	$ 209,948	$ 684,636
Marketable securities	267,166	187,213
Accounts receivable	25,155	7,096
Unbilled accounts receivable	11,875	18,213
Inventory	21,817	8,581
Prepaid expenses and other current assets	18,064	22,020
Total current assets	554,025	927,759
Marketable securities	557,529	677,873
Property and equipment, net	30,700	34,129
Operating lease right-of-use assets, net	90,162	67,539
Restricted cash	5,171	5,168
Other assets	14,638	5,925
Total assets	$ 1,252,225	$ 1,718,393
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	8,333	4,370
Accrued expenses	121,829	105,938
Current portion of operating lease liabilities	8,093	7,935
Current portion of deferred revenue	11,510	12,559
Total current liabilities	149,765	130,802
Operating lease liabilities, net of current portion	103,315	81,669
Deferred revenue, net of current portion	25,066	28,599
Other long-term liabilities	3,344	7,235
Total liabilities	281,490	248,305
Commitments and Contingencies (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; 59,141,086 and 57,793,533 shares issued and outstanding at December 31, 2021 and December 31, 2020, respectively	59	58
Additional paid-in capital	2,250,250	2,106,600
Accumulated other comprehensive loss	(4,133)	(5,214)
Accumulated deficit	(1,275,441)	(631,356)
Total stockholders' equity	970,735	1,470,088
Total liabilities and stockholders' equity	$ 1,252,225	$ 1,718,393

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,		
	2021	2020	2019
Revenues:			
Product revenue, net	$ 57,687	$ 22,134	$ —
Collaboration revenue	122,393	771,601	66,512
Total revenues	180,080	793,735	66,512
Cost and operating expenses:			
Cost of sales	17,934	425	—
Collaboration loss sharing	7,801	—	—
Research and development	601,033	326,860	331,450
Selling, general and administrative	195,293	157,743	96,388
Total cost and operating expenses	822,061	485,028	427,838
Other income (expense):			
Interest income, net	2,386	6,599	13,732
Other expense, net	(1,489)	(366)	(100)
Total other income	897	6,233	13,632
Income (loss) before income taxes	(641,084)	314,940	(347,694)
Income tax expense	3,001	1,058	—
Net income (loss)	$ (644,085)	$ 313,882	$ (347,694)
Other comprehensive income (loss):			
Unrealized gain (loss) on pension benefit obligations	4,255	(2,843)	(2,985)
Unrealized gain (loss) on available-for-sale investments	(3,649)	441	671
Currency translation adjustments	475	(278)	(40)
Comprehensive income (loss)	$ (643,004)	$ 311,202	$ (350,048)
Net income (loss) per share — basic	$ (11.01)	$ 5.76	$ (7.27)
Net income (loss) per share — diluted	$ (11.01)	$ 5.59	$ (7.27)
Weighted-average number of common shares used in net income (loss) per share — basic	58,518	54,534	47,829
Weighted-average number of common shares used in net income (loss) per share — diluted	58,518	56,168	47,829

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, 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, 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
Issuance of common stock under stock plan	1,304,386	1	47,302	—	—	47,303
Purchase of common stock under ESPP	43,167	—	3,313	—	—	3,313
Stock-based compensation expense	—	—	93,035	—	—	93,035
Other comprehensive income	—	—	—	1,081	—	1,081
Net income (loss)	—	—	—	—	(644,085)	(644,085)
Balance at December 31, 2021	59,141,086	$ 59	$ 2,250,250	$ (4,133)	$ (1,275,441)	$ 970,735

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,		
	2021	2020	2019
Cash flows from operating activities			
Net income (loss)	$ (644,085)	$ 313,882	$ (347,694)
Adjustments to reconcile net income (loss) to net cash provided by (used in) operating activities:			
Depreciation and amortization	6,479	6,559	5,259
Noncash lease expense	6,306	5,791	4,991
Stock-based compensation	91,630	75,526	54,653
Acquired in-process research and development	259,957	—	—
Accretion of premiums and discounts on investments	1,361	466	(4,949)
Other	3,379	429	—
Changes in assets and liabilities:			
Accounts receivable	(18,143)	(6,387)	(599)
Unbilled accounts receivable	6,338	4,536	(22,597)
Inventory	(12,561)	(6,707)	—
Prepaid expenses and other current assets	4,693	(12,620)	(3,338)
Other assets	(1,786)	1,440	20
Accounts payable	4,221	(791)	1,448
Accrued expenses	6,095	16,214	36,980
Deferred revenue	(4,582)	(4,915)	(94)
Operating lease liabilities	(7,955)	(6,388)	(2,095)
Net cash provided by (used in) operating activities	(298,653)	387,035	(278,015)
Cash flows from investing activities			
Purchases of property and equipment	(3,089)	(3,159)	(14,013)
Purchase of in-process research and development asset, net of cash acquired	(258,152)	—	—
Purchases of investments	(655,449)	(969,437)	(738,387)
Maturities of investments	690,830	538,347	735,934
Net cash used in investing activities	(225,860)	(434,249)	(16,466)
Cash flows from financing activities			
Proceeds from common stock offerings, net of issuance costs	—	503,189	327,466
Net proceeds from stock option exercises and employee stock purchase plan	50,716	35,265	13,288
Proceeds from issuance of common stock related to collaboration agreement	—	79,305	—
Other financing activities	—	—	(116)
Net cash provided by financing activities	50,716	617,759	340,638
Net increase (decrease) in cash, cash equivalents, and restricted cash	(473,797)	570,545	46,157
Cash, cash equivalents and restricted cash at beginning of period	689,804	119,604	73,429
Effect of exchange rate changes on cash, cash equivalents and restricted cash	(888)	(345)	18
Cash, cash equivalents and restricted cash at end of period	$ 215,119	$ 689,804	$ 119,604
Supplemental cash flow information			
Property and equipment purchases unpaid at period end	$ 149	$ 141	$ 958
Cash paid for taxes, net	$ 694	$ 778	$ 185

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,		
	2021	2020	2019
Cash and cash equivalents	$ 209,948	$ 684,636	$ 113,938
Restricted cash included in prepaid expenses and other current assets	—	—	500
Restricted cash	5,171	5,168	5,166
Total cash, cash equivalents, and restricted cash shown in consolidated statements of cash flows	$ 215,119	$ 689,804	$ 119,604

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

The Company has two approved precision therapies and is globally advancing multiple programs for systemic mastocytosis, lung cancer and other genomically defined cancers, 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.

As of December 31, 2021, the Company had cash, cash equivalents and marketable securities of $1,034.6 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, Blueprint Medicines (Italy) S.r.L., and Lengo Therapeutics Inc (Lengo), which was acquired on December 30, 2021. All intercompany transactions and balances have been eliminated.

Use of Estimates

The preparation of financial statements in conformity with GAAP requires the Company's management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Actual results could differ from those estimates. Management considers many factors in selecting appropriate financial accounting policies and in developing the estimates and assumptions that are used in the preparation of the financial statements. Management must apply significant judgment in this process. Management's estimation process often may yield a range of potentially reasonable estimates and management must select an amount that falls within that range of reasonable estimates. Estimates are used in the following areas, among others: revenue recognition, acquisitions, 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 ongoing 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, including the identification and spread of new variants, 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 making 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 percentage of our products that are sold via these programs, and our product pricing. The amount of variable consideration that is included in the transaction price may be constrained and is included in net product revenues only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period. Actual amounts of consideration ultimately received may differ from the Company's estimates. If actual results vary from the Company's estimates, the Company adjusts these estimates, which would affect net product revenue and earnings in the period such variances become known.

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

expected value method based upon a range of possible outcomes and are established in the same period that the related revenue is recognized, resulting in a reduction of product revenue.

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

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

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

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

Collaboration 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 11, *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 years ended December 31, 2021 and 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, 2021 and 2020.

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, 2021 and 2020, the Company's cash equivalents comprised of money market funds with less than 90 days from the date of purchase. Cash equivalents are reported at fair value.

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, 2021, 2020 and 2019, advertising costs totaled $13.5 million, $9.4 million and $3.3 million, respectively.

Property and Equipment, Net

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

Impairment of Long-Lived Assets

The Company continually evaluates whether events or circumstances have occurred that indicate that the 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 associated with long-lived assets for the years ended December 31, 2021, 2020 and 2019.

Leases

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

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

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

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

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

Lease cost for operating leases consists of the lease payments plus any initial direct costs, primarily brokerage commissions, and is recognized on a straight-line basis over the lease term. Included in lease cost are any variable lease

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

The Company has made an accounting policy election to not recognize leases with an initial term of 12 months or less within 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. Until a sufficient amount of historical information regarding volatility of the Company's own share price became available, the Company computed 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;

- 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.

Acquisition

When entering an acquisition transaction, the Company first determines whether the transaction is a business combination by applying the definition in ASC Topic 805, *Business Combinations* (ASC 805). The definition of a

"business", requires considerations in the form of two steps: (1) determination of whether "substantially all" of the fair value of the gross assets acquired is concentrated in a single identifiable asset or a group of similar identifiable assets (i.e., "screen test"); if not, then (2) evaluate whether the set of transferred assets and activities meets the definition of a business which includes, at a minimum, an input and a substantive process that together significantly contribute to the ability to create outputs. If the assets acquired are not a business, the Company accounts for the transaction as an asset acquisition. If the transaction is a business combination, it is accounted for by applying the acquisition method.

In asset acquisitions, the Company allocates the cost of a group of assets acquired to the individual assets acquired or liabilities assumed based on their relative fair values. Goodwill is not recognized in an asset acquisition. Any difference between the cost of an asset acquisition and the fair value of the net assets acquired is allocated to the non-monetary identifiable assets based on their relative fair values. The Company follows the guidance in ASC Topic 730 *Research and Development* (ASC 730) and determines whether any acquired research and development assets have alternative use. If they have an alternative future use, they are recognized as assets by the Company. If they have no alternative future use, they are charged to research and development expense at the acquisition date.

In business combinations, the acquisition method is applied, where the identifiable assets acquired, the liabilities assumed, and any noncontrolling interest in the acquiree as well as any goodwill is measured and recognized based on its fair value at acquisition date.

Income Taxes

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

Foreign currency translation

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

Concentrations of Credit Risk and 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, 2021 and 2020, 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.

Government assistance

In November 2021, the FASB issued ASU No. 2021-10, *Government Assistance (Topic 832) – Disclosures by Business Entities about Government Assistance* to add annual disclosure requirements related to transactions with a government that are accounted for by applying a grant or contribution accounting model by analogy. The standard is effective for annual periods beginning after December 15, 2021, with early adoption permitted. The Company adopted the new standard on January 1, 2022 and does not expect the adoption of this standard to have a significant impact on the disclosures of its consolidated financial statements.

3. Acquisition

On November 27, 2021, the Company entered into a merger agreement for the acquisition of all the outstanding shares of Lengo Therapeutics Inc. ("Lengo"), a biopharmaceutical company committed to developing novel, best-in-class precision medicines targeting driver mutations in oncology to improve the lives of patients with cancer. The acquisition was completed on December 30, 2021.

Under the terms of the acquisition, the Company agreed to pay Lengo shareholders an upfront consideration of $250.0 million, subject to customary net indebtedness, transaction expenses, and other adjustments, as set forth in the acquisition agreement, and future contingent cash milestone payments of up to $215.0 million, upon achievement of specified regulatory approval and sales milestones. The milestone payments were determined to be contingent consideration which will be recognized when the contingency is resolved, and the consideration is paid or becomes payable.

The total net purchase price was $258.4 million upon closing of the transaction, which consists of the $250.0 million upfront payment, and $8.4 million of adjustments associated with net indebtedness, transaction expenses, and other adjustments per the terms of the agreement.

The acquisition was accounted for as acquisition of assets that did not meet the definition of a business. The asset acquisition did not constitute a business as substantially all of the fair value of the gross assets acquired was concentrated in Lengo's lead compound LNG-451, now known as BLU-451. The acquired assets and liabilities were recorded at their relative fair values and the Company immediately expensed the acquired intellectual property in the consolidated statement of operations and comprehensive loss in the amount of $260.0 million as the acquired assets represent in-process research and development with no alternative future use.

A summary of the net purchase price and the allocation of the consideration is as follows (in thousands):

Purchase price, net of cash acquired	$ 258,377
Identifiable assets and liabilities acquired:	
Net current liabilities	(1,580)
In-process research and development	259,957
Total identifiable net assets acquired	$ 258,377

4. Marketable Securities

Marketable securities consisted of the following at December 31, 2021 and 2020 (in thousands):

December 31, 2021	Amortized Cost	Unrealized Gain	Unrealized Losses	Fair Value
Marketable securities, available-for-sale:				
U.S. government agency securities	$ 498,582	$ 21	$ (1,460)	$ 497,143
U.S. treasury obligations	328,801	—	(1,249)	327,552
Total	$ 827,383	$ 21	$ (2,709)	$ 824,695

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

As of December 31, 2021 and 2020, the Company held 74 and 8 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, 2021 and 2020 were $750.5 million and $125.7 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, 2021 and 2020.

As of December 31, 2021, 56 securities with an aggregate fair value of $557.5 million had remaining maturities between one and five years. As of December 31, 2020, 65 securities with an aggregate fair value of $677.9 million had remaining maturities between one and five years.

The Company received proceeds of $690.8 million and $538.3 million from maturities of debt securities for the years ended December 31, 2021 and 2020, respectively. The Company did not realize any gains or losses from maturities of debt securities for the years ended December 31, 2021 and 2020.

5. Fair Value of Financial Instruments

The following table summarizes the Company's cash equivalents and marketable securities measured at fair value on a recurring basis as of December 31, 2021 (in thousands):

Description	December 31, 2021	Active Markets (Level 1)	Observable Inputs (Level 2)	Unobservable Inputs (Level 3)
Cash equivalents:				
Money market funds	$ 118,880	$ 118,880	$ —	$ —
Marketable securities, available-for-sale:				
U.S. government agency securities	497,143	—	497,143	—
U.S. treasury obligations	327,552	327,552	—	—
Total	$ 943,575	$ 446,432	$ 497,143	$ —

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	$ —

6. Product Revenue Reserves and Allowances

In January 2020, the U.S. Food and Drug Administration (FDA) approved AYVAKIT for the treatment of adults with unresectable or metastatic gastrointestinal stromal tumor (GIST) harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations. In September 2020, the European Commission granted conditional marketing authorization to AYVAKYT as a monotherapy for the treatment of adult patients with unresectable or metastatic GIST harboring the PDGFRA D842V mutation. In June 2021, the FDA granted a subsequent approval for AYVAKIT, expanding the labeled indications to include adult patients with advanced systemic mastocytosis (Advanced SM), including aggressive SM (ASM), SM with an associated hematological neoplasm (SM-AHN) and mast cell leukemia (MCL).

In September 2020, the FDA granted accelerated approval of GAVRETO for the treatment of adult patients with metastatic RET fusion-positive non-small cell lung cancer (NSCLC) as detected by an FDA approved test. In December 2020, the FDA granted a subsequent accelerated approval for GAVRETO, expanding the labeled indications to include adult and pediatric patients 12 years of age and older with advanced or metastatic RET-mutant medullary thyroid cancer (MTC) who require systemic therapy, 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).

The Company recorded net product revenue from the U.S. product sales of GAVRETO through June 30, 2021, and on July 1, 2021, the Company transferred certain responsibilities associated with product sales to customers, pricing and distribution matters related to U.S. product sales of GAVRETO to its collaboration partner and did not record any net product revenue from product sales of GAVRETO during the second half of 2021. Products sales of GAVRETO were reflected as part of collaboration loss sharing in the consolidated statements of operations and comprehensive income (loss). For additional information, see Note 11, *Collaboration and License Agreements*.

The following table summarizes revenue recognized from product sales for the years ended December 31, 2021 2020, and 2019 (in thousands):

	Year Ended December 31,		
	2021	2020	2019
AYVAKIT/AYVAKYT	$ 52,981	$ 21,262	$ —
GAVRETO	4,706	872	—
Total product revenue	$ 57,687	$ 22,134	$ —

The following table summarizes activity in each of the product revenue allowance and reserve categories for the years ended December 31, 2021 and 2020 (in thousands):

	Year Ended December 31,	
	2021	2020
Beginning balance at January 1	$ 1,192	$ —
Provision related to sales in the current period	8,624	2,515
Adjustment related to prior periods sales	(396)	—
Credits and payments made	(5,075)	(1,323)
Ending balance at December 31	$ 4,345	$ 1,192

The total reserves above, which are included in the Company's consolidated balance sheets as of December 31, 2021 and 2020, are summarized as follows (in thousands):

	As of December 31,	
	2021	2020
Reduction of accounts receivable, net	$ 419	$ 226
Component of accrued expenses	3,926	966
Total revenue-related reserves	$ 4,345	$ 1,192

7. Inventory

Capitalized inventory consists of the following at December 31, 2021 and 2020 (in thousands):

	As of December 31,	
	2021	2020
Raw materials	$ 10,788	$ —
Work in process	17,702	9,488
Finished goods	3,916	914
Total	$ 32,406	$ 10,402

Balance sheet classification

	As of December 31,	
	2021	2020
Inventory	$ 21,817	$ 8,581
Other assets	10,589	1,821
Total	$ 32,406	$ 10,402

Inventory amounts written down as a result of excess, obsolescence, unmarketability or other reasons are charged to cost of sales. For the year ended December 31, 2021, the Company recognized a write-down of $0.6 million. For the year ended December 31, 2020, no write-down was recorded. Long-term inventory, which primarily consists of work in process, is included in other assets in the consolidated balance sheets.

8. Restricted Cash

At December 31, 2021 and 2020, respectively, $5.2 million and $5.2 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. For additional information, see Note 16, *Leases*.

9. Property and Equipment, Net

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

	Estimated Useful Life (Years)	As of December 31, 2021	As of December 31, 2020
Lab equipment	5	$ 13,120	$ 11,418
Furniture and fixtures	4	3,714	3,420
Computer equipment	3	1,714	1,513
Leasehold improvements	Term of lease	36,945	36,946
Software	3	412	412
Construction-in-progress		213	151
Total cost		56,118	53,860
Less: accumulated depreciation and amortization		(25,418)	(19,731)
Total		$ 30,700	$ 34,129

Property, plant and equipment are recorded at historical cost, net of accumulated depreciation. Depreciation expense for the years ended December 31, 2021, 2020 and 2019 was $6.5 million, $6.6 million and $5.3 million, respectively.

10. Accrued Expenses

Accrued expenses consist of the following (in thousands):

	As of December 31, 2021	As of December 31, 2020
External research and development	$ 68,164	$ 60,255
Employee compensation	29,166	27,622
Accrued professional fees	12,611	10,986
Revenue-related reserves	3,926	966
Other	7,962	6,109
Total	$ 121,829	$ 105,938

11. Collaboration and License Agreements

Zai Lab

On November 8, 2021, the Company entered into a collaboration (the Zai Lab agreement) with Zai Lab (Shanghai) Co., Ltd., (Zai Lab), pursuant to which the Company granted Zai Lab exclusive rights to develop and commercialize the Company's drug candidates BLU-701 and BLU-945 for the treatment of EGFR-driven non-small cell lung cancer in in Greater China, including Mainland China, Hong Kong, Macau and Taiwan (collectively, the Zai Lab territory), either as a monotherapy or as part of a combination therapy. The Company retains exclusive rights to the licensed products outside the Zai Lab territory.

The Company received an upfront cash payment of $25.0 million through December 31, 2021, and subject to the term of Zai Lab agreement, in addition to the upfront payment received, the Company is eligible to receive up to $590.0 million in contingent payments, including specified development, regulatory and sales-based milestones and tiered percentage royalties on a licensed product-by-licensed product basis ranging from the low-teens to mid-teens on annual net sales of each licensed product in the Zai Lab territory, subject to adjustment in specified circumstances. Zai

Lab will be responsible for costs related to clinical trials in the Zai Lab territory, other than the specified shared services costs as defined in the Zai Lab agreement which will be shared by the Company and Zai Lab.

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

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

The Company evaluated the Zai Lab agreement to determine whether it is a collaborative arrangement in scope of ASC 808. The Company concluded that the Zai Lab agreement is a collaborative agreement under ASC 808 as both parties are expected to participate in the activities at least through the completion of the clinical trials, both parties will incur significant costs to support the development activities, and the parties will share in the reward. The Company determined that the Zai Lab agreement contained two material components: (i) licenses granted to Zai Lab to exploit and develop each licensed product in the Zai Lab territory and related activities in the Zai Lab territory, including manufacturing, and (ii) the parties' participation in the global development of the licensed products. The Company used the criteria specified in ASC 606 to determine which of the components of the Zai Lab agreement are performance obligations with a customer and concluded that Zai Lab is the Company's customer for the licenses and related activities in the Zai Lab territory under ASC 606. The global development activities under the agreement does not present a transaction with a customer and the payments received by the Company for global development activities, including manufacturing, will be accounted for as a reduction of related expenses.

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

The Company evaluated the license under ASC 606 and concluded that the license is a functional intellectual property license. The Company determined that Zai Lab benefited from the license along with the initial know-how transfer at the time of grant, and therefore the related performance obligation is satisfied at a point in time. Additionally, the Company is entitled to sales milestones and royalties from Zai Lab upon future sales of the licensed products in the

Zai Lab territory, and revenue will be recognized when the related sales occur. Costs that are incurred associated with Zai Lab territory specific activities are reimbursable from Zai and will be recognized as revenue.

For the purposes of ASC 606, the transaction price of the Zai Lab agreement as of the outset of the arrangement was determined to be $25.0 million, which consisted of the upfront cash payment. The other potential milestone payments that the Company is eligible to receive were excluded from the transaction price, as all milestone amounts were fully constrained based on the probability of achievement. The Company satisfied the performance obligation upon delivery of the licenses and initial know-how transfer and recognized the upfront payment of $25.0 million as revenue during the year ended December 31, 2021.

The Company will reevaluate the transaction price at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur, and if necessary, the Company will adjust its estimate of the transaction price, and any addition to the transaction price would be recognized as revenue when it becomes probable that inclusion would not lead to a significant revenue reversal.

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, and through December 31, 2021, the Company has achieved $105.0 million in specified regulatory and commercialization milestones. In addition to upfront and milestone payments received through December 31, 2021, the Company is eligible to receive up to $822.0 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 agreed to work together to co-commercialize pralsetinib and equally share responsibilities, profits and losses. In addition, the Company is eligible to receive tiered royalties ranging from high-teens to mid-twenties on annual net sales of pralsetinib outside the U.S., excluding Greater China (the Roche territory). The Company and Roche 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 years ended December 31, 2021 and 2020, cash consideration associated with regulatory or commercialization milestones of $50.0 million and $55.0 million respectively, were added to the estimated transaction price of the Roche pralsetinib agreement and recognized revenue in such periods. The other potential milestone payments that the Company is eligible to receive under the Roche pralsetinib agreement have been excluded from the transaction price, as all the remaining milestone amounts were fully constrained based on the probability of achievement. The Company will reevaluate the transaction price at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur, and if necessary, the Company will adjust its estimate of the transaction price, and any addition to the transaction price would be recognized as revenue when it becomes probable that inclusion would not lead to a significant revenue reversal.

The following table summarizes revenue recognized under the Roche pralsetinib collaboration during the years ended December 31, 2021, 2020 and 2019 (in thousands):

	Year Ended December 31,		
	2021	2020	2019
Upfront license revenue	$ —	$ 695,694	$ —
License milestone revenue	50,000	55,000	—
Manufacturing and other services related to Roche territory-specific activities	6,022	2,406	—
Total Roche pralsetinib collaboration revenue	$ 56,022	$ 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 are accounted for as an increase to or reduction of research and development expenses. Prior to July 1, 2021, the Company was the principal for product sales to customers in the U.S. and recognized revenues on sales to third parties in product revenue, net in its consolidated statements of operations and comprehensive income (loss). On July 1, 2021, Roche took over certain responsibilities associated with product sales to customers, pricing and distribution matters for GAVRETO in the U.S. and became the principal for recording product sales to customers in the U.S., and the Company recognized its portion of the commercial losses sharing as collaboration loss sharing in its consolidated statements of operations and comprehensive income (loss).

The following table summarizes the amount from collaboration loss sharing after Roche became the principal for product sales of GAVRETO to customers in the U.S. (in thousands):

	Year Ended December 31,		
	2021	2020	2019
The Company's share of loss in the U.S. for pralsetinib	$ 7,801	$ —	$ —

The following table summarizes the amounts recognized as reductions to selling, general and administrative expenses related to the commercialization of GAVRETO in the U.S., and reductions to research and development expenses related to global development activities for pralsetinib under the Roche pralsetinib collaboration during the years ended December 31, 2021, 2020 and 2019 (in thousands):

	Year Ended December 31,		
	2021	2020	2019
Reductions to selling, general and administrative expenses	$ 18,753	$ 10,631	$ —
Reductions to research and development expenses	11,192	20,459	—

The following table summarizes the contract assets associated with the Roche pralsetinib collaboration as of December 31, 2021 and 2020 (in thousands):

	December 31, 2021	December 31, 2020
Accounts receivable, net	$ 2,679	$ —
Unbilled accounts receivable	$ 6,802	$ 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 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, 2021, 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, 2021, 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 and received in 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, 2021 and 2020, no material revenue was recognized from the Clementia collaboration. During the year ended December 31, 2019, the Company recognized $46.2 million as revenue for the delivery of the license, the technology transfer and the transfer of existing manufacturing inventory. There was no revenue deferred as a contract liability associated with the Clementia agreement as of December 31, 2021 and 2020.

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 received an upfront cash payment of $40.0 million, and through December 31, 2021, the Company has achieved $23.0 million in milestone payments under this collaboration. Subject to the terms of the CStone agreement, in addition to the upfront payments received and milestones achieved through December 31, 2021, the Company will be eligible to receive up to approximately $323.0 million in additional milestone payments, including $95.5 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, 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 expenses payable to CStone during the years ended December 31, 2021, 2020 and 2019 is as follows (in thousands):

	Year Ended December 31,		
	2021	2020	2019
Manufacturing and research and development services related to global development activities, net of expenses payable to CStone	$ 2,358	$ 3,060	$ 3,286

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 year ended December 31, 2018.

During the years ended December 31, 2021, 2020, and 2019, cash consideration associated with achieved development milestones of $9.0 million, $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.

During the year ended December 31, 2021, the Company entered into commercial supply agreements and an avapritinib manufacturing technology transfer agreement with CStone related to drug substance of avapritinib and drug product of avapritinib and pralsetinib to assist CStone’s commercialization activities conducted specifically for the CStone territory. The manufacturing activities in these agreements were considered as distinct performance obligations from the CStone collaboration agreement and collaboration revenue is recognized upon delivery of the drug substance and drug product to CStone.

A summary of revenue recognized under the CStone agreement during the years ended December 31, 2021, 2020 and 2019 is as follows (in thousands):

	Year Ended December 31,		
	2021	2020	2019
License milestone revenue	$ 9,000	$ 2,000	$ 12,000
Manufacturing services and royalty revenue related to CStone territory-specific activities	24,395	1,630	144
Total CStone collaboration revenue	$ 33,395	$ 3,630	$ 12,144

The following table presents the contract assets associated with the CStone collaboration as of December 31, 2021 and 2020 (in thousands):

	As of December 31,	
	2021	2020
Accounts receivable, net	$ 8,164	$ 563
Unbilled accounts receivable	$ 5,034	$ —

As of December 31, 2021, the Company had $4.8 million of deferred revenue as a contract liability associated with the CStone collaboration. This contract liability mainly resulted from advance payments made by CStone in connection with commercial supply of pralsetinib for the CStone territory. The contract liability associated with the CStone collaboration was $6.5 million at December 31, 2020.

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 BLU-852, a development candidate for 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 prior periods, 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 preclinical 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, 2021, the Company has achieved $23.5 million in milestone payments under this collaboration. Subject to the terms of the Roche immunotherapy agreement, as amended, in addition to upfront payments received and milestones achieved through December 31, 2021, the Company is eligible to receive up to approximately $319.3 million in contingent option fees and milestone payments related to specified research, preclinical, 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, 2021, the Company has achieved $23.5 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.

A summary of revenue recognized under the Roche immunotherapy agreement during the years ended December 31, 2021, 2020 and 2019 is as follows (in thousands):

	Year Ended December 31,		
	2021	2020	2019
Roche collaboration research and development services revenue	$ 7,636	$ 14,580	$ 8,165

During the years ended December 31, 2021, 2020 and 2019, the Company recognized the following revenue due to the changes in the contract liability balances (in thousands):

	Year Ended December 31,		
	2021	2020	2019
Amounts included in the contract liability at the beginning of the period	$ 5,080	$ 11,546	$ 4,578

As of December 31, 2021, the Company had revenue deferred as a contract liability related to the Roche immunotherapy agreement of $31.4 million, of which $6.3 million was included in current liabilities, and the research and development services related to the performance obligation are expected to be performed over a remaining period of approximately 3.25 years. 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.

12. 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. The Company did not sell any shares of its common stock under ATM Facility during the year ended December 31, 2021.

13. 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, 2021 and 2022, the number of shares reserved for issuance under the 2015 Plan was increased by 2,311,741 and 2,365,643 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. As of December 31, 2021, there were 3,027,882 shares available for future grant under the 2015 Plan.

2020 Inducement Plan

In March 2020, the Company's board of directors adopted the 2020 Inducement Plan (the Inducement Plan), pursuant to which the Company may grant, subject to the terms of the Inducement Plan and Nasdaq rules, nonstatutory stock options, stock appreciation rights, restricted stock awards, restricted stock units, and other stock-based awards. The Company initially reserved a total of 1,000,000 shares of common stock for the issuance of awards under the Inducement Plan. 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, 2021, there were 288,982 shares available for future grant under the Inducement Plan.

Stock-based Compensation Expense

The Company recognized stock-based compensation expense totaling $91.6 million, $75.5 million and $54.7 million for the years ended December 31, 2021, 2020 and 2019, respectively.

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

	Year Ended December 31,		
	2021	2020	2019
Stock options	$ 57,912	$ 57,237	$ 47,726
Restricted stock units	33,939	18,407	6,445
Employee stock purchase plan	1,184	958	482
Subtotal	93,035	76,602	54,653
Capitalized stock-based compensation costs	(1,405)	(1,076)	—
Stock-based compensation expense included in total cost and operating expenses	$ 91,630	$ 75,526	$ 54,653

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

	Year Ended December 31,		
	2021	2020	2019
Research and development	$ 39,670	$ 33,642	$ 28,596
Selling, general and administrative	51,960	41,884	26,057
Total stock-based compensation expense included in operating expenses	$ 91,630	$ 75,526	$ 54,653

At December 31, 2021, there was $199.8 million of total unrecognized compensation cost related to non-vested stock awards, which is expected to be recognized over a weighted-average period of 2.6 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,		
	2021	2020	2019
Risk-free interest rate	0.96 %	1.02 %	2.21 %
Expected dividend yield	— %	— %	— %
Expected term (years)	6.0	6.0	6.0
Expected stock price volatility	58.03 %	60.48 %	63.83 %

The following table summarizes the stock option activity for the year ended December 31, 2021:

	Shares	Weighted-Average Exercise Price	Remaining Contractual Life (in Years)	Aggregate Intrinsic Value(1) (in thousands)
Outstanding at December 31, 2020	6,030,641	$ 61.28	7.41	$ 306,810
Granted	1,125,514	98.50		
Exercised	(982,791)	48.13		
Canceled	(491,342)	79.27		
Outstanding at December 31, 2021	5,682,022	$ 69.37	6.99	$ 214,675
Exercisable at December 31, 2021	3,499,094	$ 61.30	6.13	$ 160,313

(1) Intrinsic value represents the amount by which the fair market value as of December 31, 2021 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, 2021, 2020 and 2019 was $52.93, $34.77 and $48.96, respectively. The total intrinsic value of options exercised in the years ended December 31, 2021, 2020, and 2019 was $52.3 million, $43.3 million, and $33.8 million, respectively.

At December 31, 2021, the total unrecognized compensation expense related to unvested stock option awards was $93.8 million, which is expected to be recognized over a weighted-average period of approximately 2.4 years.

Restricted stock units

Restricted stock units granted by the Company generally vest ratably over four years. The following table summarizes the restricted stock units activity for the year ended December 31, 2021:

	Shares	Weighted-Average Grant Date Fair Value
Unvested shares at December 31, 2020	1,171,686	$ 65.37
Granted	999,504	98.62
Vested	(321,645)	66.87
Forfeited	(259,385)	78.31
Unvested shares at December 31, 2021	1,590,160	$ 83.85

The total fair value of restricted stock units vested during the years ended December 31, 2021, 2020 and 2019 was $31.6 million, $7.4 million and $0.7 million, respectively. As of December 31, 2021, the total unrecognized compensation expense related to unvested restricted stock units was $105.9 million, which is expected to be recognized over a weighted-average period of approximately 2.7 years.

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, 2021 and 2022, the number of shares reserved for issuance under the 2015 ESPP was increased by 577,935 and 591,410 shares, respectively. The Company issued 43,167, 38,516, and 20,724 shares under the ESPP during the years ended December 31, 2021, 2020, and 2019 respectively.

14. Net income (loss) 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, 2021, 2020 and 2019 are as follows (in thousands, except per share data):

	Year Ended December 31,		
	2021	2020	2019
Net income (loss) - basic and diluted	$ (644,085)	$ 313,882	$ (347,694)
Weighted average shares outstanding - basic	58,518	54,534	47,829
Effect of dilutive securities:			
Stock options	—	1,303	—
Restricted stock units	—	331	—
Weighted average shares outstanding - diluted	58,518	56,168	47,829
Net income (loss) per share - basic	$ (11.01)	$ 5.76	$ (7.27)
Net income (loss) per share - diluted	(11.01)	5.59	(7.27)

For the years ended December 31, 2021, 2020 and 2019, the following dilutive securities were not included in the computation of net income (loss) per share because the effect would be anti-dilutive (in thousands):

	Year Ended December 31,		
	2021	2020	2019
Stock options	5,682	4,480	5,796
Restricted stock units	1,590	13	420
ESPP shares	24	19	14
Total	7,296	4,512	6,230

15. 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, 2021, 2020 and 2019:

	Year Ended December 31,		
	2021	2020	2019
Federal income tax (benefit) at statutory rate	21.00 %	21.00 %	21.00 %
Permanent differences	0.07	(0.47)	1.11
In-process research and development	(8.53)	—	—
Federal research and development credits	0.76	(0.96)	0.77
Federal orphan drug credits	4.02	(10.35)	6.90
State income tax, net of federal benefit	1.26	0.08	7.46
Other	(0.05)	1.50	2.13
Foreign rate differential	(0.10)	0.37	(0.03)
Deferred rate change	0.79	2.60	(0.08)
Foreign tax credit	0.39	—	—
Change in valuation allowance	(20.08)	(13.42)	(39.26)
Effective income tax rate	(0.47)%	0.35 %	— %

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

	Year Ended December 31,		
	2021	2020	2019
Deferred tax assets:			
Net operating loss carryforwards	$ 243,670	$ 140,769	$ 219,935
Research and development credit carryforwards	36,345	23,679	19,240
Orphan drug credit carryforwards	150,859	125,153	92,538
Accrued expenses and other	40,617	32,206	25,842
Deferred revenue	6,598	7,317	10,971
Deferred lease incentive	—	—	—
Deferred rent	24,798	19,308	26,196
Jublient license	448	—	—
Interest expense	29	—	—
Total gross deferred tax asset	503,364	348,432	394,722
Deferred tax liability			
Depreciation	(5,157)	(5,451)	(4,474)
Right of use assets	(20,059)	(14,539)	(19,869)
UNICAP	(1,966)	—	—
Prepaid expenses	(2)	—	—
Valuation allowance	(476,180)	(328,442)	(370,379)
Net deferred tax asset	$ —	$ —	$ —

Management has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets and has determined that it is more likely than not that the Company will not recognize the benefits of its net federal, foreign and state deferred tax assets, and as a result, a valuation allowance of $476.2 million, $328.4 million and $370.4 million has been established at December 31, 2021, 2020 and 2019, respectively. The change in the valuation allowance was $147.7 million, ($42.0) million and $136.9 million for the years ended December 31, 2021, 2020 and 2019, respectively. The increase of deferred tax asset between December 31, 2021 and 2020 is primarily driven by increased net operating losses (NOL) and credits generated from R&D activities during the year.

The Company has incurred NOL since inception with the exception of year 2020. As of December 31, 2021, the Company had federal and state NOL carryforwards of $872.6 million and $997.1 million, respectively, which begin to expire in 2030, and of which $851.1 million of the Company's federal NOL is post 2017 NOL that will be carried forward indefinitely. As a result of Lengo acquisition (a stock acquisition for tax purposes) in 2021, the Company has a carryover inside tax basis in Lengo's assets and liabilities, including its tax attributes. The Company acquired $66.6 million and $67.1 million of the federal and state NOL carryforwards, respectively, from the acquisition of Lengo. All such acquired NOL is post 2017 NOL and will be carried forward indefinitely for federal purposes. As of December 31, 2021, the Company had federal and state research and development tax credit carryforwards of $19.4 million and $17.7 million, respectively, which begin to expire in 2030. The Company acquired $0.3 million and $0.2 million of the federal and state research development tax credit carryforwards, respectively, from the acquisition of Lengo. As of December 31, 2021, the Company had federal orphan drug credits of $150.9 million, which begin to expire in 2035 and state investment tax credits of $0.6 million, which have begun to expire in 2021. As of December 31, 2021, the Company has foreign tax credits of $2.5 million which will expire in 2031.

The Company has analyzed and validated its research and development tax credits as well as its orphan drug credits for 2011-2020. The Company generated research credits in 2021 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, 2021 until such study is completed and the adjustment is known. A valuation allowance has been provided against the Company's research and development credits and, if an adjustment is required, this adjustment would be offset by an adjustment to the deferred tax asset established for the research and development credit carry-forwards and the valuation allowance.

The Internal Revenue Code of 1986, as amended (the Code), provides for a limitation of the annual use of NOL and other tax attributes (such as research and development tax credit carryforwards) following certain ownership changes (as defined by the Code) that could limit the Company's ability to utilize these carryforwards. We may have experienced such ownership changes in the past, and we may experience ownership changes in the future as a result of

shifts in our stock ownership, some of which are outside our control. Approximately $2 million of the Company's NOL carryforwards may not be available for utilization within their applicable carryforward periods based on the Section 382 study in 2020. 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.

With respect to the net operating losses and research and development tax credit carryforwards acquired from the acquisition of Lengo, the Company has not completed a study to assess whether an ownership change under Section 382 of the Code has occurred, or whether there have been multiple ownership changes since Lengo's formation. Accordingly, the Company's ability to utilize the aforementioned carryforwards may be limited and in turn, 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, 2021 and 2020, the Company has no unrecognized tax benefits or accrued interest related to unrecognized tax benefits. As of December 31, 2021, 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.

16. Leases

38 Sidney Street

On February 12, 2015, the Company entered into a lease for approximately 39,000 rentable square feet of office and laboratory space at 38 Sidney Street in Cambridge, Massachusetts, which the initial term of the lease agreement will expire on October 31, 2022. On December 15, 2021, the Company extended the lease term to expire on November 30, 2029, and agreed to pay an initial annual base rent of approximately $4.5 million, which rises annually until it reaches approximately $5.5 million. The lease extension provided the Company with an allowance for leasehold improvements of $0.8 million improvements to be made to the premises. Security deposit of $0.9 million was recorded as restricted cash on the Company's consolidated balance sheet as of December 31, 2021. The Company is subleasing the space to third parties and the term of the subleases will expire on February 28, 2022 and September 30, 2022.

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. On September 19, 2018, the Company entered into an amendment to the lease agreement to expand the rentable square footage to approximately 139,216 square feet. The initial term of the lease agreement will expire on November 30, 2029, unless terminated sooner. The lease agreement also provides the Company with an option to extend the lease agreement for two consecutive five-year periods at the then fair market annual rent, as defined in the lease agreement.

The Company has agreed to pay for the 99,833 rentable square feet an initial annual base rent of approximately $7.7 million, which increases annually until it reaches approximately $10.6 million in the last year of the initial term. The Company has also agreed to pay an initial annual base rent of approximately $3.2 million for the expansion premises, which increases annually until it reaches approximately $4.2 million in the last year of the initial term for the expansion premises. The amended lease provided the Company with a total tenant improvement allowance of approximately $17.4 million for improvements to be made to the premises. Security deposit of $3.8 million was recorded as restricted cash on the Company's consolidated balance sheet as of December 31, 2021.

The lease agreements do not contain residual value guarantees and the components of lease cost for the years ended December 31, 2021, 2020 and 2019 were as follows (in thousands):

	Year Ended December 31,		
Operating leases:	2021	2020	2019
Lease cost	$ 18,299	$ 17,600	$ 16,162
Sublease income	(2,174)	(2,919)	(2,834)
Net lease cost	$ 16,125	$ 14,681	$ 13,328

The Company has not entered into any material short-term leases or financing leases as of December 31, 2021.

Supplemental cash flow information related to leases for the years ended December 31, 2021 and 2020 was as follows (in thousands):

	Year Ended December 31,	
	2021	2020
Cash paid for amounts included in the measurement of lease liabilities:	$ 14,896	$ 14,444
Lease liabilities arising from obtaining right-of-use assets:		
Operating leases	$ 28,929	$ 479

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	7.8
Weighted average discount rate	7.4%

Future minimum lease payments under non-cancellable leases as of December 31, 2021 were as follows (in thousands):

2022	15,825
2023	17,691
2024	18,183
2025	18,557
2026	19,089
Thereafter	58,912
Total future minimum lease payments	148,257
Less imputed interest	(36,849)
Total	$ 111,408

* Minimum lease payments have not been reduced by minimum net sublease receivables of $2.0 million due in the future under the Company's non-cancelable subleases for the office and laboratory space located at 38 Sidney Street, Cambridge, Massachusetts.

17. Employee Benefit Plans

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

401(k) Savings Plan

The Company maintains a 401(k) plan for employees (the 401(k) Plan). The 401(k) Plan is intended to qualify

under Section 401(k) of the Code, so that contributions to the 401(k) Plan by 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. The expenses related to the 401(k) Plan for the years ended December 31, 2021, 2020 and 2019 were $3.0 million, $1.9 million and $1.2 million, respectively.

Switzerland Defined Benefit Plan

The Company maintains a pension plan covering employees of its Swiss subsidiary, Blueprint Medicines (Switzerland) GmbH (the "Swiss Plan"). The Swiss Plan is a government-mandated retirement fund that provides employees with a minimum benefit. Employer and employee contributions are made to the Swiss Plan based on various percentages of salary and wages that vary according to employee age and other factors. As is customary with Swiss pension plans, the assets of the Swiss Plan are invested in a collective fund with multiple employers. The Company has no investment authority over the assets of the Swiss Plan, which are held and invested by a Swiss insurance company. The investment strategy of the Swiss Plan is managed by an independent asset manager with the objective of achieving a consistent long-term return which will provide sufficient funding for future pension obligations while limiting risk. As of December 31, 2021, the Swiss Plan had an unfunded status of $3.4 million, which resulted from fair value of plan assets of $4.5 million and projected benefit obligation of $7.9 million. The accumulated benefit obligation at December 31, 2021 was $6.5 million. The Company's net periodic benefit cost for the year ended December 31, 2021 was $2.0 million. The net periodic benefit cost for the years ended December 31, 2020 and 2019 were not material. The contributions to the Swiss Plan for the years ended December 31, 2021, 2020 and 2019 were not material.

18. Commitments and Contingencies

Purchase Commitments Associated with Commercial Supply Agreements

In connection with the commercialization of AYVAKIT/AYVAKYT and GAVRETO, the Company has negotiated manufacturing agreements with certain vendors that require the Company to meet minimum purchase obligations on an annual basis. The aggregate amount of future minimum purchase obligations under these manufacturing agreements over the period of next five years is approximately $34.2 million as of December 31, 2021.

Legal Proceedings

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

Indemnification Agreements

In the ordinary course of business, the Company may provide indemnification of varying scope and terms to vendors, lessors, business partners, and other parties with respect to certain matters including, but not limited to, losses arising out of breach of such agreements or from intellectual property infringement claims made by third parties. In addition, the Company has entered into indemnification agreements with members of its board of directors and senior management that will require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors or officers. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is, in many cases, unlimited. To date, the Company has not incurred any material costs as a result of such indemnifications. The Company is not aware of any claims under indemnification arrangements, and it has not accrued any liabilities related to such obligations in its consolidated financial statements as of December 31, 2021 or 2020.

19. Subsequent Events

During the first quarter of 2022, a $30.0 million development milestone was achieved under our license agreement with Clementia.

Exhibit 1.1

Execution Version

BLUEPRINT MEDICINES CORPORATION

$300,000,000

COMMON STOCK

SALES AGREEMENT

February 17, 2022

Cowen and Company, LLC
599 Lexington Avenue
New York, NY 10022

Ladies and Gentlemen:

Blueprint Medicines Corporation, a Delaware Corporation (the "**Company**"), confirms its agreement (this "**Agreement**") with Cowen and Company, LLC ("**Cowen**"), as follows:

1. Issuance and Sale of Shares. The Company agrees that, from time to time during the term of this Agreement, on the terms and subject to the conditions set forth herein and any Terms Agreement (defined below), it may issue and sell to or through Cowen, acting as agent and/or principal, shares (the "**Shares**") of the Company's common stock, par value $0.001 per share (the "**Common Stock**"), having an aggregate offering price of up to $300,000,000 (the "**Maximum Amount**"). Notwithstanding anything to the contrary contained herein, the parties hereto agree that compliance with the limitation set forth in this Section 1 on the number of shares of Common Stock issued and sold under this Agreement and any Terms Agreement shall be the sole responsibility of the Company, and Cowen shall have no obligation in connection with such compliance. The issuance and sale of Common Stock through Cowen will be effected pursuant to the Registration Statement (as defined below) filed by the Company and which became effective automatically upon filing with the Securities and Exchange Commission (the "**Commission**") under Rule 462(c) of the Securities Act (as defined below), although nothing in this Agreement shall be construed as requiring the Company to use the Registration Statement (as defined below) to issue the Common Stock.

The Company has filed, in accordance with the provisions of the Securities Act of 1933, as amended, and the rules and regulations thereunder (collectively, the "**Securities Act**"), with the Commission a registration statement on Form S-3ASR (File No. 333-236424), including a base prospectus, relating to certain securities, including the Common Stock, to be issued from time to time by the Company, and which incorporates by reference documents that the Company has filed or will file in accordance with the provisions of the Securities Exchange Act of 1934, as amended, and the rules and regulations thereunder (collectively, the "**Exchange Act**"). The Company has prepared a prospectus supplement specifically relating to the Shares (the "**Prospectus Supplement**") to the base prospectus included as part of such registration statement. The Company has furnished to Cowen, for use by Cowen, copies of the prospectus included as part of such registration statement, as supplemented by the Prospectus Supplement, relating to the Shares. Except where the context otherwise requires, such registration statement, and any post-effective

amendment thereto, as amended when it became effective, including all documents filed as part thereof or incorporated by reference therein, and including any information contained in a Prospectus (as defined below) subsequently filed with the Commission pursuant to Rule 424(b) under the Securities Act or deemed to be a part of such registration statement pursuant to Rule 430B of the Securities Act, or any subsequent registration statement on Form S-3 filed pursuant to Rule 415(a)(6) under the Securities Act by the Company with respect to the Shares, is herein called the "**Registration Statement.**" The base prospectus, including all documents incorporated therein by reference, included in the Registration Statement, as it may be supplemented by the Prospectus Supplement, in the form in which such prospectus and/or Prospectus Supplement have most recently been filed by the Company with the Commission pursuant to Rule 424(b) under the Securities Act, together with any "issuer free writing prospectus," as defined in Rule 433 under the Securities Act ("**Rule 433**"), relating to the Shares that (i) is consented to by Cowen (including any free writing prospectus prepared by the Company solely for use in connection with the offering contemplated by a particular Terms Agreement), hereinafter referred to as a "**Permitted Free Writing Prospectus**," (ii) is required to be filed with the Commission by the Company or (iii) is exempt from filing pursuant to Rule 433(d)(5)(i), in each case in the form filed or required to be filed with the Commission or, if not required to be filed, in the form retained in the Company's records pursuant to Rule 433(g), is herein called the "**Prospectus**." Any reference herein to the Registration Statement, the Prospectus or any amendment or supplement thereto shall be deemed to refer to and include the documents incorporated by reference therein, and any reference herein to the terms "amend," "amendment" or "supplement" with respect to the Registration Statement or the Prospectus shall be deemed to refer to and include the filing after the execution hereof of any document with the Commission deemed to be incorporated by reference therein. For purposes of this Agreement, all references to the Registration Statement, the Prospectus or to any amendment or supplement thereto shall be deemed to include any copy filed with the Commission pursuant to the Electronic Data Gathering Analysis and Retrieval System ("**EDGAR**").

The Registration Statement is an "automatic shelf registration statement" (as defined in Rule 405 under the Securities Act) and the Shares have been and remain eligible for registration by the Company on such automatic shelf registration statement.

2. Agency and Principal Transactions. (a) Each time that the Company wishes to issue and sell the Shares hereunder through Cowen, acting as agent (each, an "**Agency Transaction**"), it will notify Cowen by email notice (or other method mutually agreed to in writing by the parties) (a "**Placement Notice**") containing the parameters in accordance with which it desires the Shares to be sold, which shall at a minimum include the number of Shares to be issued, the time period during which sales are requested to be made, any limitation on the number of Shares that may be sold in any one Trading Day (as defined in Section 3) and any minimum price below which sales may not be made, a form of which containing such minimum sales parameters necessary is attached hereto as Schedule 1. The Placement Notice shall originate from any of the individuals from the Company set forth on Schedule 2 (with a copy to each of the other individuals from the Company listed on such schedule), and shall be addressed to each of the individuals from Cowen set forth on Schedule 2, as such Schedule 2 may be amended from time to time. The Placement Notice shall be effective upon receipt by Cowen unless and until (i) in accordance with the notice requirements set forth in Section 4, Cowen declines to accept the terms contained therein for any reason, in its sole discretion, (ii) the entire amount of the Shares have been sold, (iii) in accordance with the notice requirements set forth in Section 4, the Company suspends or terminates the Placement

Notice, (iv) the Company issues a subsequent Placement Notice with parameters superseding those on the earlier dated Placement Notice, or (v) this Agreement has been terminated under the provisions of Section 11. The amount of any discount, commission or other compensation to be paid by the Company to Cowen in connection with the sale of the Shares shall be calculated in accordance with the terms set forth in Schedule 3**.** It is expressly acknowledged and agreed that neither the Company nor Cowen will have any obligation whatsoever with respect to an Agency Transaction or any Shares unless and until the Company delivers a Placement Notice to Cowen and Cowen does not decline such Placement Notice pursuant to the terms set forth above, and then only upon the terms specified therein and herein. In the event of a conflict between the terms of this Agreement and the terms of a Placement Notice, the terms of the Placement Notice will control.

(b) The Company may also offer to sell the Shares directly to Cowen, as principal, in which event such parties shall enter into a separate agreement (each, a "**Terms Agreement**") in substantially the form of Schedule 2(b) hereto (with such changes thereto as may be agreed upon by the Company and Cowen), relating to such sale in accordance with Section 3(b) hereof (each such transaction being referred to as a "**Principal Transaction**").

3. Sale of Shares by Cowen. (a) Subject to the terms and conditions herein set forth, upon the Company's delivery of a Placement Notice with respect to an Agency Transaction, and unless the sale of the Shares described therein has been declined, suspended, or otherwise terminated in accordance with the terms of this Agreement, Cowen, for the period specified in the Placement Notice, will use its commercially reasonable efforts consistent with its normal trading and sales practices and applicable state and federal laws, rules and regulations and the rules of the Nasdaq Stock Market, Inc. ("**Nasdaq**") to sell such Shares up to the amount specified in such Placement Notice, and otherwise in accordance with the terms of such Placement Notice. Cowen will provide written confirmation to the Company (including by email correspondence to each of the individuals of the Company set forth on Schedule 2, if receipt of such correspondence is actually acknowledged by any of the individuals to whom the notice is sent, other than via auto-reply) no later than the opening of the Trading Day (as defined below) immediately following the Trading Day on which it has made sales of Shares hereunder setting forth the number of Shares sold on such day, the volume-weighted average price of the Shares sold, and the Net Proceeds (as defined below) payable to the Company. In the event the Company engages Cowen for a sale of Shares in an Agency Transaction that would constitute a "block" within the meaning of Rule 10b-18(a)(5) under the Exchange Act (a "**Block Sale**"), the Company will provide Cowen, at Cowen's request and upon reasonable advance notice to the Company, on or prior to the Settlement Date (as defined below), the opinions of counsel, accountant's letter and officers' certificates set forth in Section 8 hereof, each dated the Settlement Date, and such other documents and information as Cowen shall reasonably request. Cowen may sell Shares by any method permitted by law deemed to be an "at the market" offering as defined in Rule 415 of the Securities Act. The Company acknowledges and agrees that (i) there can be no assurance that Cowen will be successful in selling Shares, and (ii) Cowen will incur no liability or obligation to the Company or any other person or entity if it does not sell Shares for any reason other than a failure by Cowen to use its commercially reasonable efforts consistent with its normal trading and sales practices to sell such Shares as required under this Section 3. For the purposes hereof, "**Trading Day**" means any day on which

the Company's Common Stock is purchased and sold on the principal market on which the Common Stock is listed or quoted.

(b)

(i) If the Company wishes to issue and sell the Shares to Cowen pursuant to this Agreement in a Principal Transaction, it will notify Cowen of the proposed terms of the Principal Transaction. If Cowen, acting as principal, wishes to accept such proposed terms (which it may decline to do for any reason in its sole discretion) or, following discussions with the Company, wishes to accept amended terms, the Company and Cowen shall enter into a Terms Agreement setting forth the terms of such Principal Transaction.

(ii) The terms set forth in a Terms Agreement shall not be binding on the Company or Cowen unless and until the Company and Cowen have each executed and delivered such Terms Agreement accepting all of the terms of such Terms Agreement. In the event of a conflict between the terms of this Agreement and the terms of a Terms Agreement, the terms of such Terms Agreement shall control.

(iii) Each sale of the Shares to Cowen in a Principal Transaction shall be made in accordance with the terms of this Agreement and a Terms Agreement, which shall provide for the sale of such Shares to, and the purchase thereof by, Cowen. A Terms Agreement may also specify certain provisions relating to the reoffering of such Shares by Cowen. The commitment of Cowen to purchase the Shares pursuant to any Terms Agreement shall be deemed to have been made on the basis of the representations, warranties and agreements of the Company contained, and shall be subject to the terms and conditions set forth, in this Agreement and such Terms Agreement. Any such Terms Agreement shall specify the number of the Shares to be purchased by Cowen pursuant thereto, the price to be paid to the Company for such Shares, any provisions relating to rights of, and default by, Cowen in the reoffering of the Shares, and the time, date (each such time and date being referred to herein as a "**Principal Settlement Date**") and place of delivery of and payment for such Shares.

(c) Notwithstanding any other provision of this Agreement, the Company shall not offer, sell or deliver, or request the offer or sale, of any Shares pursuant to this Agreement (whether in an Agency Transaction or a Principal Transaction) and, by notice to Cowen given by telephone (confirmed promptly by email), shall cancel any instructions for the offer or sale of any Shares, and Cowen shall not be obligated to offer or sell any Shares, (i) during any period in which the Company is, or could be deemed to be, in possession of material non-public information, or (ii) at any time from and including the date on which the Company shall issue a press release containing, or shall otherwise publicly announce, its earnings, revenues or other results of operations (an "**Earnings Announcement**") through and including the time that the Company files a Quarterly Report on Form 10-Q or an Annual Report on Form 10-K that includes consolidated financial statements as of and for the same period or periods, as the case may be, covered by such Earnings Announcement.

4. Suspension of Sales.

(a) The Company or Cowen may, upon notice to the other party in writing (including by email correspondence to each of the individuals of the other party set forth on Schedule 2, if

receipt of such correspondence is actually acknowledged by any of the individuals to whom the notice is sent, other than via auto-reply) or by telephone (confirmed immediately by email correspondence to each of the individuals of the other party set forth on Schedule 2), suspend any sale of Shares; *provided, however*, that such suspension shall not affect or impair either party's obligations with respect to any Shares sold hereunder prior to the receipt of such notice. Each of the parties agrees that no such notice under this Section 4 shall be effective against the other unless it is made to one of the individuals named on Schedule 2 hereto, as such schedule may be amended from time to time.

(b) If either Cowen or the Company has reason to believe that the exemptive provisions set forth in Rule 101(c)(1) of Regulation M under the Exchange Act are not satisfied with respect to the Common Stock, it shall promptly notify the other party, and Cowen may, at its sole discretion, suspend sales of the Shares under this Agreement.

(c) The Registration Statement became effective upon filing on February 13, 2020. Notwithstanding any other provision of this Agreement, during any period in which the Registration Statement is no longer effective under the Securities Act, the Company shall promptly notify Cowen, the Company shall not request the sale of any Shares, and Cowen shall not be obligated to sell or offer to sell any Shares.

5. Settlement.

(a) Settlement of Shares. Unless otherwise specified in the applicable Placement Notice, settlement for sales of Shares in an Agency Transaction will occur on the second (2nd) Trading Day (or such earlier day as is industry practice for regular-way trading) following the date on which such sales are made (each, an "**Agency Settlement Date**" and the first such Agency Settlement Date, the "**First Delivery Date**"; and any Agency Settlement Date and Principal Settlement Date shall be referred to as a "**Settlement Date**"). The amount of proceeds to be delivered to the Company on a Settlement Date against receipt of the Shares sold (the "**Net Proceeds**") will be equal to the aggregate sales price received by Cowen at which such Shares were sold, after deduction for (i) Cowen's commission, discount or other compensation for such sales payable by the Company pursuant to Section 2 hereof or pursuant to any applicable Terms Agreement, (ii) any other amounts due and payable by the Company to Cowen hereunder pursuant to Section 7(g) (Expenses) hereof, and (iii) any transaction fees imposed by any governmental or self-regulatory organization in respect of such sales.

(b) Delivery of Shares. On or before each Settlement Date, the Company will, or will cause its transfer agent to, electronically transfer the Shares being sold by crediting Cowen's or its designee's account (provided Cowen shall have given the Company written notice of such designee prior to the Settlement Date) at The Depository Trust Company through its Deposit and Withdrawal at Custodian System or by such other means of delivery as may be mutually agreed upon by the parties hereto which in all cases shall be freely tradeable, transferable, registered shares in good deliverable form. On each Settlement Date, Cowen will deliver the related Net Proceeds in same day funds to an account designated by the Company on, or prior to, the Settlement Date. The Company agrees that if the Company, or its transfer agent (if applicable), defaults in its obligation to deliver duly authorized Shares on a Settlement Date through no fault of Cowen, the Company agrees that in addition to and in no way limiting the rights and obligations

set forth in Section 9(a) (Indemnification and Contribution) hereto, it will (i) hold Cowen harmless against any loss, claim, damage, or reasonable and documented expense (including reasonable and documented legal fees and expenses), as incurred, arising out of or in connection with such default by the Company and (ii) pay to Cowen (without duplication) any commission, discount, or other compensation to which it would otherwise have been entitled absent such default.

6. Representations and Warranties of the Company. The Company represents and warrants to, and agrees with, Cowen that as of (i) the date of this Agreement, (ii) each date on which the Company executes and delivers a Terms Agreement, (iii) each Time of Sale (defined below), (iv) each Settlement Date, and (v) each Bring-Down Date (as defined below)(each such date included in (i) through (v) above, a "**Representation Date**"):

(a) Compliance with Registration Requirements. The Registration Statement became effective automatically upon filing with the Commission under the Securities Act. The Company has complied to the Commission's satisfaction with all requests of the Commission for additional or supplemental information. No stop order suspending the effectiveness of the Registration Statement is in effect and no proceedings for such purpose have been instituted or are pending or, to the best knowledge of the Company, contemplated or threatened by the Commission. The Company meets the requirements for use of Form S-3 under the Securities Act. The sale of the Shares hereunder meets the requirements of General Instruction I.B.1 of Form S-3ASR.

(b) No Misstatement or Omission. The Prospectus when filed complied and, as amended or supplemented, if applicable, will comply in all material respects with the Securities Act. Each of the Registration Statement, the Prospectus and any post-effective amendments or supplements thereto, at the time it became effective or its date, as applicable, complied and as of each Representation Date, complied and will comply in all material respects with the Securities Act and did not and, as of each Representation Date, did not and will not contain any untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary to make the statements therein not misleading. The Prospectus, as amended or supplemented, as of its date, did not and, as of each Representation Date, will not contain any untrue statement of a material fact or omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading. The representations and warranties set forth in the two immediately preceding sentences do not apply to statements in or omissions from the Registration Statement or any post-effective amendment thereto, or the Prospectus, or any amendments or supplements thereto, made in reliance upon and in conformity with information relating to Agent's Information (defined below). There are no contracts or other documents required to be described in the Prospectus or to be filed as exhibits to the Registration Statement which have not been described or filed as required. As used herein, "**Time of Sale**" means (i) with respect to each offering of Shares pursuant to this Agreement, the time of Cowen's initial entry into contracts with purchasers for the sale of such Shares and (ii) with respect to each offering of Shares pursuant to any relevant Terms Agreement, the time of sale of such Shares to Cowen.

(c) Offering Materials Furnished to Cowen. The Company has delivered to Cowen one complete copy of the Registration Statement and a copy of each consent and certificate of experts filed as a part thereof, and conformed copies of the Registration Statement (without exhibits) and the Prospectus, as amended or supplemented, in such quantities and at such places as Cowen has reasonably requested. The Registration Statement, the Prospectus and any Permitted Free Writing

Prospectus (to the extent any such Permitted Free Writing Prospectus was required to be filed with the Commission) delivered to Cowen for use in connection with the public offering of the Shares contemplated herein or by any Terms Agreement have been and will be identical to the versions of such documents transmitted to the Commission for filing via EDGAR, except to the extent permitted by Regulation S-T.

(d) Not an Ineligible Issuer. The Company currently is not an "ineligible issuer," as defined in Rule 405 under the Securities Act. The Company agrees to notify Cowen promptly upon the Company becoming an "ineligible issuer."

(e) Distribution of Offering Material By the Company. The Company has not distributed and will not distribute, prior to the completion of Cowen's distribution of the Shares, any offering material in connection with the offering and sale of the Shares other than the Prospectus or the Registration Statement.

(f) The Sales Agreement; Terms Agreement. This Agreement has been duly authorized, executed and delivered by, and is a valid and binding agreement of, the Company, enforceable in accordance with its terms, except as rights to indemnification hereunder may be limited by applicable law and except as the enforcement hereof may be limited by bankruptcy, insolvency, reorganization, moratorium or other similar laws relating to or affecting the rights and remedies of creditors or by general equitable principles. Any Terms Agreement will have been duly authorized, executed and delivered by the Company and, assuming due authorization, execution and delivery by the other parties thereto, will be a legal, valid and binding agreement of the Company enforceable in accordance with its terms, except as may be limited by bankruptcy, insolvency, reorganization, moratorium or similar laws affecting creditors' rights generally, and by general equitable principles.

(g) Authorization of the Common Stock. The Shares, when issued and delivered, will be duly authorized for issuance and sale pursuant to this Agreement and any Terms Agreement and, when issued and delivered by the Company against payment therefor pursuant to this Agreement, will be duly authorized, validly issued, fully paid and nonassessable, free and clear of any pledge, lien, encumbrance, security interest or other claim, and the issuance and sale of the Shares by the Company is not subject to preemptive or other similar rights arising by operation of law, under the organizational documents of the Company or under any agreement to which the Company or any Subsidiary (as defined below) is a party or otherwise.

(h) No Applicable Registration or Other Similar Rights. There are no persons with registration or other similar rights to have any equity or debt securities registered for sale under the Registration Statement or included in the offering contemplated by this Agreement or any Terms Agreement, except for such rights as have been duly waived, and the issuance of the Shares is not subject to any preemptive rights, rights of first refusal or similar rights pursuant to the General Corporation Law of the State of Delaware or the Company's Certificate of Incorporation or Bylaws or any agreement or other instrument to which the Company is a party, except for such rights that have been complied with or effectively waived prior to the date hereof.

(i) No Material Adverse Change. Except as otherwise disclosed in the Prospectus, subsequent to the respective dates as of which information is given in the Prospectus: (i) there has not been any material adverse change, or any development involving a prospective material

adverse change, in or affecting the general affairs, management, financial position, stockholders' equity, results of operations or prospects of the Company and its Subsidiaries (any such change is called a "**Material Adverse Change**"); (ii) neither the Company nor any of its Subsidiaries has incurred any liability or obligation, direct or contingent, other than liabilities and obligations which were incurred in the ordinary course of business; (iii) neither the Company nor any of its Subsidiaries has declared or paid any dividends on its capital stock and there has not been any change in the capital stock (other than as a result of the exercise of stock options or the award of stock options, restricted stock units or other equity awards in the ordinary course of business pursuant to the Company's equity plans that are described or incorporated by reference in the Prospectus) or long-term debt of the Company or any of its Subsidiaries.

(j) Independent Accountants. Ernst & Young LLP, who has expressed its opinion with respect to the financial statements (which term as used in this Agreement includes the related notes thereto) and supporting schedules filed with the Commission or incorporated by reference as a part of the Registration Statement and included in the Prospectus, is an independent registered public accounting firm as required by the Securities Act and the Exchange Act.

(k) Preparation of the Financial Statements. The financial statements filed with the Commission as a part of or incorporated by reference in the Registration Statement and included in the Prospectus present fairly the consolidated financial position of the Company and its Subsidiaries as of and at the dates indicated and the results of their operations and cash flows for the periods specified. The supporting schedules, if any, included in or incorporated in the Registration Statement present fairly the information required to be stated therein. Such financial statements and supporting schedules, if any, have been prepared in conformity with generally accepted accounting principles as applied in the United States applied on a consistent basis throughout the periods involved, except as may be expressly stated in the related notes thereto. No other financial statements or supporting schedules are required to be included in or incorporated in the Registration Statement. The financial data set forth or incorporated in the Prospectus under the caption "Selected Financial Data" fairly present the information set forth therein on a basis consistent with that of the audited financial statements contained, incorporated or deemed to be incorporated in the Registration Statement.

(l) XBRL. The interactive data in eXtensible Business Reporting Language included or incorporated by reference in the Registration Statement fairly presents the information called for in all material respects and has been prepared in accordance with the Commission's rules and guidelines applicable thereto.

(m) Incorporation and Good Standing of the Company and its Subsidiaries. The Company has been duly incorporated and is validly existing as a corporation in good standing under the laws of the jurisdiction of its incorporation and has corporate power and authority to own, lease and operate its properties and to conduct its business as described in the Prospectus and to enter into and perform its obligations under this Agreement and any Terms Agreement and to consummate the transactions contemplated herein and therein. Each subsidiary of the Company (each a "**Subsidiary**") has been duly organized and is validly existing as a corporation or limited liability company in good standing under the laws of the jurisdiction of its organization and has the requisite power and authority to own, lease and operate its properties and to conduct its business as described in the Prospectus. Each of the Company and its Subsidiaries is duly qualified as a foreign corporation or foreign partnership to transact business and is in good standing under the laws of

the jurisdiction of its incorporation or formation and each other jurisdiction in which such qualification is required, whether by reason of the ownership or leasing of property or the conduct of business, except for such jurisdictions where the failure to so qualify or to be in good standing would not, individually or in the aggregate, result in a Material Adverse Change. Except as described in the Prospectus, all of the issued and outstanding equity interests of the Subsidiaries have been duly authorized and validly issued, are fully paid and nonassessable and are owned by the Company free and clear of any security interest, mortgage, pledge, lien, encumbrance or claim. The Company does not own or control, directly or indirectly, any corporation, association or other entity other than the Subsidiaries listed in Exhibit 21.1 to the Company's Annual Report on Form 10-K for the most recently ended fiscal year and other than (i) those Subsidiaries not required to be listed on Exhibit 21.1 by Item 601 of Regulation S-K under the Exchange Act and (ii) those Subsidiaries formed since the last day of the most recently ended fiscal year.

(n) Capital Stock Matters. The Common Stock conforms in all material respects to the description thereof contained in the Prospectus. All of the issued and outstanding shares of Common Stock have been duly authorized and validly issued, are fully paid and nonassessable and have been issued in compliance with federal and state securities laws. None of the outstanding shares of Common Stock were issued in violation of any preemptive rights, rights of first refusal or other similar rights to subscribe for or purchase securities of the Company. There are no authorized or outstanding options, warrants, preemptive rights, rights of first refusal or other rights to purchase, or equity or debt securities convertible into or exchangeable or exercisable for, any capital stock of the Company or any of its Subsidiaries other than those accurately described in all material respects in the Prospectus. The description of the Company's equity incentive plans and other equity plans or arrangements, and the equity awards or other rights granted thereunder, set forth in the Prospectus accurately and fairly presents in all material respects the information required to be shown with respect to such plans, arrangements, equity awards and rights.

(o) Non-Contravention of Existing Instruments; No Further Authorizations or Approvals Required. Neither the Company nor any of its Subsidiaries is in violation of its charter or by-laws or is in default (or, with the giving of notice or lapse of time, would be in default) ("**Default**") under any indenture, mortgage, loan or credit agreement, note, contract, franchise, lease or other instrument to which the Company or any of its Subsidiaries is a party or by which it or any of them may be bound, or to which any of the property or assets of the Company or any of its Subsidiaries is subject (each, an "**Existing Instrument**"), except for such Defaults as would not, individually or in the aggregate, result in a Material Adverse Change. The Company's execution, delivery and performance of this Agreement and any Terms Agreement and consummation of the transactions contemplated hereby and thereby and by the Prospectus (i) have been duly authorized by all necessary corporate action and will not result in any violation of the provisions of the charter or by-laws of the Company or any Subsidiary, (ii) will not conflict with or constitute a breach of, or Default under, or result in the creation or imposition of any lien, charge or encumbrance upon any property or assets of the Company or any of its Subsidiaries pursuant to, or require the consent of any other party to, any Existing Instrument, except for such conflicts, breaches, Defaults, liens, charges or encumbrances as would not, individually or in the aggregate, result in a Material Adverse Change and (iii) will not result in any violation of any law, administrative regulation or administrative or court decree applicable to the Company or any Subsidiary. No consent, approval, authorization or other order of, or registration or filing with, any court or other governmental or regulatory authority or agency, is required for the Company's

execution, delivery and performance of this Agreement and consummation of the transactions contemplated hereby or by any Terms Agreement and by the Prospectus, except such as have been obtained or made by the Company and are in full force and effect under the Securities Act, applicable state securities or blue sky laws and from the Financial Industry Regulatory Authority ("**FINRA**").

(p) No Material Actions or Proceedings. Except as disclosed in the Prospectus, there are no legal or governmental actions, suits or proceedings pending or, to the best of the Company's knowledge, threatened (i) against or affecting the Company or any of its Subsidiaries, (ii) which has as the subject thereof any officer or director of, or property owned or leased by, the Company or any of its Subsidiaries or (iii) relating to environmental or discrimination matters, where in any such case (A) there is a reasonable possibility that such action, suit or proceeding might be determined adversely to the Company or such Subsidiary and (B) any such action, suit or proceeding, if so determined adversely, would reasonably be expected to result in a Material Adverse Change or adversely affect the consummation of the transactions contemplated by this Agreement or any Terms Agreement. No material labor dispute with the employees of the Company or any of its Subsidiaries exists or, to the Company's knowledge, is threatened or imminent.

(q) All Necessary Permits, etc. The Company and each Subsidiary possess all material permits, licenses, approvals, clearances, exemptions, registrations, consents and other authorizations (collectively, "**Permits**") issued by the appropriate Regulatory Authorities, including without limitation, all such Permits required by the FDA or any component thereof, necessary to conduct the businesses now operated by it, except where the failure to possess such Permit would not, individually or in the aggregate, reasonably be expected to result in a Material Adverse Change; the Company is in compliance with the terms and conditions of all such Permits, except where the failure to comply would not, individually or in the aggregate, reasonably be expected to have a Material Adverse Change; no event has occurred which allows, or after notice or lapse of time would allow, revocation or termination thereof, or results in any other impairment of the rights of the holder of any Permit, except where such event would not, individually or in the aggregate, reasonably be expected to have a Material Adverse Change; all of the Permits are valid and in full force and effect; the Company has not received notice of proceedings relating to the revocation or material modification of any such Permits; and to the knowledge of the Company, no Regulatory Authority granting any such Permit has taken any action to limit, suspend or revoke the same in any material respect.

(r) Tax Law Compliance. The Company and its consolidated Subsidiaries have filed all necessary federal, state and foreign income, property and franchise tax returns and have paid all taxes required to be paid by any of them and, if due and payable, any related or similar assessment, fine or penalty levied against any of them except as may be being contested in good faith and by appropriate proceedings. The Company has made adequate charges, accruals and reserves in the applicable financial statements referred to in Section 6(k) above in respect of all federal, state and foreign income, property and franchise taxes for all periods as to which the tax liability of the Company or any of its consolidated Subsidiaries has not been finally determined.

(s) Company Not an "Investment Company". The Company has been advised of the rules and requirements under the Investment Company Act of 1940, as amended (the "**Investment**

Company Act"). The Company is not, and after receipt of payment for the Common Stock will not be, an "investment company" within the meaning of the Investment Company Act.

(t) Insurance. The Company and its Subsidiaries have insurance covering their properties, operations, personnel and businesses, including business interruption insurance, which insurance insures against such risks and is in such amounts as are, in the Company's reasonable judgment, commercially reasonable for the conduct of its and its Subsidiaries business; and neither the Company nor any of its Subsidiaries has (i) received written notice from any insurer or agent of such insurer that capital improvements or other expenditures are required or necessary to be made in order to continue such insurance or (ii) any reason to believe that it will not be able to renew its existing insurance coverage as and when such coverage expires or to obtain similar coverage from similar insurers as may be necessary to continue its business.

(u) No Price Stabilization or Manipulation. The Company has not taken and will not take, directly or indirectly, any action designed to or that might be reasonably expected to cause or result in stabilization or manipulation of the price of any security of the Company to facilitate the sale or resale of the Shares.

(v) Related Party Transactions. There are no relationships, direct or indirect, or related-party transactions involving the Company or any other person required to be described in the Prospectus which have not been described as required.

(w) Exchange Act Compliance. The documents incorporated or deemed to be incorporated by reference in the Prospectus, at the time they were or hereafter are filed with the Commission, complied and will comply in all material respects with the requirements of the Exchange Act, and, when read together with the other information in the Prospectus, at the Settlement Dates, will not contain an untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary to make the fact required to be stated therein or necessary to make the statements therein, in the light of the circumstances under which they were made, not misleading.

(x) No Unlawful Contributions or Other Payments. Neither the Company, any of its Subsidiaries, nor, to the knowledge of the Company, any director, officer, agent, employee, affiliate or other person associated with or acting on behalf of the Company or any of its Subsidiaries has (i) used any corporate funds for any unlawful contribution, gift, entertainment or other unlawful expense relating to political activity; (ii) made any direct or indirect unlawful payment to any foreign or domestic government official or employee from corporate funds; (iii) violated or is in violation of any provision of the Foreign Corrupt Practices Act of 1977; (iv) violated or is in violation of any provision of the Bribery Act 2010 of the United Kingdom; or (v) made any bribe, rebate, payoff, influence payment, kickback or other unlawful payment.

(y) Compliance with Money Laundering Laws. The operations of the Company and its Subsidiaries are and have been conducted at all times in material compliance with applicable financial recordkeeping and reporting requirements of the Currency and Foreign Transactions Reporting Act of 1970, as amended, the money laundering statutes of all jurisdictions, the rules and regulations thereunder and any related or similar rules, regulations or guidelines, issued, administered or enforced by any governmental agency having jurisdiction over the Company and its Subsidiaries (collectively, the "**Money Laundering Laws**") and no action, suit or proceeding

by or before any court or governmental agency, authority or body or any arbitrator involving the Company or any of its Subsidiaries with respect to the Money Laundering Laws is pending or, to the knowledge of the Company, threatened.

(z) Compliance with OFAC.

(A) Neither the Company, its Subsidiaries, nor, to the knowledge of the Company, any director, officer, agent, employee or affiliate of the Company or any of its Subsidiaries is currently the subject or the target of any sanctions administered or enforced by the U.S. Government, including, without limitation, the Office of Foreign Assets Control of the U.S. Department of the Treasury ("OFAC"), or other relevant sanctions authority (collectively, "**Sanctions**").

(B) The Company will not, directly or indirectly, use the Net Proceeds, or lend, contribute or otherwise make available such proceeds to any Subsidiary, joint venture partner or other person or entity (i) to fund any activities of or business with any person, or in any country or territory, that, at the time of such funding, is the subject of Sanctions or (ii) in any other manner that will result in a violation by any person (including any person participating in the transaction, whether as underwriter, advisor, investor or otherwise) of Sanctions (including Cowen)

(aa) Company's Accounting System. The Company maintains a system of internal control over financial reporting (as such term is defined in Rule 13a-15(f) under the Exchange Act) that complies with the requirements of the Exchange Act applicable to the Company and has been designed by the Company's principal executive officer and principal financial officer, or under their supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with U.S. generally accepted accounting principles ("**GAAP**"). The Company's internal accounting controls have been designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with GAAP. The Company's internal accounting controls are sufficient to provide reasonable assurance that (i) transactions are executed in accordance with the general or specific authorizations of the Company's management; (ii) transactions are recorded as necessary to permit preparation of financial statements in conformity with GAAP and to maintain asset accountability; (iii) access to assets is permitted only in accordance with the general or specific authorization of the Company's management; and (iv) the recorded accountability for assets is compared with the existing assets at reasonable intervals and appropriate action is taken with respect to any differences. The Company is not aware of any material weaknesses in its internal control over financial reporting. Since the date of the latest audited financial statements included or incorporated by reference in the Prospectus, there has been no change in the Company's internal control over financial reporting that has materially and adversely affected, or is reasonably likely to materially and adversely affect, the Company's internal control over financial reporting.

(bb) Disclosure Controls. The Company maintains disclosure controls and procedures (as such term is defined in Rule 13a-15(e) under the Exchange Act) that are designed to comply with the requirements of the Exchange Act; such disclosure controls and procedures have been designed to ensure that material information relating to the Company and its Subsidiaries is made

known to the Company's principal executive officer and principal financial officer by others within those entities; and such disclosure controls and procedures are effective.

(cc) Compliance with Environmental Laws. The Company and its Subsidiaries (i) are in compliance with all, and have not violated any, laws, regulations, ordinances, rules, orders, judgments, decrees, permits or other legal requirements of any Regulatory Authority, including without limitation any international, national, state, provincial, regional, or local authority, relating to the protection of human health or safety, the environment, or natural resources, or to hazardous or toxic substances or wastes, pollutants or contaminants ("Environmental Laws") applicable to the Company or its Subsidiaries, which compliance includes, without limitation, obtaining, maintaining and complying with all permits and authorizations and approvals required by Environmental Laws to conduct its business, and (ii) have not received written notice of any actual or alleged violation of Environmental Laws, or of any potential liability for or other obligation concerning the presence, disposal or release of hazardous or toxic substances or wastes, pollutants or contaminants, except in the case of (i) and (ii) where the failure to comply or the potential liability or obligation would not, individually or in the aggregate, reasonably be expected to result in a Material Adverse Change. Except as described in the Prospectus, (A) there are no proceedings that are pending against the Company under Environmental Laws in which a Regulatory Authority is also a party and (B) the Company is not aware of any non-compliance with Environmental Laws, or liabilities under Environmental Laws, which would reasonably be expected to result in a Material Adverse Change.

(dd) Intellectual Property. Except as disclosed in the Prospectus, the Company and its Subsidiaries own or have valid, binding and enforceable licenses or other rights under the patents and patent applications, copyrights, trademarks, trademark registrations, service marks, service mark registrations, trade names, service names, know-how (including trade secrets and other unpatented and/or unpatentable proprietary or confidential information, systems or procedures) and other intellectual property (collectively, "**Intellectual Property**") that is necessary for, or used in the conduct of, or the proposed conduct of, the business of the Company in the manner described in the Prospectus (collectively, the "**Company Intellectual Property**"). To the Company's knowledge, none of the patents and patent applications contained in the Company Intellectual Property, are invalid or unenforceable, in whole or in part, and the Company is unaware of any facts that would form a reasonable basis for such a determination. None of the rights within the Company Intellectual Property, other than patents and patent applications, are invalid or unenforceable, in whole or in part, and the Company is unaware of any facts that would form a reasonable basis for such a determination. Except as disclosed in the Prospectus, the Company is not obligated to pay a material royalty, grant a license or provide other material consideration to any third party in connection with the Company Intellectual Property. There is no pending or, to the Company's knowledge, threatened action, suit, proceeding or claim by a third party (i) challenging the Company's rights in or to any Company Intellectual Property, including with respect to ownership and inventorship; (ii) challenging the validity, enforceability or scope of any Company Intellectual Property; or (iii) asserting that the Company has infringed, misappropriated or otherwise violated, or would, upon the commercialization of any products described in the Prospectus as under development, infringe, misappropriate or otherwise violate, any Intellectual Property rights of others; and, in each of the foregoing cases, the Company (a) is unaware of any facts that would form a reasonable basis for any such action, suit, proceeding or claim and (b) has not received any written notice alleging any such claim or conflict. To the knowledge of the

Company, (1) neither the commercial development nor the sale of any of the products, proposed products or processes of the Company, as described in the Prospectus, infringes, misappropriates or otherwise violates, or would, upon the commercialization of such products or proposed products, infringe, misappropriate or otherwise violate, any Intellectual Property rights of any third party; (2) the Company believes it can acquire, on reasonable terms, any licenses under third-party Intellectual Property that may be necessary for or used in its business, as currently conducted or as proposed to be conducted, as described in the Prospectus; (3) no third party has any ownership right in or to any Company Intellectual Property that is owned by the Company, other than any co-owner of a patent or patent application within the Company Intellectual Property who is listed on the records of the U.S. Patent and Trademark Office (the "**USPTO**") as co-owner of such patent or named in such patent application; (4) no third party has any ownership right in or to any Company Intellectual Property, in any field of use, other than the respective licensor to the Company of such Company Intellectual Property; (5) no employee of the Company is in or has ever been in violation, in any material respect, of any term of any employment contract, patent disclosure agreement, invention assignment agreement, non-competition agreement, non-solicitation agreement, nondisclosure agreement or other restrictive covenant to or with a former employer where the basis of such violation relates to such employee's employment, or to actions undertaken by the employee while employed, with the Company; and (6) each current and former employee and consultant of the Company (A) has executed an inventions assignment and confidentiality agreement with the Company, on or about the respective date of hire, in substantially the form made available to the Underwriter and its counsel; and (B) has assigned or agreed to assign to the Company any and all Intellectual Property rights he or she may possess or may have possessed that are related to the Company's business, as currently conducted and as proposed to be conducted, as described in the Prospectus.

(ee) Patents and Patent Applications. All patents and patent applications owned by or licensed to the Company or under which the Company has rights have, to the knowledge of the Company, been duly and properly filed and maintained; to the knowledge of the Company, the parties prosecuting such applications have complied with their duty of candor and disclosure to the USPTO in connection with such applications; and the Company is not aware of any facts required to be disclosed to the USPTO that were not disclosed to the USPTO and which would preclude the grant of a patent in connection with any such application or could form the basis of a finding of invalidity with respect to any patents that have issued with respect to such applications.

(ff) Listing. The Company is subject to and in compliance in all material respects with the reporting requirements of Section 13 or Section 15(d) of the Exchange Act. The Common Stock is registered pursuant to Section 12(b) or Section 12(g) of the Exchange Act and is listed on the Nasdaq, and the Company has taken no action designed to, or reasonably likely to have the effect of, terminating the registration of the Common Stock under the Exchange Act or delisting the Common Stock from the Exchange, nor has the Company received any notification that the Commission or Nasdaq is contemplating terminating such registration or listing. All of the Shares that have been or may be sold under this Agreement and any Terms Agreement have been approved for listing on the Nasdaq, subject to official notice of issuance; the Company has taken all necessary actions to ensure that, upon and at all times after the Nasdaq shall have approved the Shares for listing, it will be in compliance with all applicable corporate governance requirements set forth in the Nasdaq's listing rules that are then in effect.

(gg) Brokers. Except for Cowen, there is no broker, finder or other party that is entitled to receive from the Company any brokerage or finder's fee or other fee or commission as a result of any transactions contemplated by this Agreement or by any Terms Agreement.

(hh) No Outstanding Loans or Other Indebtedness. Except as described in the Prospectus, there are no outstanding loans, advances (except normal advances for business expenses in the ordinary course of business) or guarantees or indebtedness by the Company to or for the benefit of any of the officers or directors of the Company or any of the members of any of their immediate families.

(ii) No Reliance. The Company has not relied upon Cowen or legal counsel for Cowen for any legal, tax or accounting advice in connection with the offering and sale of the Shares.

(jj) FINRA Exemption. The Company meets the requirements for use of Form S-3 under the Securities Act specified in FINRA Rule 5110(h)(1)(C) and satisfies the "experienced issuer" requirements as defined in FINRA Rule 5110(j)(6).

(kk) Compliance with Laws. The Company has not been advised, and has no reason to believe, that it and each of its Subsidiaries are not conducting business in compliance with all applicable laws, rules and regulations of the jurisdictions in which it is conducting business, except where failure to be so in compliance would not result in a Material Adverse Change.

(ll) Privacy Laws. Except as set otherwise set forth in Section 6(mm) with respect to the GDPR Privacy Law, the Company and each of its Subsidiaries are, and at all prior times were, in material compliance with all applicable data privacy and security laws and regulations, including, without limitation, the Health Insurance Portability and Accountability Act ("**HIPAA**"), as amended by the Health Information Technology for Economic and Clinical Health Act (the "**HITECH Act**") (42 U.S.C. Section 17921 et seq.) (collectively, "**Privacy Laws**"). To ensure compliance with the Privacy Laws, the Company and each of its Subsidiaries have in place, comply with, and take appropriate steps reasonably designed to ensure compliance in all material respects with their policies and procedures relating to data privacy and security and the collection, storage, use, disclosure, handling and analysis of Personal Data (the "**Policies**"). The Company provides accurate notice of its Policies to its customers, employees, third party vendors and representatives. The Policies provide accurate and sufficient notice of the Company's then-current privacy practices relating to its subject matter and such Policies do not contain any material omissions of the Company's then-current privacy practices. "**Personal Data**" means (i) a natural persons' name, street address, telephone number, email address, photograph, social security number, bank information, or customer or account number; (ii) any information which would qualify as "personally identifying information" under the Federal Trade Commission Act, as amended; (iii) Protected Health Information as defined by HIPAA; and (iv) any other piece of information that allows the identification of such natural person, or his or her family, or permits the collection or analysis of any data related to an identified person's health or sexual orientation. None of such disclosures made or contained in any of the Policies have been inaccurate, misleading, deceptive or in violation of any Privacy Laws or Policies in any material respect. The execution, delivery and performance of this Agreement, any Terms Agreement or any other agreement referred to in this Agreement will not result in a breach of any Privacy Laws or Policies. Neither the Company nor any of its Subsidiaries, (i) has received notice of any actual or potential liability under or relating to, or actual or potential violation of, any of the Privacy Laws, and has no knowledge of

any event or condition that would reasonably be expected to result in any such notice; (ii) is currently conducting or paying for, in whole or in part, any investigation, remediation or other corrective action pursuant to any Privacy Law; or (iii) is a party to any order, decree, or agreement that imposed any obligation or liability under any Privacy Law.

(mm) GDPR Privacy Law. The Company and each its Subsidiaries have taken reasonable steps to comply with the European Union General Data Protection Regulation ("**GDPR**") (EU 2016/679); provided, however, the Company and each of its Subsidiaries had relied upon the E.U.-U.S. Privacy Shield (the "**Privacy Shield**") to legitimize its transfer of certain GDPR Personal Data (as defined below) to the United States, and following the European Court of Justice's invalidation of the Privacy Shield, neither the Company nor its Subsidiaries have implemented an alternative solution to replace the Privacy Shield as a GDPR Personal Data transfer mechanism ("**GDPR Privacy Law**"). The Company and each of its Subsidiaries have in place, comply in all material respects with, and take appropriate steps reasonably designed to comply in all material respects with their policies and procedures relating to GDPR Personal Data (the "**GDPR Policies**"). "**GDPR Personal Data**" means "personal data" as defined by GDPR. The execution, delivery and performance of this Agreement, any Terms Agreement or any other agreement referred to in this Agreement will not result in a breach of GDPR Privacy Law or GDPR Policies. Neither the Company nor any of its Subsidiaries, (i) has received notice of any actual or potential liability under or relating to, or actual or potential violation of, GDPR Privacy Law; (ii) is currently conducting or paying for, in whole or in part, any investigation, remediation or other corrective action pursuant to GDPR Privacy Law; or (iii) is a party to any order, decree, or agreement that imposed any obligation or liability under GDPR Privacy Law.

(nn) IT Systems. (i)(x) To the Company's knowledge, there has been no material security breach or other compromise of or relating to any of the Company's or its Subsidiaries' information technology and computer systems, networks, hardware, software, data (including the data of their respective customers, employees, suppliers, vendors and any third party data maintained by or on behalf of them), equipment or technology (collectively, "**IT Systems and Data**") and (y) the Company and its Subsidiaries have not been notified of, and have no knowledge of any event or condition that would reasonably be expected to result in, any material security breach; (ii) the Company and its Subsidiaries are presently in compliance with all applicable laws or statutes and all judgments, orders, rules and regulations of any court or arbitrator or governmental or regulatory authority, published privacy policies and contractual obligations relating to the privacy and security of IT Systems and Data and to the protection of such IT Systems and Data from unauthorized use, access, misappropriation or modification, except as would not, in the case of this clause (ii), individually or in the aggregate, result in a Material Adverse Change; and (iii) the Company and its Subsidiaries have implemented backup and disaster recovery technology consistent with industry standards and practices.

(oo) Export and Import Laws. Each of the Company and the Subsidiaries, and, to the Company's knowledge, each of their affiliates and any director, officer, agent or employee of, or other person associated with or acting on behalf of, the Company has acted at all times in compliance with applicable Export and Import Laws (as defined below) and there are no claims, complaints, charges, investigations or proceedings pending or expected or, to the knowledge of the Company, threatened between the Company or any of the Subsidiaries and any Governmental Authority under any Export or Import Laws. The term "**Export and Import Laws**" means the

Arms Export Control Act, the International Traffic in Arms Regulations, the Export Administration Act of 1979, as amended, the Export Administration Regulations, and all other laws and regulations of the United States government regulating the provision of services to non-U.S. parties or the export and import of articles or information from and to the United States of America, and all similar laws and regulations of any foreign government regulating the provision of services to parties not of the foreign country or the export and import of articles and information from and to the foreign country to parties not of the foreign country.

(pp) Preclinical Studies and Clinical Trials. The preclinical studies and clinical trials conducted by, on behalf of or sponsored by the Company were and, if still pending are being, conducted in all material respects in accordance with the experimental protocols or clinical trial protocols established for each study or trial and with all applicable local, state and federal laws, rules and regulations, including, without limitation, the Federal Food, Drug, and Cosmetic Act and its applicable implementing regulations at 21 C.F.R. Parts 50, 54, 56, 58, 312, and 812; except where the failure to so conduct would not, individually or in the aggregate, reasonably be expected to result in a Material Adverse Change; the descriptions of the results of such studies and trials contained in any Prospectus did not include any untrue statement of a material fact or omit to state any material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading; except to the extent disclosed in the Prospectus, the Company is not aware of any studies or trials, the results of which are inconsistent with or otherwise call into question the study or trial results described or referred to in the Prospectus; and neither the U.S. Food and Drug Administration, ("**FDA**") nor any applicable foreign Regulatory Agency has commenced, or, to the knowledge of the Company, threatened to initiate, any action to place a clinical hold on, or otherwise terminate, delay or suspend, any proposed or ongoing preclinical study or clinical investigation conducted or proposed to be conducted by or on behalf of the Company.

(qq) Health Care Laws. The Company has operated and currently is in compliance in all respects with all applicable Health Care Laws (as defined in this Section 6(qq)), including, without limitation, the rules and regulations of the FDA, the U.S. Department of Health and Human Services Office of Inspector General, the Centers for Medicare & Medicaid Services, the Office for Civil Rights, the Department of Justice or any other Regulatory Authority having jurisdiction over the Company or any of its properties, and has not engaged in activities which are, as applicable, cause for false claims liability, civil penalties, or mandatory or permissive exclusion from Medicare, Medicaid, or any other state or federal health care program. For purposes of this Agreement, "Health Care Laws" shall mean the federal Anti-kickback Statute (42 U.S.C. § 1320a-7b(b)), the Physician Payments Sunshine Act (42 U.S.C. § 1320a-7h), the civil False Claims Act (31 U.S.C. §§ 3729 et seq.), the criminal False Claims Act (42 U.S.C. §§ 1320a-7b(a)), all criminal laws relating to health care fraud and abuse, including but not limited to 18 U.S.C. Sections 286 and 287, and the health care fraud criminal provisions under the Health Insurance Portability and Accountability Act of 1996 (42 U.S.C. § 1320d et seq.) ("**HIPAA**"), the exclusion laws (42 U.S.C. § 1320a-7), the civil monetary penalties law (42 U.S.C. § 1320a- 7a), HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act (42 U.S.C. §§ 17921 et seq.), Medicare (Title XVIII of the Social Security Act), Medicaid (Title XIX of the Social Security Act), the Federal Food, Drug, and Cosmetic Act (21 U.S.C. §§ 301 et seq.), the regulations promulgated pursuant to such laws, and any similar federal, state and local laws and regulations, including the collection and reporting requirements, and the processing of any applicable rebate,

chargeback or adjustment, under applicable rules and regulations relating to the Medicaid Drug Rebate Program (42 U.S.C. § 1396r-8) and any state supplemental rebate program, Medicare average sales price reporting (42 U.S.C. § 1395w-3a), the Public Health Service Act (42 U.S.C. § 256b), the VA Federal Supply Schedule (38 U.S.C. § 8126) or under any state pharmaceutical assistance program or U.S. Department of Veterans Affairs agreement, and any successor government programs. The Company has not received any FDA Form 483, notice of adverse finding, warning letter, untitled letter or other correspondence or notice from the FDA or any other Regulatory Authority alleging or asserting noncompliance with any Health Care Laws applicable to the Company. Except as would not, individually or in the aggregate, reasonably be expected to result in a Material Adverse Change, the Company has not, either voluntarily or involuntarily, initiated, conducted, or issued or caused to be initiated, conducted or issued, any post-market recall, market withdrawal or replacement, safety alert, post-sale warning, "dear doctor" letter, or other notice or action relating to any lack of safety, efficacy or regulatory compliance of any product or any alleged defect or violation with respect to any product and, to the Company's knowledge, no third party has initiated or conducted any such notice or action and, to the Company's knowledge, there are no facts which are reasonably likely to cause, and the Company has not received any written notice from the FDA or any other regulatory agency requesting, a post-market recall, market withdrawal or replacement of any product sold or intended to be sold by the Company, a change in the marketing classification or a change in the labeling of any such products, or a termination or suspension of the manufacturing of any such products. Additionally, the Company is not a party to nor has any ongoing reporting obligations pursuant to any corporate integrity agreements, deferred prosecution agreements, monitoring agreements, consent decrees, settlement orders, plans of correction or similar agreements with or imposed by any Regulatory Authority. Neither the Company, nor, to the knowledge of the Company, any of its respective employees, officers or directors has been excluded, suspended or debarred from participation in any U.S. federal health care program or human clinical research or, is subject to a governmental inquiry, investigation, proceeding, or other similar action that could reasonably be expected to result in debarment, suspension, or exclusion.

(rr) ERISA Compliance. Except as would not, individually or in the aggregate, reasonably be expected to result in a material liability to the Company or any of its Subsidiaries, (i) each "employee benefit plan" within the meaning of the Employee Retirement Income Security Act of 1974, as amended ("**ERISA**"), whether or not subject to ERISA, for which the Company or any member of its "Controlled Group" (defined as any organization which is a member of a controlled group of corporations within the meaning of Section 414 of the Internal Revenue Code of 1986, as amended (the "**Code**")) would have any liability (each a "**Plan**") has been maintained in compliance with its terms and with the requirements of all applicable statutes, rules and regulations including ERISA and the Code; (ii) neither the Company nor any member of its Controlled Group has incurred, or reasonably expects to incur, any liability under Title IV of ERISA in respect of a Plan (including a "multiemployer plan," within the meaning of Section 4001(c)(3) of ERISA); (iii) each Plan that is intended to be qualified under Section 401(a) of the Code is so qualified and nothing has occurred, whether by action or by failure to act, which would cause the loss of such qualification; (iv) there is no pending audit or investigation by the Internal Revenue Service, the U.S. Department of Labor, the Pension Benefit Guaranty Corporation or any other governmental agency with respect to any Plan that could reasonably be expected to result in material liability to the Company or any of its Subsidiaries; and (v) the Company and its Subsidiaries have not incurred any liability for any prohibited transaction, the failure of any Plan

to meet the minimum funding standards required by law, including by ERISA or the Code, or any complete or partial withdrawal liability with respect to any Plan.

(ss) No Rated Securities. There are no debt securities or preferred stock of, or guaranteed by, the Company that are rated by a "nationally recognized statistical rating organization," as such term is defined in Section 3(a)(62) of the Exchange Act.

(tt) WKSI. (i) At the original effectiveness of the Registration Statement, (ii) at the time of the most recent amendment thereto for the purposes of complying with Section 10(a)(3) of the Securities Act (whether such amendment was by post-effective amendment or incorporated report filed pursuant to Section 13 or 15(d) of the Exchange Act or in the form of a prospectus), (iii) at the time the Company or any person acting on its behalf (within the meaning, for this clause only, of Rule 163(c) under the Securities Act) made any offer relating to the Shares in reliance on the exemption of Rule 163 under the Securities Act, and (iv) as of the applicable Time of Sale, the Company was and is a "well-known seasoned issuer" (as defined in Rule 405 of the Securities Act).

Any certificate signed by an officer of the Company and delivered to Cowen or to counsel for Cowen pursuant to or in connection with this Agreement or any Terms Agreement shall be deemed to be a representation and warranty by the Company to Cowen as to the matters set forth therein.

The Company acknowledges that Cowen and, for purposes of the opinions to be delivered pursuant to Section 7 hereof, counsel to the Company and counsel to Cowen, will rely upon the accuracy and truthfulness of the foregoing representations and hereby consents to such reliance.

7. Covenants of the Company. The Company covenants and agrees with Cowen that:

(a) Registration Statement Amendments. After the date of this Agreement and during any period in which a Prospectus relating to any Shares is required to be delivered by Cowen under the Securities Act (including in circumstances where such requirement may be satisfied pursuant to Rule 172 under the Securities Act), (i) the Company will notify Cowen promptly of the time when any subsequent amendment to the Registration Statement, other than documents incorporated by reference, has been filed with the Commission and/or has become effective or any subsequent supplement to the Prospectus has been filed and of any request by the Commission for any amendment or supplement to the Registration Statement or Prospectus (insofar as it related to the transactions contemplated hereby) or for additional information, (ii) the Company will prepare and file with the Commission, promptly upon Cowen's request, any amendments or supplements to the Registration Statement or Prospectus that, in Cowen's reasonable opinion, may be necessary or advisable in connection with the distribution of the Shares by Cowen (*provided, however*, that the failure of Cowen to make such request shall not relieve the Company of any obligation or liability hereunder, or affect Cowen's right to rely on the representations and warranties made by the Company in this Agreement or any Terms Agreement); (iii) the Company will not file any amendment or supplement to the Registration Statement or Prospectus, other than documents incorporated by reference, relating to the Shares or a security convertible into the Shares unless a copy thereof has been submitted to Cowen within a reasonable period of time before the filing and Cowen has not reasonably objected thereto (*provided, however*, that (A) the failure of Cowen to make such objection shall not relieve the Company of any obligation or liability hereunder, or affect Cowen's right to rely on the representations and warranties made by the Company in this

Agreement or any Terms Agreement, (B) the Company has no obligations to provide Cowen any advance copy of such filing or to provide Cowen an opportunity to object to such filing if the filing does not name Cowen and does not relate to the transactions herein provided, and (C) the only remedy Cowen shall have with respect to the failure by the Company to provide Cowen with such copy or the filing of such amendment or supplement despite Cowen's objection shall be to cease making sales under this Agreement or any Terms Agreement) and the Company will furnish to Cowen at the time of filing thereof a copy of any document that upon filing is deemed to be incorporated by reference into the Registration Statement or Prospectus, except for those documents available via EDGAR; (iv) the Company will cause each amendment or supplement to the Prospectus, other than documents incorporated by reference, to be filed with the Commission as required pursuant to the applicable paragraph of Rule 424(b) of the Securities Act, or in the case of any document to be incorporated therein by reference, to be filed with the Commission as required pursuant to the Exchange Act, within the time period prescribed (the determination to file or not to file any amendment or supplement with the Commission under this Section 7(a) based on the Company's reasonable opinion or reasonable objections, shall be made exclusively by the Company) and (v) prior to the termination of this Agreement, the Company will notify Cowen if at any time the Registration Statement shall no longer be effective as a result of the passage of time pursuant to Rule 415 under the Securities Act or otherwise.

(b) Notice of Commission Stop Orders. The Company will advise Cowen, promptly after it receives notice or obtains knowledge thereof, of the issuance or threatened issuance by the Commission of any stop order suspending the effectiveness of the Registration Statement, of the suspension of the qualification of the Shares for offering or sale in any jurisdiction, or of the initiation or threatening of any proceeding for any such purpose; and it will promptly use its commercially reasonable efforts to prevent the issuance of any stop order or to obtain its withdrawal if such a stop order should be issued.

(c) Delivery of Prospectus; Subsequent Changes. During any period in which a Prospectus relating to the Shares is required to be delivered by Cowen under the Securities Act with respect to a pending sale of the Shares, (including in circumstances where such requirement may be satisfied pursuant to Rule 172 under the Securities Act), the Company will comply with all requirements imposed upon it by the Securities Act, as from time to time in force, and to file on or before their respective due dates (taking into account any extensions under the Exchange Act) all reports and any definitive proxy or information statements required to be filed by the Company with the Commission pursuant to Sections 13(a), 13(c), 14, 15(d) or any other provision of or under the Exchange Act. If during such period any event occurs as a result of which the Prospectus as then amended or supplemented would include an untrue statement of a material fact or omit to state a material fact necessary to make the statements therein, in the light of the circumstances then existing, not misleading, or if during such period it is necessary to amend or supplement the Registration Statement or Prospectus to comply with the Securities Act, the Company will promptly notify Cowen to suspend the offering of Shares during such period and the Company will promptly amend or supplement the Registration Statement or Prospectus (at the expense of the Company) so as to correct such statement or omission or effect such compliance; *provided*, *however*, that the Company may delay any such amendment or supplement if, in the reasonable judgment of the Company, it is in the best interest of the Company to do so, provided that no Placement Notice is in effect during such time.

(d) Listing of Shares. During any period in which the Prospectus relating to the Shares is required to be delivered by Cowen under the Securities Act with respect to a pending sale of the Shares (including in circumstances where such requirement may be satisfied pursuant to Rule 172 under the Securities Act), the Company will use its commercially reasonable efforts to cause the Shares to be listed on Nasdaq and to qualify the Shares for sale under the securities laws of such jurisdictions as Cowen reasonably designates and to continue such qualifications in effect so long as required for the distribution of the Shares; *provided, however,* that the Company shall not be required in connection therewith to qualify as a foreign corporation or dealer in securities or file a general consent to service of process in any jurisdiction.

(e) Delivery of Registration Statement and Prospectus. The Company will furnish to Cowen and its counsel (at the expense of the Company) copies of the Registration Statement, the Prospectus (including all documents incorporated by reference therein) and all amendments and supplements to the Registration Statement or Prospectus that are filed with the Commission during any period in which a Prospectus relating to the Shares is required to be delivered under the Securities Act (including all documents filed with the Commission during such period that are deemed to be incorporated by reference therein), in each case as soon as reasonably practicable and in such quantities as Cowen may from time to time reasonably request and, at Cowen's request, will also furnish copies of the Prospectus to each exchange or market on which sales of the Shares may be made; *provided, however,* that the Company shall not be required to furnish any document (other than the Prospectus) to Cowen to the extent such document is available on EDGAR.

(f) Earnings Statement. The Company will make generally available to its security holders as soon as practicable, but in any event not later than 15 months after the end of the Company's current fiscal quarter, an earnings statement covering a 12-month period that satisfies the provisions of Section 11(a) and Rule 158 of the Securities Act. For the avoidance of doubt, the Company's compliance with the reporting requirements of the Exchange Act shall be deemed to satisfy this Section 7(f).

(g) Expenses. The Company, whether or not the transactions contemplated hereunder are consummated or this Agreement is terminated, in accordance with the provisions of Section 11 hereunder, will pay the following expenses all incident to the performance of its obligations hereunder, including, but not limited to, expenses relating to (i) the preparation, printing and filing of the Registration Statement and each amendment and supplement thereto, of each Prospectus and of each amendment and supplement thereto, (ii) the preparation, issuance and delivery of the Shares, (iii) the qualification of the Shares under securities laws in accordance with the provisions of Section 7(d) of this Agreement, including filing fees (provided, however, that any fees or disbursements of counsel for Cowen in connection therewith shall be paid by Cowen except as set forth in clause (vii) below), (iv) the printing and delivery to Cowen of copies of the Prospectus and any amendments or supplements thereto, and of this Agreement and any Terms Agreement, (v) the fees and expenses incurred in connection with the listing or qualification of the Shares for trading on Nasdaq, (vi) the filing fees and expenses, if any, of the Commission, (vii) the filing fees and associated legal expenses of Cowen's outside counsel for filings with the FINRA Corporate Financing Department, such legal expense reimbursement not to exceed $10,000 and, (viii) the reasonable fees and disbursements of Cowen's outside counsel in an amount not to exceed $50,000.

(h) Use of Proceeds. The Company will use the Net Proceeds as described in the Prospectus in the section entitled "Use of Proceeds."

(i) Notice of Other Sales. During the pendency of any Placement Notice given hereunder, and for three (3) trading days following the termination of any Placement Notice given hereunder, the Company shall provide Cowen notice as promptly as reasonably possible before it offers to sell, contracts to sell, sells, grants any option to sell or otherwise disposes of any shares of Common Stock (other than Shares offered pursuant to the provisions of this Agreement or any Terms Agreement) or securities convertible into or exchangeable for Common Stock, warrants or any rights to purchase or acquire Common Stock; *provided*, that such notice shall not be required in connection with (i) the issuance, grant or sale of Common Stock, options to purchase shares of Common Stock, restricted stock units or Common Stock issuable upon the exercise of options or the vesting and settlement of restricted stock units or other equity awards pursuant to any stock option, stock bonus, employee stock purchase plan or other stock plan or arrangement described in the Prospectus or pursuant to any qualifying inducement award under Nasdaq rules, (ii) the issuance of securities in connection with an acquisition, merger or sale or purchase of assets, (iii) the issuance or sale of Common Stock pursuant to any dividend reinvestment plan that the Company may adopt from time to time provided the implementation of such is disclosed to Cowen in advance, (iv) the issuance of any shares of Common Stock issuable upon the exchange, conversion or redemption of securities or the exercise of warrants, options or other rights in effect or outstanding or (v) the issuance or sale of shares of Common Stock, or securities convertible into or exercisable for Common Stock, offered and sold in a privately negotiated transaction to vendors, customers, investors, strategic partners or potential strategic partners, financial institutions or other lenders in connection with debt arrangements, and otherwise conducted in a manner so as not to be integrated with the offering of Common Stock hereby. For avoidance of doubt, nothing herein shall be construed to restrict the Company's ability, or require the Company to provide notice to Cowen, to file a registration statement with the Commission.

(j) Change of Circumstances. The Company will, at any time during a fiscal quarter in which the Company intends to tender a Placement Notice or sell Shares hereunder or pursuant to a Terms Agreement, advise Cowen promptly after it shall have received notice or obtained knowledge thereof, of any information or fact that would alter or affect in any material respect any opinion, certificate, letter or other document provided to Cowen pursuant to this Agreement or any Terms Agreement.

(k) Due Diligence Cooperation. During the Term of this Agreement or any Terms Agreement, the Company will cooperate with any reasonable due diligence review conducted by Cowen or its agents in connection with the transactions contemplated hereby or by any Terms Agreement, including, without limitation, providing information and making available documents and senior corporate officers, during regular business hours and at the Company's principal offices, as Cowen may reasonably request.

(l) Required Filings Relating to Sale of Shares. The Company agrees that on such dates as the Securities Act shall require, the Company will (i) file a prospectus supplement with the Commission under the applicable paragraph of Rule 424(b) under the Securities Act (each and every filing under Rule 424(b), a "**Filing Date**"), and (ii) at Cowen's request, deliver such number of copies of each such prospectus supplement to each exchange or market on which such sales were effected as may be required by the rules or regulations of such exchange or market. The

Company shall disclose in its Quarterly Reports on Form 10-Q and in its Annual Report on Form 10-K, the number of the Shares sold through Cowen under this Agreement and any Terms Agreement, and the Net Proceeds to the Company from the sale of the Shares and the compensation paid by the Company with respect to sales of the Shares pursuant to this Agreement during the relevant quarter or, in the case of an Annual Report on Form 10-K, during the fiscal year covered by such Annual Report and the fourth quarter of such fiscal year.

(m) Bring-Down Dates; Certificate. On or prior to the First Delivery Date and each time (i) the Company files the Prospectus relating to the Shares or amends or supplements the Registration Statement or the Prospectus relating to the Shares (other than a prospectus supplement filed in accordance with Section 7(l) of this Agreement) by means of a post-effective amendment, sticker, or supplement but not by means of incorporation of document(s) by reference to the Registration Statement or the Prospectus relating to the Shares; (ii) the Company files an annual report on Form 10-K under the Exchange Act; (iii) the Company files its quarterly reports on Form 10-Q under the Exchange Act; or (iv) the Company files a Current Report on Form 8-K containing amended financial information (other than an earnings release or other information "furnished" pursuant to Items 2.02 or 7.01 of Form 8-K) under the Exchange Act (each date of filing of one or more of the documents referred to in clauses (i) through (iv) shall be a "**Bring-Down Date**"); the Company shall furnish Cowen with a certificate, in the form attached hereto as Exhibit 7(m) within three (3) Trading Days of any Bring-Down Date if requested by Cowen. The requirement to provide a certificate under this Section 7(m) shall be automatically waived for any Bring-Down Date occurring at a time at which no Agency Transaction is pending, which waiver shall continue until the earlier to occur of the date the Company delivers a Placement Notice hereunder (which for such calendar quarter shall be considered a Bring-Down Date) and the next occurring Bring-Down Date; *provided*, *however*, that such waiver shall not apply for any Bring-Down Date on which the Company files its annual report on Form 10-K. Notwithstanding the foregoing, if the Company subsequently decides to sell Shares in an Agency Transaction following a Bring-Down Date when the Company relied on such waiver and did not provide Cowen with a certificate under this Section 7(m), then before the Company delivers the Placement Notice or Cowen sells any Shares pursuant to such Agency Transaction, the Company shall provide Cowen with a certificate, in the form attached hereto as Exhibit 7(m), dated the date of the Placement Notice. With respect to any Principal Transaction pursuant to a Terms Agreement, the certificate in the form attached hereto as Exhibit 7(m) shall be delivered at the Principal Settlement Date.

(n) Legal Opinion. On or prior to the First Delivery Date and within three (3) Trading Days of each Bring-Down Date with respect to which the Company is obligated to deliver a certificate in the form attached hereto as Exhibit 7(m) for which no waiver is applicable, the Company shall cause to be furnished to Cowen a written opinion of Goodwin Procter LLP ("Company Counsel"), or other counsel reasonably satisfactory to Cowen, in form and substance satisfactory to Cowen and its counsel, dated the date that the opinion is required to be delivered, modified, as necessary, to relate to the Registration Statement and the Prospectus as then amended or supplemented; *provided*, *however*, that in lieu of such opinions for subsequent Bring-Down Dates, counsel may furnish Cowen with a letter (a "**Reliance Letter**") to the effect that Cowen may rely on a prior opinion delivered under this Section 7(n) to the same extent as if it were dated the date of such letter (except that statements in such prior opinion shall be deemed to relate to the Registration Statement and the Prospectus as amended or supplemented at such Bring-Down Date). With respect to any Principal Transaction pursuant to a Terms Agreement, the Company

shall cause to be furnished to Cowen on the Principal Settlement Date a written opinion of Company Counsel, or other counsel satisfactory to Cowen, in form and substance satisfactory to Cowen and its counsel, dated the Principal Settlement Date.

(o) Intellectual Property Opinion. On or prior to the First Delivery Date and within five (5) Trading Days of each Representation Date with respect to which the Company is obligated to deliver a certificate pursuant to Section 7(m) (other than pursuant to Section 7(m)(iii)) and for which no waiver is applicable, the Company shall cause to be furnished to Cowen written opinions of McCarter & English, LLP and Goodwin Procter LLP ("**Company IP Counsel**"), or other counsel reasonably satisfactory to Cowen, in form and substance reasonably satisfactory to Cowen and its counsel, substantially similar to the form previously provided to Cowen and its counsel, modified, as necessary, to relate to the Registration Statement and the Prospectus as then amended or supplemented and dated as of the date that such certificate is required to be delivered; provided, however, the Company shall be required to furnish to Cowen no more than one set of opinions hereunder per calendar year; provided, further, that in lieu of such opinions for subsequent Representation Dates on which Company IP Counsel are obligated to deliver opinions hereunder, counsel may furnish Cowen with a letter (an "**IP Reliance Letter**") to the effect that Cowen may rely on a prior opinion delivered under this Section 7(o) to the same extent as if it were dated the date of such letter (except that statements in such prior opinion shall be deemed to relate to the Registration Statement and the Prospectus as amended or supplemented as of the date of the IP Reliance Letter).

(p) Comfort Letter. On or prior to the First Delivery Date and within three (3) Trading Days of each Bring-Down Date with respect to which the Company is obligated to deliver a certificate in the form attached hereto as Exhibit 7(m) for which no waiver is applicable, the Company shall cause its independent accountants to furnish Cowen letters (the **"Comfort Letters"**), dated the date the Comfort Letter is delivered, in form and substance reasonably satisfactory to Cowen, (i) confirming that they are an independent registered public accounting firm within the meaning of the Securities Act and the PCAOB, (ii) stating, as of such date, the conclusions and findings of such firm with respect to the financial information and other matters ordinarily covered by accountants' "comfort letters" to Cowen in connection with registered public offerings (the first such letter, the **"Initial Comfort Letter"**) and (iii) updating the Initial Comfort Letter with any information that would have been included in the Initial Comfort Letter had it been given on such date and modified as necessary to relate to the Registration Statement and the Prospectus, as amended and supplemented to the date of such letter; provided, however, that (i) Cowen has provided the Company's independent accountants with a representation letter reasonably satisfactory to the Company's independent accountants and (ii) any such comfort letter will only be required on the Bring-Down Date to the extent that it contains financial statements filed with the Commission under the Exchange Act and incorporated or deemed to be incorporated by reference into a Prospectus. The Company shall not be required to furnish more than one comfort letter hereunder per annual report on Form 10-K and quarterly report on Form 10-Q filed by the Company in connection with an Agency Transaction. With respect to any Principal Transaction pursuant to a Terms Agreement, the Company shall cause its independent accountants to furnish Cowen, in form and substance satisfactory to Cowen, Comfort Letters at the Time of Sale, dated the date of such Time of Sale, and on the Principal Settlement Date, dated the Principal Settlement Date.

(q) Market Activities. The Company will not, directly or indirectly, (i) take any action designed to cause or result in, or that constitutes or would reasonably be expected to constitute, the stabilization or manipulation of the price of any security of the Company to facilitate the sale or resale of the Shares or (ii) sell, bid for, or purchase the Common Stock to be issued and sold pursuant to this Agreement or any Terms Agreement, or pay anyone any compensation for soliciting purchases of the Shares other than Cowen; provided, however, that the Company may bid for and purchase shares of its Common Stock in accordance with Rule 10b-18 under the Exchange Act.

(r) Insurance. The Company and its Subsidiaries shall maintain, or cause to be maintained, insurance in such amounts and covering such risks and in such amounts as in the Company's reasonable judgement is reasonable and customary for the business for which it is engaged.

(s) Compliance with Laws. The Company and each of its Subsidiaries shall maintain, or cause to be maintained, all material environmental permits, licenses and other authorizations required by federal, state and local law in order to conduct their businesses as described in the Prospectus, and the Company and each of its Subsidiaries shall conduct their businesses, or cause their businesses to be conducted, in substantial compliance with such permits, licenses and authorizations and with applicable environmental laws, except where the failure to maintain or be in compliance with such permits, licenses and authorizations could not reasonably be expected to result in a Material Adverse Change.

(t) Investment Company Act. The Company will conduct its affairs in such a manner so as to reasonably ensure that neither it nor its Subsidiaries will be or become, at any time prior to the termination of this Agreement, an "investment company," as such term is defined in the Investment Company Act, assuming no change in the Commission's current interpretation as to entities that are not considered an investment company.

(u) Securities Act and Exchange Act. The Company will use its best efforts to comply with all requirements imposed upon it by the Securities Act and the Exchange Act as from time to time in force, so far as necessary to permit the continuance of sales of, or dealings in, the Shares as contemplated by the provisions hereof and the Prospectus.

(v) No Offer to Sell. Other than a Permitted Free Writing Prospectus, neither Cowen nor the Company (including its agents and representatives, other than Cowen in its capacity as such) will make, use, prepare, authorize, approve or refer to any written communication (as defined in Rule 405 under the Securities Act), required to be filed with the Commission, that constitutes an offer to sell or solicitation of an offer to buy Common Stock hereunder.

(w) Sarbanes-Oxley Act. The Company and its Subsidiaries will use their best efforts to comply with all effective applicable provisions of the Sarbanes-Oxley Act.

(x) Affirmation. Each Placement Notice delivered by the Company to Cowen and each execution and delivery by the Company of a Terms Agreement shall be deemed to be (i) an affirmation that the representations, warranties and agreements of the Company herein contained and contained in any certificate delivered to Cowen pursuant hereto are true and correct at the time of delivery of such Placement Notice or the date of such Terms Agreement, as the case may be,

and (ii) an undertaking that such representations, warranties and agreements will be true and correct on any applicable Time of Sale and Settlement Date, as though made at and as of each such time (it being understood that such representations, warranties and agreements shall relate to the Registration Statement and the Prospectus as amended and supplemented to the time of such Placement Notice acceptance or Terms Agreement, as the case may be).

(y) Renewal. If immediately prior to the third anniversary (the "**Renewal Deadline**") of the initial effective date of the Registration Statement, the aggregate gross sales price of Shares sold by the Company is less than the Maximum Amount and this Agreement has not expired or been terminated, the Company will, prior to the Renewal Deadline, file, if it has not already done so and is eligible to do so, file a new shelf registration statement relating to the Shares, in a form reasonably satisfactory to Cowen, and, if not automatically effective, will use its commercially reasonable efforts to cause such registration statement to be declared effective within 60 days after the Renewal Deadline. The Company will take all other action necessary or appropriate to permit the issuance and sale of the Shares to continue as contemplated in the expired registration statement relating to the Shares. References herein to the Registration Statement shall include such new shelf registration statement.

8. Conditions to Cowen's Obligations. The obligations of Cowen hereunder with respect to a Placement Notice or pursuant to any Terms Agreement will be subject to the continuing accuracy and completeness of the representations and warranties made by the Company herein, to the due performance by the Company of its obligations hereunder and thereunder, to the completion by Cowen of a due diligence review satisfactory to Cowen in its reasonable judgment, and to the continuing satisfaction (or waiver by Cowen in its sole discretion) of the following additional conditions:

(a) Registration Statement Effective. The Registration Statement shall be effective and shall be available for (i) all sales of Shares issued pursuant to all prior Placement Notices or any Terms Agreements and (ii) the sale of all Shares contemplated to be issued pursuant to Placement Notice or any Terms Agreement.

(b) No Material Notices. None of the following events shall have occurred and be continuing: (i) receipt by the Company or any of its Subsidiaries of any request for additional information from the Commission or any other federal or state governmental authority during the period of effectiveness of the Registration Statement, the response to which would require any post-effective amendments or supplements to the Registration Statement or the Prospectus; (ii) the issuance by the Commission or any other federal or state governmental authority of any stop order suspending the effectiveness of the Registration Statement or the initiation of any proceedings for that purpose; (iii) receipt by the Company of any notification with respect to the suspension of the qualification or exemption from qualification of any of the Shares for sale in any jurisdiction or the initiation or threatening of any proceeding for such purpose; or (iv) the occurrence of any event that makes any material statement made in the Registration Statement or the Prospectus or any material document incorporated or deemed to be incorporated therein by reference untrue in any material respect or that requires the making of any changes in the Registration Statement, related Prospectus or such documents so that, in the case of the Registration Statement, it will not contain any materially untrue statement of a material fact or omit to state any material fact required to be stated therein or necessary to make the statements therein not misleading and, that in the case of

the Prospectus, it will not contain any materially untrue statement of a material fact or omit to state any material fact required to be stated therein or necessary to make the statements therein, in the light of the circumstances under which they were made, not misleading.

(c) No Misstatement or Material Omission. Cowen shall not have advised the Company that the Registration Statement or Prospectus, or any amendment or supplement thereto, contains an untrue statement of fact that in Cowen's reasonable opinion is material, or omits to state a fact that in Cowen's opinion is material and is required to be stated therein or is necessary to make the statements therein not misleading.

(d) Material Changes. Except as contemplated in the Prospectus, or disclosed in the Company's reports filed with the Commission, there shall not have been any material adverse change, on a consolidated basis, in the authorized capital stock of the Company or any Material Adverse Change or any development that could reasonably be expected to result in a Material Adverse Change, or any downgrading in or withdrawal of the rating assigned to any of the Company's securities (other than asset backed securities) by any rating organization or a public announcement by any rating organization that it has under surveillance or review its rating of any of the Company's securities (other than asset backed securities), the effect of which, in the case of any such action by a rating organization described above, in the reasonable judgment of Cowen (without relieving the Company of any obligation or liability it may otherwise have), is so material as to make it impracticable or inadvisable to proceed with the offering of the Shares on the terms and in the manner contemplated in the Prospectus.

(e) Company Counsel Legal Opinion. Cowen shall have received the opinions of Company Counsel required to be delivered pursuant to Section 7(n) on or before the date on which such delivery of such opinion is required pursuant to Section 7(n).

(f) Cowen Counsel Legal Opinion. Cowen shall have received from Latham & Watkins LLP, counsel for Cowen, such opinion or opinions, on or before the date on which the delivery of the Company Counsel legal opinion is required pursuant to Section 7(n), with respect to such matters as Cowen may reasonably require, and the Company shall have furnished to such counsel such documents as they request for enabling them to pass upon such matters.

(g) Comfort Letter. Cowen shall have received the Comfort Letter required to be delivered pursuant to Section 7(p) on or before the date on which such delivery of such Comfort Letter is required pursuant to Section 7(p).

(h) Representation Certificate. Cowen shall have received the certificate required to be delivered pursuant to Section 7(m) on or before the date on which delivery of such certificate is required pursuant to Section 7(m).

(i) Secretary's Certificate. On or prior to the First Delivery Date and at each Principal Settlement Date, Cowen shall have received a certificate, signed on behalf of the Company by its corporate secretary, in form and substance reasonably satisfactory to Cowen and its counsel.

(j) No Suspension. Trading in the Common Stock shall not have been suspended on Nasdaq.

(k) Other Materials. On each date on which the Company is required to deliver a certificate pursuant to Section 7(m), the Company shall have furnished to Cowen such appropriate further information, certificates and documents as Cowen may have reasonably requested. All such information, certificates and other documents shall have been in compliance with the provisions hereof. The Company will furnish Cowen with such conformed copies of such information, certificates and other documents as Cowen shall have reasonably requested.

(l) Securities Act Filings Made. All filings with the Commission required by Rule 424 under the Securities Act to have been filed prior to the issuance of any Placement Notice hereunder or prior to any Principal Settlement Date shall have been made within the applicable time period prescribed for such filing by Rule 424. The Company shall file a prospectus supplement or a supplement to a prospectus supplement in connection with any Principal Transaction pursuant to a Terms Agreement within the applicable time period prescribed for such filing by Rule 424.

(m) Approval for Listing. The Shares shall either have been (i) approved for listing on Nasdaq, subject only to notice of issuance, or (ii) the Company shall have filed an application for listing of the Shares on Nasdaq at, or prior to, the issuance of any Placement Notice.

(n) No Termination Event. There shall not have occurred any event that would permit Cowen to terminate this Agreement pursuant to Section 11(a).

9. Indemnification and Contribution.

(a) Company Indemnification. The Company agrees to indemnify and hold harmless Cowen, the directors, officers, partners, employees and agents of Cowen and each person, if any, who (i) controls Cowen within the meaning of Section 15 of the Securities Act or Section 20 of the Exchange Act, or (ii) is controlled by or is under common control with Cowen from and against any and all losses, claims, liabilities, expenses and damages (including, but not limited to, any and all reasonable investigative, legal and other expenses incurred in connection with, and any and all amounts paid in settlement (in accordance with Section 9(c)) of, any action, suit or proceeding between any of the indemnified parties and any indemnifying parties or between any indemnified party and any third party, or otherwise, or any claim asserted), as and when incurred, to which Cowen, or any such person, may become subject under the Securities Act, the Exchange Act or other federal or state statutory law or regulation, at common law or otherwise, insofar as such losses, claims, liabilities, expenses or damages arise out of or are based, directly or indirectly, on (x) any untrue statement or alleged untrue statement of a material fact contained in the Registration Statement or the Prospectus or any amendment or supplement to the Registration Statement or the Prospectus or in any free writing prospectus or in any application or other document executed by or on behalf of the Company in connection with this Agreement or any Terms Agreement or based on written information furnished by or on behalf of the Company filed in any jurisdiction in order to qualify the Common Stock under the securities laws thereof or filed with the Commission, (y) the omission or alleged omission to state in any such document a material fact required to be stated in it or necessary to make the statements in it not misleading or (z) any breach by any of the indemnifying parties of any of their respective representations, warranties and agreements contained in this Agreement or any Terms Agreement; *provided, however*, that this indemnity agreement shall not apply to the extent that such loss, claim, liability, expense or damage arises from the sale of the Shares pursuant to this Agreement or any Terms Agreement and is caused directly or indirectly by an untrue statement or omission or alleged untrue statement or omission

made in reliance upon and in conformity with solely Agent's Information. As used herein, "**Agent's Information**" means, solely, the following information in the Prospectus: the ninth paragraph under the caption "Plan of Distribution" in the Prospectus. This indemnity agreement will be in addition to any liability that the Company might otherwise have.

(b) Cowen Indemnification. Cowen agrees to indemnify and hold harmless the Company and its directors and each officer of the Company that signed the Registration Statement, and each person, if any, who (i) controls the Company within the meaning of Section 15 of the Securities Act or Section 20 of the Exchange Act or (ii) is controlled by or is under common control with the Company against any and all loss, liability, claim, damage and expense described in the indemnity contained in Section 9(a), as incurred, but only with respect to untrue statements or omissions, or alleged untrue statements or omissions, made in the Registration Statement (or any amendments thereto) or the Prospectus (or any amendment or supplement thereto) in reliance upon and in conformity with the Agent's Information.

(c) Procedure. Any party that proposes to assert the right to be indemnified under this Section 9 will, promptly after receipt of notice of commencement of any action against such party in respect of which a claim is to be made against an indemnifying party or parties under this Section 9, notify each such indemnifying party of the commencement of such action, enclosing a copy of all papers served, but the omission so to notify such indemnifying party will not relieve the indemnifying party from (i) any liability that it might have to any indemnified party otherwise than under this Section 9 and (ii) any liability that it may have to any indemnified party under the foregoing provision of this Section 9 unless, and only to the extent that, such omission results in the forfeiture of substantive rights or defenses by the indemnifying party. If any such action is brought against any indemnified party and it notifies the indemnifying party of its commencement, the indemnifying party will be entitled to participate in and, to the extent that it elects by delivering written notice to the indemnified party promptly after receiving notice of the commencement of the action from the indemnified party, jointly with any other indemnifying party similarly notified, to assume the defense of the action, with counsel reasonably satisfactory to the indemnified party, and after notice from the indemnifying party to the indemnified party of its election to assume the defense, the indemnifying party will not be liable to the indemnified party for any legal or other expenses except as provided below and except for the reasonable costs of investigation subsequently incurred by the indemnified party in connection with the defense. The indemnified party will have the right to employ its own counsel in any such action, but the fees, expenses and other charges of such counsel will be at the expense of such indemnified party unless (1) the employment of counsel by the indemnified party has been authorized in writing by the indemnifying party, (2) the indemnified party has reasonably concluded (based on advice of counsel) that there may be legal defenses available to it or other indemnified parties that are different from or in addition to those available to the indemnifying party, (3) a conflict or potential conflict exists (based on advice of counsel to the indemnified party) between the indemnified party and the indemnifying party (in which case the indemnifying party will not have the right to direct the defense of such action on behalf of the indemnified party) or (4) the indemnifying party has not in fact employed counsel to assume the defense of such action within a reasonable time after receiving notice of the commencement of the action, in each of which cases the reasonable fees, disbursements and other charges of counsel will be at the expense of the indemnifying party or parties. It is understood that the indemnifying party or parties shall not, in connection with any proceeding or related proceedings in the same jurisdiction, be liable for the reasonable fees,

disbursements and other charges of more than one separate firm admitted to practice in such jurisdiction at any one time for all such indemnified party or parties. All such fees, disbursements and other charges will be reimbursed by the indemnifying party promptly as they are incurred after the indemnifying party receives a written invoice related to such fees, disbursements and other charges. An indemnifying party will not, in any event, be liable for any settlement of any action or claim effected without its written consent. No indemnifying party shall, without the prior written consent of each indemnified party, settle or compromise or consent to the entry of any judgment in any pending or threatened claim, action or proceeding relating to the matters contemplated by this Section 9 (whether or not any indemnified party is a party thereto), unless such settlement, compromise or consent includes an unconditional release of each indemnified party from all liability arising or that may arise out of such claim, action or proceeding.

(d) Contribution. In order to provide for just and equitable contribution in circumstances in which the indemnification provided for in the foregoing paragraphs of this Section 9 is applicable in accordance with its terms but for any reason is held to be unavailable from the Company or Cowen, the Company and Cowen will contribute to the total losses, claims, liabilities, expenses and damages (including any investigative, legal and other expenses reasonably incurred in connection with, and any amount paid in settlement of, any action, suit or proceeding or any claim asserted, but after deducting any contribution received by the Company from persons other than Cowen, such as persons who control the Company within the meaning of the Securities Act, officers of the Company who signed the Registration Statement and directors of the Company, who also may be liable for contribution) to which the Company and Cowen may be subject in such proportion as shall be appropriate to reflect the relative benefits received by the Company on the one hand and Cowen on the other. The relative benefits received by the Company on the one hand and Cowen on the other hand shall be deemed to be in the same proportion as the total Net Proceeds from the sale of the Shares (before deducting expenses) received by the Company bear to the total compensation received by Cowen from the sale of Shares on behalf of the Company. If, but only if, the allocation provided by the foregoing sentence is not permitted by applicable law, the allocation of contribution shall be made in such proportion as is appropriate to reflect not only the relative benefits referred to in the foregoing sentence but also the relative fault of the Company, on the one hand, and Cowen, on the other, with respect to the statements or omission that resulted in such loss, claim, liability, expense or damage, or action in respect thereof, as well as any other relevant equitable considerations with respect to such offering. Such relative fault shall be determined by reference to, among other things, whether the untrue or alleged untrue statement of a material fact or omission or alleged omission to state a material fact relates to information supplied by the Company or Cowen, the intent of the parties and their relative knowledge, access to information and opportunity to correct or prevent such statement or omission. The Company and Cowen agree that it would not be just and equitable if contributions pursuant to this Section 9(d) were to be determined by pro rata allocation or by any other method of allocation that does not take into account the equitable considerations referred to herein. The amount paid or payable by an indemnified party as a result of the loss, claim, liability, expense, or damage, or action in respect thereof, referred to above in this Section 9(d) shall be deemed to include, for the purpose of this Section 9(d), any legal or other expenses reasonably incurred by such indemnified party in connection with investigating or defending any such action or claim to the extent consistent with Section 9(c) hereof. Notwithstanding the foregoing provisions of this Section 9(d), Cowen shall not be required to contribute any amount in excess of the commissions received by it under this Agreement and no person found guilty of fraudulent misrepresentation (within the meaning of

Section 11(f) of the Securities Act) will be entitled to contribution from any person who was not guilty of such fraudulent misrepresentation. For purposes of this Section 9(d), any person who controls a party to this Agreement or any Terms Agreement within the meaning of the Securities Act, and any officers, directors, partners, employees or agents of Cowen, will have the same rights to contribution as that party, and each director of the Company and each officer of the Company who signed the Registration Statement will have the same rights to contribution as the Company, subject in each case to the provisions hereof. Any party entitled to contribution, promptly after receipt of notice of commencement of any action against such party in respect of which a claim for contribution may be made under this Section 9(d), will notify any such party or parties from whom contribution may be sought, but the omission to so notify will not relieve that party or parties from whom contribution may be sought from any other obligation it or they may have under this Section 9(d) except to the extent that the failure to so notify such other party materially prejudiced the substantive rights or defenses of the party from whom contribution is sought. Except for a settlement entered into pursuant to the last sentence of Section 9(c) hereof, no party will be liable for contribution with respect to any action or claim settled without its written consent if such consent is required pursuant to Section 9(c) hereof.

10. Representations and Agreements to Survive Delivery. The indemnity and contribution agreements contained in Section 9 of this Agreement and all representations and warranties of the Company herein or in certificates delivered pursuant hereto shall survive, as of their respective dates, regardless of (i) any investigation made by or on behalf of Cowen, any controlling persons, or the Company (or any of their respective officers, directors or controlling persons), (ii) delivery and acceptance of the Shares and payment therefor or (iii) any termination of this Agreement.

11. Termination.

(a) Cowen shall have the right by giving notice as hereinafter specified at any time to terminate this Agreement if (i) any Material Adverse Change, or any development that could reasonably be expected to result in a Material Adverse Change has occurred that, in the reasonable judgment of Cowen, may materially impair the ability of Cowen to sell the Shares hereunder, (ii) the Company shall have failed, refused or been unable to perform any agreement on its part to be performed hereunder; or (iii) any other condition of Cowen's obligations hereunder is not fulfilled, or (iv), any suspension or limitation of trading in the Shares or in securities generally on Nasdaq shall have occurred. Any such termination shall be without liability of any party to any other party except that the provisions of Section 7(g) (Expenses), Section 9 (Indemnification and Contribution), Section 10 (Representations and Agreements to Survive Delivery), Section 16 (Applicable Law; Consent to Jurisdiction) and Section 17 (Waiver of Jury Trial) hereof shall remain in full force and effect notwithstanding such termination. If Cowen elects to terminate this Agreement as provided in this Section 11(a), Cowen shall provide the required notice as specified in Section 12 (Notices).

(b) In the case of any purchase by Cowen pursuant to a Terms Agreement, the obligations of Cowen pursuant to such Terms Agreement shall be subject to termination by Cowen at any time prior to or at the Principal Settlement Date if (A) since the time of execution of the Terms Agreement or the respective dates as of which information is given in the Registration Statement or the Prospectus, (i) there has been any Material Adverse Change or material change in the senior management of the Company, whether or not arising in the ordinary course of

business; or (ii) there has occurred any outbreak or escalation of hostilities or other national or international calamity or crisis or change in economic, political or other conditions, the effect of which on the United States or international financial markets is such as to make it, in Cowen's judgment, impracticable to market the Shares or enforce contracts for the sale of the Shares; or (iii) if trading in any securities of the Company has been suspended by the Commission or by the Nasdaq, or if trading generally on the Nasdaq over-the-counter market or the New York Stock Exchange has been suspended (including an automatic halt in trading pursuant to market-decline triggers, other than those in which solely program trading is temporarily halted), or limitations on prices for trading (other than limitations on hours or numbers of days of trading) have been fixed, or maximum ranges for prices for securities have been required, by such exchange or FINRA or the over-the-counter market or by order of the Commission or any other governmental authority; or (iv) if there has been any downgrade in the rating of any of the Company's debt securities or preferred stock by any "nationally recognized statistical rating organization" (as defined under Section 3(a)(62) of the Exchange Act); or (v) any federal, state, local or foreign statute, regulation, rule or order of any court or other governmental authority has been enacted, published, decreed or otherwise promulgated which, in the opinion of Cowen, would reasonably be expected to result in a Material Adverse Change; or (vi) any action has been taken by any federal, state, local or foreign government or agency in respect of its monetary or fiscal affairs which, in the opinion of Cowen, would reasonably be expected to have a material adverse effect on the securities markets in the United States. If Cowen elects to terminate its obligations pursuant to this Section 11(b), the Company shall be notified promptly in writing.

(c) The Company shall have the right, by giving ten (10) days' notice as hereinafter specified to terminate this Agreement in its sole discretion at any time after the date of this Agreement. Any such termination shall be without liability of any party to any other party except that the provisions of Section 7(g), Section 9, Section 10, Section 16 and Section 17 hereof shall remain in full force and effect notwithstanding such termination.

(d) Cowen shall have the right, by giving ten (10) days' notice as hereinafter specified to terminate this Agreement in its sole discretion at any time after the date of this Agreement. Any such termination shall be without liability of any party to any other party except that the provisions of Section 7(g), Section 9, Section 10, Section 16 and Section 17 hereof shall remain in full force and effect notwithstanding such termination.

(e) Unless earlier terminated pursuant to this Section 11, this Agreement shall automatically terminate upon the issuance and sale of all of the Shares through Cowen on the terms and subject to the conditions set forth herein; *provided* that the provisions of Section 7(g), Section 9, Section 10, Section 16 and Section 17 hereof shall remain in full force and effect notwithstanding such termination.

(f) This Agreement shall remain in full force and effect unless terminated pursuant to Sections 11(a), (b), (c), (d), or (e) above or otherwise by mutual agreement of the parties; *provided, however,* that any such termination by mutual agreement shall in all cases be deemed to provide that Section 7(g), Section 9, Section 10, Section 16 and Section 17 shall remain in full force and effect.

(g) Any termination of this Agreement shall be effective on the date specified in such notice of termination; *provided, however,* that such termination shall not be effective until the close

of business on the date of receipt of such notice by Cowen or the Company, as the case may be. If such termination shall occur prior to the Settlement Date for any sale of Shares, such Shares shall settle in accordance with the provisions of this Agreement.

(h) Subject to the additional limitation set forth in Section 7 of this Agreement, in the event of termination of this Agreement prior to the sale of any Shares, Cowen shall be entitled only to the reimbursement of its out of pocket expenses actually incurred.

12. Notices. All notices or other communications required or permitted to be given by any party to any other party pursuant to the terms of this Agreement or any Terms Agreement shall be in writing, unless otherwise specified in this Agreement, and if sent to Cowen, shall be delivered to Cowen at Cowen and Company, LLC, 599 Lexington Avenue, New York, NY 10022, Attention: General Counsel, email: Bradley.friedman@cowen.com; or if sent to the Company, shall be delivered to Blueprint Medicines Corporation, 45 Sidney Street, Cambridge, Massachusetts 02139, Attention: Michael Landsittel, Chief Financial Officer, email: MLandsittel@blueprintmedicines.com with copies (which shall not constitute notice) to Blueprint Medicines Corporation, 45 Sidney Street, Cambridge, Massachusetts 02139, Attention: Legal Department, email: legal@blueprintmedicines.com and Goodwin Procter LLP, 100 Northern Avenue, Boston, MA 02210, Attention: Danielle Lauzon, email: dlauzon@goodwinlaw.com. Each party to this Agreement may change such address for notices by sending to the parties to this Agreement written notice of a new address for such purpose. Each such notice or other communication shall be deemed given (i) when delivered personally on or before 4:30 p.m., New York City time, on a Business Day (as defined below), or, if such day is not a Business Day on the next succeeding Business Day, (ii) on the next Business Day after timely delivery to a nationally-recognized overnight courier. (iii) on the Business Day actually received if deposited in the U.S. mail (certified or registered mail, return receipt requested, postage prepaid) and (iv) when delivered by email communication ("**Electronic Notice**"), at the time the party sending Electronic Notice receives verification of receipt by the receiving party, other than via auto reply. For purposes of this Agreement, "**Business Day**" shall mean any day on which the Nasdaq and commercial banks in the City of New York are open for business.

13. Successors and Assigns. This Agreement and any Terms Agreement shall inure to the benefit of and be binding upon the Company and Cowen and their respective successors and the affiliates, controlling persons, officers and directors referred to in Section 9 hereof. References to any of the parties contained in this Agreement or any Terms Agreement shall be deemed to include the successors and permitted assigns of such party. Nothing in this Agreement or any Terms Agreement, express or implied, is intended to confer upon any party other than the parties hereto or their respective successors and permitted assigns any rights, remedies, obligations or liabilities under or by reason of this Agreement or any such Terms Agreement, except as expressly provided in this Agreement or such Terms Agreement. Neither party may assign its rights or obligations under this Agreement or any Terms Agreement without the prior written consent of the other party; *provided*, *however*, that Cowen may assign its rights and obligations hereunder or under any Terms Agreement to an affiliate of Cowen without obtaining the Company's consent, so long as such affiliate is a registered broker-dealer.

14. Adjustments for Share Splits. The parties acknowledge and agree that all share-related numbers contained in this Agreement or any Terms Agreement shall be adjusted to take

into account any share split, share dividend or similar event effected with respect to the Common Stock.

15. Entire Agreement; Amendment; Severability. This Agreement (including all schedules and exhibits attached hereto and Placement Notices issued pursuant hereto), together with any Terms Agreement, constitutes the entire agreement and supersedes all other prior and contemporaneous agreements and undertakings, both written and oral, among the parties hereto with regard to the subject matter hereof. Neither this Agreement, nor any Terms Agreement, nor any term hereof may be amended except pursuant to a written instrument executed by the Company and Cowen. In the event that any one or more of the provisions contained herein, or the application thereof in any circumstance, is held invalid, illegal or unenforceable as written by a court of competent jurisdiction, then such provision shall be given full force and effect to the fullest possible extent that it is valid, legal and enforceable, and the remainder of the terms and provisions herein shall be construed as if such invalid, illegal or unenforceable term or provision was not contained herein, but only to the extent that giving effect to such provision and the remainder of the terms and provisions hereof shall be in accordance with the intent of the parties as reflected in this Agreement and any Terms Agreement.

16. Applicable Law; Consent to Jurisdiction. This Agreement and any Terms Agreement shall be governed by, and construed in accordance with, the internal laws of the State of New York without regard to the principles of conflicts of laws. Each party hereby irrevocably submits to the non-exclusive jurisdiction of the state and federal courts sitting in the City of New York, borough of Manhattan, for the adjudication of any dispute hereunder or in connection with any transaction contemplated hereby or by any Terms Agreement, and hereby irrevocably waives, and agrees not to assert in any suit, action or proceeding, any claim that it is not personally subject to the jurisdiction of any such court, that such suit, action or proceeding is brought in an inconvenient forum or that the venue of such suit, action or proceeding is improper. Each party hereby irrevocably waives personal service of process and consents to process being served in any such suit, action or proceeding by mailing a copy thereof (certified or registered mail, return receipt requested) to such party at the address in effect for notices to it under this Agreement and agrees that such service shall constitute good and sufficient service of process and notice thereof. Nothing contained herein shall be deemed to limit in any way any right to serve process in any manner permitted by law.

17. Waiver of Jury Trial. The Company and Cowen each hereby irrevocably waives any right it may have to a trial by jury in respect of any claim based upon or arising out of this Agreement, any Terms Agreement or any transaction contemplated hereby or thereby.

18. Absence of Fiduciary Relationship. The Company acknowledges and agrees that:

(a) Cowen has been retained solely to act as an arm's length contractual counterparty to the Company in connection with the sale of the Shares contemplated hereby and any Terms Agreement and that no fiduciary, advisory or agency relationship between the Company and Cowen has been created in respect of any of the transactions contemplated by this Agreement or any Terms Agreement, irrespective of whether Cowen has advised or is advising the Company on other matters;

(b) the Company is capable of evaluating and understanding and understands and accepts the terms, risks and conditions of the transactions contemplated by this Agreement or any Terms Agreement;

(c) the Company has been advised that Cowen and its affiliates are engaged in a broad range of transactions which may involve interests that differ from those of the Company and that Cowen has no obligation to disclose such interests and transactions to the Company by virtue of any fiduciary, advisory or agency relationship; and

(d) the Company waives, to the fullest extent permitted by law, any claims it may have against Cowen, for breach of fiduciary duty or alleged breach of fiduciary duty in connection with the sale of Shares under this Agreement and any Terms Agreement and agrees that Cowen shall have no liability (whether direct or indirect) to the Company in respect of such a fiduciary claim or to any person asserting a fiduciary duty claim on behalf of or in right of the Company, including stockholders, partners, employees or creditors of the Company.

19. Counterparts. This Agreement and any Terms Agreement may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. Delivery of an executed Agreement or any Terms Agreement by one party to the other may be made by electronic transmission.

[Remainder of Page Intentionally Blank]

If the foregoing correctly sets forth the understanding between the Company and Cowen, please so indicate in the space provided below for that purpose, whereupon this letter shall constitute a binding agreement between the Company and Cowen.

Very truly yours,

COWEN AND COMPANY, LLC

By: /s/ Michael Murphy
Name: Michael Murphy
Title: Managing Director

ACCEPTED as of February 17, 2022:

BLUEPRINT MEDICINES CORPORATION

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

SCHEDULE 1

FORM OF PLACEMENT NOTICE

From: [ ]
Cc: [ ]
To: [ ]
Subject: Cowen At the Market Offering—Placement Notice

Gentlemen:

Pursuant to the terms and subject to the conditions contained in the Sales Agreement between Blueprint Medicines Corporation (the "Company"), and Cowen and Company, LLC ("Cowen") dated [●], 2022 (the "Agreement"), I hereby request on behalf of the Company that Cowen sell up to [[ ] shares]/[$[ ] of shares] of the Company's common stock, par value $0.001 per share, at a minimum market price of $_____ per share. Sales should begin on the date of this Notice and shall continue until [DATE] [all shares are sold].

SCHEDULE 2

Notice Parties

Company

Jeff Albers	President and Chief Executive Officer
Michael Landsittel	Chief Financial Officer
Tracey L. McCain	Executive Vice President, Chief Legal and Compliance Officer
Kate Haviland	Chief Operating Officer

Cowen

Michael J. Murphy	Managing Director
William Follis	Managing Director

BLUEPRINT MEDICINES CORPORATION

[_____] SHARES

TERMS AGREEMENT

____, 20__

Cowen and Company, LLC
599 Lexington Avenue
New York, NY 10022

Ladies & Gentlemen:

Blueprint Medicines Corporation, a Delaware corporation (the "**Company**"), proposes, subject to the terms and conditions stated herein and in the Sales Agreement, dated [•], 2022 (the "**Sales Agreement**"), between the Company and Cowen and Company, LLC ("**Cowen**"), to issue and sell to Cowen the securities specified in the Schedule hereto (the "**Purchased Securities**"). Unless otherwise defined below, terms defined in the Sales Agreement shall have the same meanings when used herein.

Each of the provisions of the Sales Agreement not specifically related to the solicitation by Cowen, as agent of the Company, of offers to purchase securities is incorporated herein by reference in its entirety, and shall be deemed to be part of this Terms Agreement to the same extent as if such provisions had been set forth in full herein. Each of the representations, warranties and agreements set forth therein shall be deemed to have been made as of the date of this Terms Agreement and the Settlement Date set forth in the Schedule hereto.

An amendment to the Registration Statement or a supplement to the Prospectus, as the case may be, relating to the Purchased Securities, in the form heretofore delivered to Cowen, is now proposed to be filed with the Commission.

Subject to the terms and conditions set forth herein and in the Sales Agreement which are incorporated herein by reference, the Company agrees to issue and sell to Cowen, and Cowen agrees to purchase from the Company, the Purchased Securities at the time and place and at the purchase price set forth in the Schedule hereto.

Notwithstanding any provision of the Sales Agreement or this Terms Agreement to the contrary, the Company consents to Cowen trading in the Common Stock for Cowen's own account and for the account of its clients at the same time as sales of the Purchased Securities occur pursuant to this Terms Agreement.

If the foregoing is in accordance with your understanding, please sign and return to us a counterpart hereof, whereupon this Terms Agreement, including those provisions of the Sales Agreement incorporated herein by reference, shall constitute a binding agreement between Cowen and the Company.

BLUEPRINT MEDICINES CORPORATION

By: _____
Name:
Title:

Accepted and agreed as of
the date first above written:

COWEN AND COMPANY, LLC

By: _____
Name:
Title:

Schedule to Terms Agreement

Title of Purchased Securities:

Common Stock, par value $0.001 per share

Number of Shares of Purchased Securities:

[●] Shares

Purchase Price Payable by Cowen:

$**[●]** per Share

Method of and Specified Funds for Payment of Purchase Price:

[By wire transfer to a bank account specified by the Company in same day funds.**]**

Method of Delivery:

[To Cowen's account, or the account of Cowen's designee, at The Depository Trust Company via DWAC in return for payment of the purchase price.**]**

Settlement Date:

[●], 20**[●]**

Closing Location:

[●]

Documents to be Delivered:

The following documents referred to in the Sales Agreement shall be delivered on the Settlement Date as a condition to the closing for the Purchased Securities (which documents shall be dated on or as of the Settlement Date and shall be appropriately updated to cover any Permitted Free Writing Prospectuses and any amendments or supplements to the Registration Statement, the Prospectus, any Permitted Free Writing Prospectuses and any documents incorporated by reference therein):

(1) the opinion and negative assurance letter referred to in Section 8(e);
(2) the opinion and negative assurance letter referred to in Section 8(f)
(3) the "comfort letter" referred to in Section 8(g);
(4) the representation certificate referred to in Section 8(h);
(5) the secretary's certificate referred to in Section 8(i); and
(6) such other documents as Cowen shall reasonably request.

Time of sale: **[●] [**a.m./p.m.**]** (New York City time) on **[●]**, **[●]**

Time of sale information:

- The number of shares of Purchased Securities set forth above.

SCHEDULE 3

Compensation

Cowen shall be paid compensation up to 3.0 % of the gross proceeds from the sales of Shares in an Agency Transaction pursuant to the terms of this Agreement.

Exhibit 7(m)

OFFICER CERTIFICATE

The undersigned, the duly qualified and elected _____, of **Blueprint Medicines Corporation** ("**Company**"), a Delaware corporation, does hereby certify on behalf of the Company (and not in the undersigned's individual capacity), pursuant to Section 7(m) of the Sales Agreement dated [●], 2022 (the "**Sales Agreement**") between the Company and Cowen and Company, LLC, that to the best of the knowledge of the undersigned.

(i) The representations and warranties of the Company in Section 6 of the Sales Agreement (A) to the extent such representations and warranties are subject to qualifications and exceptions contained therein relating to materiality or Material Adverse Change, are true and correct on and as of the date hereof with the same force and effect as if expressly made on and as of the date hereof, except for those representations and warranties that speak solely as of a specific date and which were true and correct as of such date, and (B) to the extent such representations and warranties are not subject to any qualifications or exceptions, are true and correct in all material respects as of the date hereof as if made on and as of the date hereof with the same force and effect as if expressly made on and as of the date hereof except for those representations and warranties that speak solely as of a specific date and which were true and correct as of such date; and

(ii) The Company has complied with all agreements and satisfied all conditions on its part to be performed or satisfied pursuant to the Sales Agreement at or prior to the date hereof.

By: _____
Name:
Title:

Date: _____

Exhibit 5.1

Goodwin Procter LLP
100 Northern Avenue
Boston, MA 02210
goodwinlaw.com
+1 617 570 1000

February 17, 2022

Blueprint Medicines Corporation
45 Sidney Street
Cambridge, MA 02139

Re: Securities Registered under Registration Statement on Form S-3ASR

We have acted as counsel to you in connection with your filing of a Registration Statement on Form S-3ASR (File No. 333-236424) (as amended or supplemented, the "**Registration Statement**") filed on February 13, 2020 with the Securities and Exchange Commission (the "**Commission**") pursuant to the Securities Act of 1933, as amended (the "**Securities Act**"), relating to the registration of the offering by Blueprint Medicines Corporation, a Delaware corporation (the "**Company**") of any combination of securities of the types specified therein. The Registration Statement was declared effective by the Commission on February 13, 2020. Reference is made to our opinion letter dated February 13, 2020 and included as Exhibit 5.1 to the Registration Statement. We are delivering this supplemental opinion letter in connection with the prospectus supplement (the "**Prospectus Supplement**") filed on February 17, 2022 by the Company with the Commission pursuant to Rule 424 under the Securities Act. The Prospectus Supplement relates to the offering by the Company of up to $300,000,000 in shares (the "**Shares**") of the Company's common stock, par value $0.001 per share ("**Common Stock**") covered by the Registration Statement. The Shares are being offered and sold by the sales agent named in, and pursuant to, the sales agreement among the Company and such sales agent.

We have reviewed such documents and made such examination of law as we have deemed appropriate to give the opinion set forth below. We have relied, without independent verification, on certificates of public officials and, as to matters of fact material to the opinion set forth below, on certificates of officers of the Company.

For purposes of the opinion set forth below, we have assumed that the Shares are issued for a price per share equal to or greater than the minimum price authorized by the Company's board of directors (or a duly authorized committee of the Company's board of directors) (the "**Minimum Price**") and that no event occurs that causes the number of authorized shares of Common Stock available for issuance by the Company to be less than the number of then unissued Shares that may be issued for the Minimum Price.

For purposes of the opinion set forth below, we refer to the following as "Future Approval and Issuance": (a) the approval by the Company's board of directors (or a duly authorized committee of the board of directors) of the issuance of the Shares (the "**Approval**") and (b) the issuance of the Shares in accordance with the Approval and the receipt by the Company of the consideration

(which shall not be less than the par value of such Shares) to be paid in accordance with the Approval.

The opinion set forth below is limited to the Delaware General Corporation Law.
Based on the foregoing, we are of the opinion that the Shares have been duly authorized and, upon Future Approval and Issuance, will be validly issued, fully paid and nonassessable.

This opinion is being furnished to you for submission to the Commission as an exhibit to the Company's Annual Report on Form 10-K relating to the Shares (the "**Annual Report**"), which is incorporated by reference in the Registration Statement. We hereby consent to the filing of this opinion letter as an exhibit to the Annual Report and its incorporation by reference and the reference to our firm in that report. In giving our consent, we do not admit that we are in the category of persons whose consent is required under Section 7 of the Securities Act or the rules and regulations thereunder.

Very truly yours,

/s/ Goodwin Procter LLP

GOODWIN PROCTER LLP

THIRD AMENDMENT TO LEASE

THIS THIRD AMENDMENT TO LEASE (this "Amendment") is entered into as of this 15th day of December, 2021, by and between BRE-BMR 38 SIDNEY LLC, a Delaware limited liability company ("Landlord," as successor-in-interest to Thirty-Eight Sidney Street LLC, which was successor-in-interest to Thirty-Eight Sidney Street Limited Partnership), and BLUEPRINT MEDICINES CORPORATION, a Delaware corporation ("Tenant").

RECITALS

A. WHEREAS, Landlord and Tenant are parties to that certain Lease dated as of February 12, 2015, as amended by that certain First Amendment to Lease dated as of January 26, 2018 and that certain Second Amendment to Lease ("Second Amendment") dated as of April 6, 2021 (collectively, and as the same may have been further amended, amended and restated, supplemented or modified from time to time, the "Existing Lease"), whereby Tenant leases certain premises containing approximately 39,114 rentable square feet located on the second and third floors (the "Existing Premises") from Landlord in the building at 38 Sidney Street, Cambridge, Massachusetts (the "Building");

B. WHEREAS, Landlord and Tenant desire to extend the term of the Existing Lease with respect to the Existing Premises;

C. WHEREAS, Landlord and Tenant desire to make certain other amendments to the Existing Lease; and

D. WHEREAS, Landlord and Tenant desire to modify and amend the Existing Lease only in the respects and on the conditions hereinafter stated.

AGREEMENT

NOW, THEREFORE, Landlord and Tenant, in consideration of the mutual promises contained herein and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, and intending to be legally bound, agree as follows:

1. Definitions. For purposes of this Amendment, capitalized terms shall have the meanings ascribed to them in the Existing Lease unless otherwise defined herein. The Existing Lease, as amended by this Amendment, is referred to collectively herein as the "Lease." From and after the date hereof, the term "Lease," as used in the Existing Lease, shall mean the Existing Lease, as amended by this Amendment.

2. Extension Term; Term Expiration Date. The term with respect to the Existing Premises is hereby extended to November 30, 2029. The period commencing on November 1, 2022 (the "Existing Premises Extension Term Commencement Date") and ending on November 30, 2029 shall be referred to herein as the "Existing Premises Extension Term." The term "Term" as used in the Lease shall refer to the term under the Existing Lease as extended by the Existing Premises Extension Term. Notwithstanding anything in the Existing Lease to the contrary, the parties agree that the Existing Premises Extension Term does not constitute the exercise of

Tenant's Extension Option with respect to the Existing Premises per the terms of Section 2.6 of the Existing Lease (as amended by Section 3 of the Second Amendment) and that one option to extend the Term of the Existing Lease with respect to the Existing Premises for a term of five (5) years under Section 2.6 of the Existing Lease (as amended by Section 3 of the Second Amendment) remains.

3. Rent During Existing Premises Extension Term. Monthly and annual installments of Annual Fixed Rent for the Existing Premises during the Existing Premises Extension Term will be as follows:

Dates	Rentable Square Feet of the Existing Premises	Annual Fixed Rent per Rentable Square Foot	Annual Fixed Rent per month	Annual Fixed Rent per year
11/1/2022-10/31/2023	39,114	$115.00 annually	$374.842.50	$4,498,110
11/1/2023-10/31/2024	39,114	$118.45 annually	$386,087.78	$4,633,053.30
11/1/2024-10/31/2025	39,114	$122.00 annually	$397,659	$4,771,908
11/1/2025-10/31/2026	39,114	$125.66 annually	$409,588.77	$4,915,065.24
11/1/2026-10/31/2027	39,114	$129.43 annually	$421,877.09	$5,062,525.02
11/1/2027-10/31/2028	39,114	$133.32 annually	$434,556.54	$5,214,678.48
11/1/2028-10/31/2029	39,114	$137.32 annually	$447,594.54	$5,371,134.48
11/1/2029-11/30/2029	39,114	$141.44 annually	$461,023.68	$5,532,284.16*

**to be pro-rated for partial year*

4. Tenant Improvements. As of the Existing Premises Extension Term Commencement Date, Landlord shall make available to Tenant a tenant improvement allowance of Eight Hundred Twenty-One Thousand Three Hundred Ninety-Four and 00/100 Dollars ($821,394.00) (based upon Twenty-One Dollars ($21.00) per Rentable Square Foot of the Existing

Premises) (the "Extension TI Allowance") in order to fund appropriate improvements to the Existing Premises ("Tenant Improvements") consistent with Permitted Uses. Tenant shall be responsible for performing and completing the Tenant Improvements. The Extension TI Allowance may be applied to the costs of (i) construction, (ii) Landlord's construction oversight fee described above, (iii) commissioning of mechanical, electrical and plumbing systems by a licensed, qualified commissioning agent hired by Tenant, and review of such party's commissioning report by a licensed, qualified commissioning agent hired by Landlord, (iv) space planning, architect, engineering and other related services performed by third parties unaffiliated with Tenant, (v) building permits and other taxes, fees, charges and levies by governmental authorities for permits or for inspections of the Tenant Improvements, and (vi) costs and expenses for labor, material, equipment and fixtures. In no event shall the Extension TI Allowance be used for (A) the cost of work that is not authorized by the Approved Plans (as defined in the Work Letter; said Work Letter is defined below) or otherwise approved in writing by Landlord, (B) payments to Tenant or any affiliates of Tenant, (C) the purchase of any furniture, personal property or other non-building system equipment, (D) costs resulting from any default by Tenant of its obligations under this Lease or (E) costs that are recoverable by Tenant from a third party (e.g., insurers, warrantors, or tortfeasors). Tenant shall have until November 1, 2023 (the "TI Deadline") to submit a Fund Request (as defined in the Work Letter) for the Extension TI Allowance, after which date Landlord's obligation to fund the Expansion TI Allowance shall expire. In no event shall any unused Extension TI Allowance entitle Tenant to a credit against Annual Fixed Rent or Additional Rent payable under the Lease. Tenant's design and installation utilizing the Extension TI Allowance shall be subject to (a) the provisions of the Lease governing alterations, and (b) the work letter attached to this Amendment as Exhibit A (the "Work Letter") (provided that in the event any terms of the attached Work Letter conflict with terms of the Lease, the provisions of the Work Letter shall govern).

5. Condition of Existing Premises. Tenant acknowledges that (a) it is in possession of and is familiar with the condition of the Existing Premises and, notwithstanding anything contained in the Lease to the contrary, agrees to take the same in its condition "as is" as of the first day of the Existing Premises Extension Term, and (b) Landlord shall have no obligation to alter, repair or otherwise prepare the Existing Premises for Tenant's continued occupancy for the Existing Premises Extension Term or to pay for any improvements to the Existing Premises, except as may be expressly provided in the Lease or as set forth herein.

6. Sublease Profits. The fourth sentence of the fourth paragraph of Section 6.8 of the Existing Lease is hereby amended by deleting the clause "one hundred percent (100%) of any amounts the Tenant receives" and replacing it with the clause "fifty percent (50%) of any amounts the Tenant receives."

7. Extension Option.

a. The first sentence of the first paragraph of Section 2.6 of the Existing Lease is hereby deleted in its entirety and replaced with the following: "Provided that there has been no Event of Default which is uncured and continuing on the part of the Tenant, and that Tenant is, as of the date of exercise of its rights under this Section 2.6, in occupancy of at least seventy percent (70%) of the Premises for its own

business purposes, the Tenant shall have the right to extend the Term hereof for one (1) period of five (5) years (the "Extension Term") on the following terms and conditions:"

b. The first sentence of clause (a) of Section 2.6 of the Existing Lease is hereby amended by deleting "at least ten (10) months prior" and replacing it with "at least twelve (12) months prior."

8. Broker. Landlord and Tenant represent to the other that it has not dealt with any broker or agent in the negotiation for or the obtaining of this Amendment, other than Jones Lang LaSalle and CBRE (each, a "Broker" and collectively, the "Brokers"). Each Broker is entitled to a leasing commission in connection with the making of this Amendment, and Landlord shall pay such commission to each Broker pursuant to a separate agreement between Landlord and each Broker.

9. No Default. Landlord and Tenant represent, warrant and covenant that, to the best of their knowledge, Landlord and Tenant are not in default of any of their respective obligations under the Existing Lease and no event has occurred that, with the passage of time or the giving of notice (or both) would constitute a default by either Landlord or Tenant thereunder.

10. Notices. Landlord confirms that, notwithstanding anything in the Lease to the contrary, notices delivered to Landlord pursuant to the Lease should be sent to:

BRE-BMR 38 Sidney LLC
4570 Executive Drive, Suite 400
San Diego, CA 92121
Attn: Legal Review
Email: legalreview@biomedrealty.com

Tenant confirms that, notwithstanding anything in the Lease to the contrary, notices delivered to Tenant pursuant to the Lease should be sent to:

Blueprint Medicines Corporation
45 Sidney Street
Cambridge, MA 02139
Attn: Legal Department
Email: legal@blueprintmedicines.com

with a copy to:

Blueprint Medicines Corporation
45 Sidney Street
Cambridge, MA 02139
Attn: Michael Landsittel, Chief Financial Officer
Email: MLandsittel@blueprintmedicines.com

11. Effect of Amendment. Except as modified by this Amendment, the Existing Lease and all the covenants, agreements, terms, provisions and conditions thereof shall remain in full force and effect and are hereby ratified and affirmed. In the event of any conflict between the terms contained in this Amendment and the Existing Lease, the terms herein contained shall supersede and control the obligations and liabilities of the parties.

12. Successors and Assigns. Each of the covenants, conditions and agreements contained in this Amendment shall inure to the benefit of and shall apply to and be binding upon the parties hereto and their respective heirs, legatees, devisees, executors, administrators and permitted successors and assigns and sublessees. Nothing in this section shall in any way alter the provisions of the Lease restricting assignment or subletting.

13. Miscellaneous. This Amendment becomes effective only upon execution and delivery hereof by Landlord and Tenant. The captions of the paragraphs and subparagraphs in this Amendment are inserted and included solely for convenience and shall not be considered or given any effect in construing the provisions hereof. All exhibits hereto are incorporated herein by reference. Submission of this instrument for examination or signature by Tenant does not constitute a reservation of or option for a lease, and shall not be effective as a lease, lease amendment or otherwise until execution by and delivery to both Landlord and Tenant.

14. Authority. Landlord and Tenant guarantee, warrant and represent that the individual or individuals signing this Amendment have the power, authority and legal capacity to sign this Amendment on behalf of and to bind all entities, corporations, partnerships, limited liability companies, joint venturers or other organizations and entities on whose behalf such individual or individuals have signed.

15. Counterparts; Facsimile and PDF Signatures. This Amendment may be executed in one or more counterparts, each of which, when taken together, shall constitute one and the same document. A facsimile or portable document format (PDF) signature, or other electronic signature (e.g., Docusign) on this Amendment shall be equivalent to, and have the same force and effect as, an original signature.

[REMAINDER OF THIS PAGE INTENTIONALLY LEFT BLANK]

IN WITNESS WHEREOF, Landlord and Tenant have executed this Amendment as a sealed Massachusetts instrument as of the date and year first above written.

LANDLORD:

BRE-BMR 38 SIDNEY LLC,
a Delaware limited liability company

By: /s/ Colleen O'Connor
Name: Colleen O'Connor
Title: VP, Leasing, East Coast & UK Markets

TENANT:

BLUEPRINT MEDICINES CORPORATION,
a Delaware corporation

By: /s/ Michael Landsittel
Name: Michael Landsittel
Title: CFO

EXHIBIT A

WORK LETTER

This Work Letter (this "Work Letter") is made and entered into as of the 15th day of December, 2021, by and between BRE-BMR 38 SIDNEY LLC, a Delaware limited liability company ("Landlord," as successor-in-interest to Thirty-Eight Sidney Street LLC, which was successor-in-interest to Thirty-Eight Sidney Street Limited Partnership), and BLUEPRINT MEDICINES CORPORATION, a Delaware corporation ("Tenant"), and is attached to and made a part of that certain Lease dated as of February 12, 2015 (as the same has been amended, supplemented or otherwise modified from time to time, the "Lease"), by and between Landlord and Tenant for the premises located at 38 Sidney Street, Cambridge, Massachusetts ("Premises"). All capitalized terms used but not otherwise defined herein shall have the meanings given them in the Lease.

1. General Requirements.

1.1. Authorized Representatives.

(a) Landlord designates, as Landlord's authorized representative ("Landlord's Authorized Representative"), (i) Salvatore Zinno as the person authorized to initial plans, drawings, approvals and to sign change orders pursuant to this Work Letter and (ii) an officer of Landlord as the person authorized to sign any amendments to this Work Letter or the Lease. Tenant shall not be obligated to respond to or act upon any such item until such item has been initialed or signed (as applicable) by the appropriate Landlord's Authorized Representative. Landlord may change either Landlord's Authorized Representative upon one (1) business day's prior written notice to Tenant.

(b) Tenant shall designate, as soon as practicable, an individual ("Tenant's Authorized Representative") as the person authorized to initial and sign all plans, drawings, change orders and approvals pursuant to this Work Letter. Landlord shall not be obligated to respond to or act upon any such item until such item has been initialed or signed (as applicable) by Tenant's Authorized Representative. Tenant may change Tenant's Authorized Representative upon one (1) business day's prior written notice to Landlord.

1.2. Schedule. The schedule for design and development of the Tenant Improvements, including the time periods for preparation and review of construction documents, approvals and performance, shall be in accordance with a schedule to be prepared by Tenant (the "Schedule"). Tenant shall prepare the Schedule so that it is a reasonable schedule for the completion of the Tenant Improvements. The Schedule shall clearly identify all activities requiring Landlord participation, including specific dates and time periods when Tenant's contractor will require access to areas of the project outside of the Premises. As soon as the Schedule is completed, Tenant shall deliver the same to Landlord for Landlord's approval, which approval shall not be unreasonably withheld, conditioned or delayed. Such Schedule shall be approved or disapproved by Landlord within ten (10) business days after delivery to Landlord. Landlord's failure to respond within such ten (10) business day period shall be deemed approval by Landlord. If Landlord disapproves the Schedule, then Landlord shall notify Tenant in writing of its objections to such Schedule, and the parties shall confer and negotiate in good faith to reach agreement on the Schedule. The Schedule shall be

subject to adjustment as mutually agreed upon in writing by the parties, or as provided in this Work Letter.

1.3. Tenant's Architects, Contractors and Consultants. The architect, engineering consultants, design team, general contractor and subcontractors responsible for the construction of the Tenant Improvements shall be selected by Tenant and approved by Landlord, which approval Landlord shall not unreasonably withhold, condition or delay. Landlord may refuse to use any architects, consultants, contractors, subcontractors or material suppliers that Landlord reasonably believes could cause labor disharmony or may not have sufficient experience, in Landlord's reasonable opinion, to perform work in an occupied Class "A" building. All Tenant contracts related to the Tenant Improvements shall provide that Tenant may assign such contracts and any warranties with respect to the Tenant Improvements to Landlord at any time.

2. Tenant Improvements. All Tenant Improvements shall be performed by Tenant's contractor, at Tenant's sole cost and expense (subject to Landlord's obligations with respect to any portion of the Extension TI Allowance) and in accordance with the Approved Plans (as defined below), the Lease and this Work Letter. To the extent that the total projected cost of the Tenant Improvements (subject to reasonable review and approval by Landlord) exceeds the Extension TI Allowance (such excess, the "Excess TI Costs"), Tenant shall pay the costs of the Tenant Improvements on a pari passu basis with Landlord as such costs become due, in the proportion of Excess TI Costs payable by Tenant to the Extension TI Allowance. If the cost of the Tenant Improvements (subject to reasonable review and approval by Landlord) increases over Landlord's initial projection, then Landlord may notify Tenant and Tenant shall pay any additional Excess TI Costs in the same way that Tenant paid the initial Excess TI Costs. If Tenant fails to pay, or is late in paying, any sum due to Landlord under this Work Letter, then Landlord shall have all of the rights and remedies set forth in the Lease for nonpayment of Annual Fixed Rent (including the right to interest and the right to assess a late charge), and for purposes of any litigation instituted with regard to such amounts the same shall be considered Annual Fixed Rent. All material and equipment furnished by Tenant or its contractors as the Tenant Improvements shall be new or "like new;" the Tenant Improvements shall be performed in a first-class, workmanlike manner; and the quality of the Tenant Improvements shall be of a nature and character not less than the building standard. Tenant shall take, and shall require its contractors to take, commercially reasonable steps to protect the Premises during the performance of any Tenant Improvements, including covering or temporarily removing any window coverings so as to guard against dust, debris or damage. All Tenant Improvements shall be performed in accordance with Article 4 (Alterations) of the Lease; provided that, notwithstanding anything in the Lease or this Work Letter to the contrary, in the event of a conflict between this Work Letter and the Lease, the terms of this Work Letter shall govern.

2.1. Work Plans. Tenant shall prepare and submit to Landlord for approval schematics covering the Tenant Improvements prepared in conformity with the applicable provisions of this Work Letter (the "Draft Schematic Plans"). The Draft Schematic Plans shall contain sufficient information and detail to accurately describe the proposed design to Landlord and such other information as Landlord may reasonably request. Landlord shall notify Tenant in writing within ten (10) business days after receipt of the Draft Schematic Plans whether Landlord approves or objects to the Draft Schematic Plans and of the manner, if any, in which the Draft Schematic Plans are unacceptable. Landlord's failure to respond within such ten (10) business day period shall be deemed approval by Landlord. If Landlord reasonably objects to the Draft Schematic Plans, then

Tenant shall revise the Draft Schematic Plans and cause Landlord's objections to be remedied in the revised Draft Schematic Plans. Tenant shall then resubmit the revised Draft Schematic Plans to Landlord for approval, such approval not to be unreasonably withheld, conditioned or delayed. Landlord's approval of or objection to revised Draft Schematic Plans and Tenant's correction of the same shall be in accordance with this Section until Landlord has approved the Draft Schematic Plans in writing or been deemed to have approved them. The iteration of the Draft Schematic Plans that is approved or deemed approved by Landlord without objection shall be referred to herein as the "Approved Schematic Plans."

2.2. Construction Plans. Tenant shall prepare final plans and specifications for the Tenant Improvements that (a) are consistent with and are logical evolutions of the Approved Schematic Plans and (b) incorporate any other Tenant-requested (and Landlord-approved) Changes (as defined below). As soon as such final plans and specifications ("Construction Plans") are completed, Tenant shall deliver the same to Landlord for Landlord's approval, which approval shall not be unreasonably withheld, conditioned or delayed. All such Construction Plans shall be submitted by Tenant to Landlord in electronic .pdf, CADD and full-size hard copy formats, and shall be approved or disapproved by Landlord within ten (10) business days after delivery to Landlord. Landlord's failure to respond within such ten (10) business day period shall be deemed approval by Landlord. If the Construction Plans are disapproved by Landlord, then Landlord shall notify Tenant in writing of its objections to such Construction Plans, and the parties shall confer and negotiate in good faith to reach agreement on the Construction Plans. Promptly after the Construction Plans are approved by Landlord and Tenant, two (2) copies of such Construction Plans shall be initialed and dated by Landlord and Tenant, and Tenant shall promptly submit such Construction Plans to all appropriate Governmental Authorities for approval. The Construction Plans so approved, and all change orders specifically permitted by this Work Letter, are referred to herein as the "Approved Plans."

2.3. Changes to the Tenant Improvements. Any changes to the Approved Plans (each, a "Change") shall be requested and instituted in accordance with the provisions of this Article 2 and shall be subject to the written approval of the non-requesting party in accordance with this Work Letter.

(a) Change Request. Either Landlord or Tenant may request Changes after Landlord approves the Approved Plans by notifying the other party thereof in writing in substantially the same form as the AIA standard change order form (a "Change Request"), which Change Request shall detail the nature and extent of any requested Changes, including (a) the Change, (b) the party required to perform the Change and (c) any modification of the Approved Plans and the Schedule, as applicable, necessitated by the Change. If the nature of a Change requires revisions to the Approved Plans, then the requesting party shall be solely responsible for the cost and expense of such revisions and any increases in the cost of the Tenant Improvements as a result of such Change. Change Requests shall be signed by the requesting party's Authorized Representative.

(b) Approval of Changes. All Change Requests shall be subject to the other party's prior written approval, which approval shall not be unreasonably withheld, conditioned or delayed. The non-requesting party shall have five (5) business days after receipt of a Change Request to notify the requesting party in writing of the non-requesting party's decision either to

approve or object to the Change Request. The non-requesting party's failure to respond within such five (5) business day period shall be deemed approval by the non-requesting party.

2.4. Preparation of Estimates. Tenant shall, before proceeding with any Change, using its best efforts, prepare as soon as is reasonably practicable (but in no event more than five (5) business days after delivering a Change Request to Landlord or receipt of a Change Request) an estimate of the increased costs or savings that would result from such Change, as well as an estimate of such Change's effects on the Schedule. Landlord shall have five (5) business days after receipt of such information from Tenant to (a) in the case of a Tenant-initiated Change Request, approve or reject such Change Request in writing, or (b) in the case of a Landlord-initiated Change Request, notify Tenant in writing of Landlord's decision either to proceed with or abandon the Landlord-initiated Change Request.

2.5. Quality Control Program; Coordination. Tenant shall provide Landlord with information regarding the following (together, the "QCP"): (a) Tenant's general contractor's quality control program and (b) evidence of subsequent monitoring and action plans. The QCP shall be subject to Landlord's reasonable review and approval and shall specifically address the Tenant Improvements. Tenant shall ensure that the QCP is regularly implemented on a scheduled basis and shall provide Landlord with reasonable prior notice and access to attend all inspections and meetings between Tenant and its general contractor. At the conclusion of the Tenant Improvements, Tenant shall deliver the quality control log to Landlord, which shall include all records of quality control meetings and testing and of inspections held in the field, including inspections relating to concrete, steel roofing, piping pressure testing and system commissioning.

3. Completion of Tenant Improvements. Tenant, at its sole cost and expense (except for the Extension TI Allowance), shall perform and complete the Tenant Improvements in all respects (a) in substantial conformance with the Approved Plans, (b) otherwise in compliance with provisions of the Lease and this Work Letter and (c) in accordance with applicable laws, the requirements of Tenant's insurance carriers, the requirements of Landlord's insurance carriers (to the extent Landlord provides its insurance carriers' requirements to Tenant) and the board of fire underwriters having jurisdiction over the Premises. The Tenant Improvements shall be deemed completed at such time as Tenant shall furnish to Landlord (t) evidence satisfactory to Landlord that (i) all Tenant Improvements have been completed and paid for in full (which shall be evidenced by the architect's certificate of completion and the general contractor's and each subcontractor's and material supplier's final unconditional waivers and releases of liens, each in a form acceptable to Landlord and complying with applicable laws, and a Certificate of Substantial Completion in the form of the American Institute of Architects document G704, executed by the project architect and the general contractor, together with a statutory notice of substantial completion from the general contractor), (ii) all Tenant Improvements have been accepted by Landlord, (iii) any and all liens related to the Tenant Improvements have either been discharged of record (by payment, bond, order of a court of competent jurisdiction or otherwise) or waived by the party filing such lien and (iv) no security interests relating to the Tenant Improvements are outstanding, (u) all certifications and approvals with respect to the Tenant Improvements that may be required from any governmental authority and any board of fire underwriters or similar body for the use and occupancy of the Premises (including a certificate of occupancy (or its substantial equivalent) for the Premises for the Permitted Use), (v) certificates of insurance required by the Lease to be purchased and maintained by Tenant, (w) an affidavit from Tenant's architect certifying that all work performed in, on or about the

Premises is in accordance with the Approved Plans, (x) complete "as built" drawing print sets, project specifications and shop drawings and electronic CADD files on disc (showing the Tenant Improvements as an overlay on the Building "as built" plans (provided that Landlord provides the Building "as-built" plans provided to Tenant) of all contract documents for work performed by their architect and engineers in relation to the Tenant Improvements, (y) a commissioning report prepared by a licensed, qualified commissioning agent hired by Tenant and approved by Landlord for all new or affected mechanical, electrical and plumbing systems (which report Landlord may hire a licensed, qualified commissioning agent to peer review, and whose reasonable recommendations Tenant's commissioning agent shall perform and incorporate into a revised report) and (z) such other "close out" materials as Landlord reasonably requests consistent with Landlord's own requirements for its contractors, such as copies of manufacturers' warranties, operation and maintenance manuals and the like.

4. Insurance.

4.1. Property Insurance. At all times during the period beginning with commencement of construction of the Tenant Improvements and ending with final completion of the Tenant Improvements, Tenant shall maintain, or cause to be maintained (in addition to the insurance required of Tenant pursuant to the Lease), property insurance for the project and including the Landlord, BioMed Realty, L.P., Massachusetts Institute of Technology and their respective officers, employees, directors, representatives, agents, general partners, members, subsidiaries, affiliates, lenders, mortgagees, ground lessors and beneficiaries (collectively with Landlord, the "Landlord Parties"), as a Loss Payee as their interests may appear. Such policy shall, on a completed replacement cost basis for the full insurable value at all times, insure against loss or damage by fire, vandalism and malicious mischief and other such risks as are customarily covered by the so-called "broad form extended coverage endorsement" upon all Tenant Improvements and the general contractor's and any subcontractors' machinery, tools and equipment, all while each forms a part of, or is contained in, the Tenant Improvements or any temporary structures on the Premises, or is adjacent thereto; provided that, for the avoidance of doubt, insurance coverage with respect to the general contractor's and any subcontractors' machinery, tools and equipment shall be carried on a primary basis by such general contractor or the applicable subcontractor(s). Tenant agrees to pay any deductible, and Landlord is not responsible for any deductible, for a claim under such insurance.

4.2. Other Insurance. During all construction by Tenant at the Premises, insurance required in Exhibit A-1 (as attached to the Second Amendment) must be in place.

4.3. Waivers of Subrogation. Any insurance provided pursuant to this Article shall waive subrogation against the Landlord Parties and Tenant shall hold harmless and indemnify the Landlord Parties for any loss or expense incurred as a result of a failure to obtain such waivers of subrogation from insurers.

5. Liability. Tenant assumes sole responsibility and liability for any and all injuries or the death of any persons, including Tenant's contractors and subcontractors and their respective employees, agents and invitees, and for any and all damages to property arising from any act or omission on the part of Tenant, Tenant's contractors or subcontractors, or their respective employees, agents and invitees in the prosecution of the Tenant Improvements. Tenant agrees to indemnify the Landlord and its affiliates, employees, agents and contractors, and any lender,

mortgagee, ground lessor or beneficiary, from and against all claims due to, because of or arising from any and all such injuries, death or damage, whether real or alleged, and Tenant and Tenant's contractors and subcontractors shall assume and defend at their sole cost and expense all such claims; provided, however, that nothing contained in this Work Letter shall be deemed to indemnify Landlord from or against liability to the extent arising directly from Landlord's negligence or willful misconduct. Any deficiency in design or construction of the Tenant Improvements shall be solely the responsibility of Tenant, notwithstanding the fact that Landlord may have approved of the same in writing.

6. Extension TI Allowance.

6.1. Approval of Budget for the Tenant Improvements. Notwithstanding anything to the contrary set forth elsewhere in this Work Letter or the Lease, Landlord shall not have any obligation to expend any portion of the Extension TI Allowance until Landlord and Tenant shall have approved in writing the budget for the Tenant Improvements (the "Approved Budget"). Prior to Landlord's approval of the Approved Budget, Tenant shall pay all of the costs and expenses incurred in connection with the Tenant Improvements as they become due. Landlord shall not be obligated to reimburse Tenant for costs or expenses relating to the Tenant Improvements that exceed the amount of the Extension TI Allowance. Landlord shall not unreasonably withhold, condition or delay its approval of any budget for Tenant Improvements that is proposed by Tenant.

6.2. Fund Requests. Upon submission by Tenant to Landlord as of or prior to the Extension TI Deadline of (a) a statement (a "Fund Request") setting forth the total amount of the TI Allowance requested, (b) a summary of the Tenant Improvements performed using AIA standard form Application for Payment (G 702) executed by the general contractor and by the architect, (c) invoices from the general contractor, the architect, and any subcontractors, material suppliers and other parties requesting payment with respect to the amount of the TI Allowance then being requested, and (d) except with respect to the final Fund Request, conditional lien releases from the general contractor and each subcontractor and material supplier with respect to the Tenant Improvements performed that correspond to the Fund Request each in a form acceptable to Landlord and complying with applicable laws, then Landlord shall, within thirty (30) days following receipt by Landlord of a Fund Request and the accompanying materials required by this Section, pay to (as elected by Landlord) the applicable contractors, subcontractors and material suppliers or Tenant (for reimbursement for payments made by Tenant to such contractors, subcontractors or material suppliers either prior to Landlord's approval of the Approved Budget or as a result of Tenant's decision to pay for the Tenant Improvements itself and later seek reimbursement from Landlord in the form of one lump sum payment in accordance with the Lease and this Work Letter), the amount of Tenant Improvement costs set forth in such Fund Request or Landlord's pari passu share thereof if Excess TI Costs exist based on the Approved Budget; provided, however, that Landlord shall not be obligated to make any payments under this Section until the budget for the Tenant Improvements is approved in accordance with Section 6.1. Notwithstanding anything in this Section to the contrary, Tenant shall not submit a Fund Request after the TI Deadline or more often than every thirty (30) days. Any additional Fund Requests submitted by Tenant after the TI Deadline or more often than every thirty (30) days shall be void and of no force or effect.

6.3. Accrual Information. In addition to the other requirements of this Section 6, Tenant shall, no later than the second (2nd) business day of each quarter until the Tenant Improvements are

complete, provide Landlord with an estimate of (a) the percentage of design and other soft cost work that has been completed, (b) design and other soft costs spent through the end of the previous month, both from commencement of the Tenant Improvements and solely for the previous month, (c) the percentage of construction and other hard cost work that has been completed, (d) construction and other hard costs spent through the end of the previous month, both from commencement of the Tenant Improvements and solely for the previous month, and (e) the date of Substantial Completion of the Tenant Improvements.

[REMAINDER OF THIS PAGE INTENTIONALLY LEFT BLANK]

IN WITNESS WHEREOF, Landlord and Tenant have executed this Work Letter to be effective on the date first above written.

LANDLORD:

BRE-BMR 38 SIDNEY LLC,
a Delaware limited liability company

By: /s/ Colleen O'Connor
Name: Coleen O'Connor
Title: VP, Leasing, East Coast & UK Markets

TENANT:

BLUEPRINT MEDICINES CORPORATION,
a Delaware corporation

By: /s/ Michael Landsittel
Name: Michael Landsittel
Title: CFO

CERTAIN CONFIDENTIAL INFORMATION CONTAINED IN THIS DOCUMENT, MARKED BY [***], HAS BEEN OMITTED BECAUSE IT IS BOTH (I) NOT MATERIAL AND (II) IS THE TYPE THAT THE REGISTRANT TREATS AS PRIVATE OR CONFIDENTIAL

Confidential
Execution Version

LICENSE AND COLLABORATION AGREEMENT

by and between

Blueprint Medicines Corporation

and

Zai Lab (Shanghai) Co., Ltd

Dated as of November 8, 2021

TABLE OF CONTENTS

Schedules

LICENSE AND COLLABORATION AGREEMENT

This LICENSE AND COLLABORATION AGREEMENT (this "**Agreement**") is made as of November 8, 2021 (the "**Effective Date**") by and between Blueprint Medicines Corporation, a Delaware corporation ("**Blueprint**"), having a place of business at 45 Sidney Street, Cambridge MA 02139, USA, and Zai Lab (Shanghai) Co., Ltd, an exempted company organized and existing under the laws of P.R. of China ("**Zai**"), having a place of business at 4F, Bldg 1, Jinchuang Plaza, 4560 Jinke Rd, Shanghai, China, 201210. Blueprint and Zai are referred to in this Agreement individually as a "**Party**" and collectively as the "**Parties**."

RECITALS

WHEREAS, Blueprint is a biopharmaceutical company that is developing (a) a mutant EGFR inhibitor known as BLU-701, and (b) a mutant EGFR inhibitor known as BLU-945, in each case, that are being studied by Blueprint for the treatment of NSCLC and other cancers with certain mutations;

WHEREAS, Blueprint Controls certain Know-How and Patent Rights relating to BLU-945 and BLU-701;

WHEREAS, Zai is a biopharmaceutical company engaged in the research, development, and commercialization of pharmaceutical and biologic products in the Territory;

WHEREAS, Zai wishes to obtain from Blueprint an exclusive license to develop, perform medical affairs for, manufacture (subject to the terms in the Agreement) and commercialize, the Blueprint Compounds and Licensed Products, in each case, in the Territory, and Blueprint is willing to grant such a license to Zai, all in accordance with the terms and conditions set forth herein; and

WHEREAS, Blueprint and Zai both recognize the importance of accelerating Global Clinical Trials to address patient needs and Zai is willing to commit to participation in certain Clinical Trials as agreed to by both Parties for each Licensed Product.

AGREEMENT

NOW, **THEREFORE**, the Parties hereby agree as follows:

Article 1
DEFINITIONS

Unless specifically set forth to the contrary herein, the following terms will have the respective meanings set forth below, whether used in the singular or plural:

1.1 "**Accounting Standards**" means GAAP for both Parties, unless a Party elects to change its general accounting principles to IFRS (or any change thereafter between IFRS and GAAP) and provides notice to the other Party of such change in accordance with Section 10.7 (Accounting Standards).

1.2 "**Acquiree**" has the meaning set forth in Section 2.8.3(b).

1.3 "**Acquiror**" has the meaning set forth in Section 2.8.3(a).

1.4 "**Active Ingredient**" means those clinically active materials that provide pharmacological activity in a pharmaceutical or biologic product (excluding [****]).

1.5 "**Affiliate**" means, with respect to a Person, any other Person that controls, is controlled by, or is under common control with such Person. For the purpose of this definition only, "control" (including, with correlative meaning, the terms "controlled by" and "under the common control") means the actual power, either directly or indirectly through one or more intermediaries, to direct or cause the direction of the management and policies of any Person, whether by the ownership of more than 50% of the voting security of such Person, by contract, or otherwise.

1.6 "**Agreement**" has the meaning set forth in the Preamble.

1.7 "**Alliance Manager**" has the meaning set forth in Section 3.1 (Alliance Managers).

1.8 "**Anti-Corruption Laws**" has the meaning set forth in Section 12.1.5 (Representations and Warranties of Each Party).

1.9 "**Applicable Law**" means collectively all laws, rules, regulations, ordinances, decrees, judicial and administrative orders (and any license, franchise, permit, or similar right granted under any of the foregoing), and any policies and other requirements of any applicable Governmental Authority that govern or otherwise apply to a Party, including all Anti-Corruption Laws.

1.10 "**Approved Labeling**" means, with respect to a Licensed Product: (a) the Regulatory Authority-approved full prescribing information for such Licensed Product; and (b) the Regulatory Authority-approved labels and other written, printed, or graphic materials on any container, wrapper, or any package insert that is used with or for such Licensed Product.

1.11 "**Arbitration Notice**" has the meaning set forth in Section 16.3.1 (Rules).

1.12 "**Arbitrators**" has the meaning set forth in Section 16.3.2 (Selection of Arbitrator).

1.13 "**Assigned Collaboration Know-How**" means any Collaboration Know-How that [****].

1.14 "**Assigned Collaboration Patent Rights**" means all Collaboration Patent Rights that Cover Assigned Collaboration Know-How.

1.15 "**Assigned Collaboration Technology**" means the Assigned Collaboration Know-How and the Assigned Collaboration Patent Rights.

1.16 "**Average Patient Cost**" means with respect to additional patients enrolled in a Global Clinical Trial for a Licensed Product by a Party [****].

1.17 "**BLU-701**" means (a) Blueprint's mutant [****] EGFR inhibitor known as "BLU-701"; (b) its named back-up forms [****] and any other backup form that Blueprint identifies and designates after the Effective Date as a back-up form for BLU-701 in accordance with Blueprint's then-current business practices; (c) prodrugs that convert to the compounds in (a) and (b); (d) stereoisomers and isotopic variants of the compounds in (a), (b), and (c); (e) [****]; (f) salt forms of the compounds in (a) through (e); and (g) solvates, hydrates, and solid forms (including crystalline, polymorphic, amorphous and co-crystalline forms) of the compounds in (a) through (f).

1.18 [****]

1.19 "**BLU-945**" means (a) Blueprint's mutant [****] EGFR inhibitor known as "BLU-945"; (b) its named back-up forms [****] and any other backup form that Blueprint identifies and designates after the Effective Date as a back-up form for BLU-945 in accordance with Blueprint's then-current business practices; (c) prodrugs that convert to the compounds in (a) and (b); (d) stereoisomers and isotopic variants of the compounds in (a), (b), and (c); (e) [****]; (f) salt forms of the compounds in (a) through (e); and (g) solvates, hydrates, and solid forms (including crystalline, polymorphic, amorphous and co-crystalline forms) of the compounds in (a) through (f).

1.20 [****]

1.21 "**Blueprint**" has the meaning set forth in the Preamble.

1.22 "**Blueprint Collaboration Know-How**" means Collaboration Know-How, other than Blueprint/Zai Combination Know-How, developed or invented solely by Blueprint's or its Affiliates', licensees', Sublicensees', or Subcontractors' employees, agents, or independent contractors, or any Persons that are contractually required to assign or license such Collaboration Know-How (or Patent Rights Covering such Know-How) to Blueprint or any Affiliate of Blueprint, in each case, in the performance of activities under this Agreement during the Term.

1.23 "**Blueprint Collaboration Patent Rights**" means all Collaboration Patent Rights that Cover Blueprint Collaboration Know-How.

1.24 "**Blueprint Compound**" means BLU-701 or BLU-945 and includes [****].

1.25 "**Blueprint Identified Rights**" has the meaning set forth in Section 2.6.1 (Blueprint Identified Rights).

1.26 "**Blueprint Indemnitee(s)**" has the meaning set forth in Section 13.1 (By Zai).

1.27 "**Blueprint In-Licensed Rights**" has the meaning set forth in Section 2.6.3 (Third Party IP Agreements).

1.28 "**Blueprint Know-How**" means, subject to Section 2.6.5 (Right to Decline Blueprint In-Licensed Rights), all Know-How (excluding Blueprint's interest in the Blueprint/Zai Combination Know-How and other Joint Collaboration Know-How) that is (a) Controlled by Blueprint or any of its Affiliates as of the Effective Date or during the Term, and (b) necessary or reasonably useful to Develop, perform Medical Affairs for, or Commercialize a Blueprint Compound or a Licensed Product in the Territory, including all Assigned Collaboration Know-How and Blueprint Collaboration Know-How, but expressly excluding Blueprint Manufacturing Know-How.

1.29 "**Blueprint Manufacturing Know-How**" means all Know-How Controlled by Blueprint or any of its Affiliates as of the Effective Date or during the Term that is actually used for the Manufacture of each Licensed Product in the Field in the Territory.

1.30 "**Blueprint Manufacturing Patent Rights**" means all Patent Rights Controlled by Blueprint or any of its Affiliates as of the Effective Date or during the Term that are actually practiced for the Manufacture of each Licensed Product in the Field in the Territory.

1.31 "**Blueprint Manufacturing Technology**" means the Blueprint Manufacturing Know-How and the Blueprint Manufacturing Patent Rights.

1.32 "**Blueprint Patent Rights**" means, subject to Section 2.6.5 (Right to Decline Blueprint In-Licensed Rights), all Patent Rights (excluding Blueprint's interest in the Blueprint/Zai Combination Patent Rights and other Joint Collaboration Patent Rights) that are (a) Controlled by Blueprint or any of its Affiliates as of the Effective Date or during the Term, and (b) necessary or reasonably useful (or, with respect to patent applications, would be necessary or reasonably useful if such patent applications were to issue as patents) to Develop, perform Medical Affairs for, or Commercialize a Blueprint Compound or a Licensed Product in the Territory, including all Assigned Collaboration Patent Rights and Blueprint Collaboration Patent Rights, but expressly excluding Blueprint Manufacturing Patent Rights. **Schedule 1.32** (Blueprint Patent Rights) includes the Blueprint Patent Rights that are owned or exclusively licensed by Blueprint in the Territory and that exist as of the Effective Date.

1.33 "**Blueprint Publication**" has the meaning set forth in Section 11.5.1.

1.34 "**Blueprint Specifications**" has the meaning set forth in Section 7.2.3 (Specifications).

1.35 "**Blueprint Technology**" means Blueprint Know-How, Blueprint Patent Rights, and Blueprint's interest in the Joint Collaboration Technology.

1.36 "**Blueprint/Zai Combination**" means any Combination Product or Combination Regimen that includes a Blueprint Compound together with any Zai Product.

1.37 "**Blueprint/Zai Combination Know-How**" means any Collaboration Know-How that (a) [****] relates to any Blueprint/Zai Combination (and not to any Zai Product alone or any other Licensed Product that is not a Blueprint/Zai Combination), including any composition, method of use or method of Manufacturing, in each case, that is specific to a Blueprint/Zai Combination (including any composition, method of use, or method of Manufacturing that is [****]), or any Companion Diagnostic [****] for use with a Blueprint/Zai Combination, and (b) is developed or invented during the Term by a Party's or its Affiliates', licensees', Sublicensees', or Sublicensees' employees, agents, or independent contractors, or any Persons that are contractually required to assign or license such Know-How (or Patent Rights Covering such Know-How) to a Party or any Affiliate of a Party, either alone or jointly with the other Party's or its Affiliates', licensees', Sublicensees', Subcontractors' employees, agents, or independent contractors, or any Persons that are contractually required to assign or license such Know-How (or Patent Rights Covering such Know-How) to the other Party or any Affiliate of the other Party, in each case, in the performance of activities under this Agreement during the Term.

1.38 "**Blueprint/Zai Combination Patent Rights**" means all Collaboration Patent Rights that Cover Blueprint/Zai Combination Know-How. For clarity, Blueprint/Zai Combination Patent Rights do not include any Patent Rights that Cover (a) a Zai Product alone or (b) any other Licensed Product that is not a Blueprint/Zai Combination or a Companion Diagnostic that is for use with a Zai Product alone or any other Licensed Product that is not a Blueprint/Zai Combination.

1.39 "**Blueprint/Zai Combination Technology**" means the Blueprint/Zai Combination Know-How and the Blueprint/Zai Combination Patent Rights.

1.40 "**Breach Notification**" has the meaning set forth in Section 15.2.2(a) (Notice and Cure Period).

1.41 "**Business Day**" means a day other than a Saturday, Sunday, or a day on which banking institutions in Cambridge, Massachusetts or Shanghai, China are required by Applicable Law to remain closed.

1.42 "**Buyers**" has the meaning set forth in Section 1.136 (Net Sales).

1.43 "**Calendar Quarter**" means the respective periods of three consecutive calendar months ending on March 31, June 30, September 30, and December 31.

1.44 "**Calendar Year**" means each 12-month period commencing on January 1.

1.45 "**cGMP**" means all applicable current Good Manufacturing Practices, including, as applicable, (a) the principles detailed in the U.S. Current Good Manufacturing Practices, 21 C.F.R. Parts 4, 210, 211, 601, 610 and 820, (b) European Directive 2003/94/EC and Eudralex 4, (c) the principles detailed in the International Conference on Harmonization's Q7 guidelines, and (d) the equivalent Applicable Law in any relevant country or region, each as may be amended and applicable from time to time.

1.46 "**Change of Control**" means, with respect to a Party, that: (a) any Third Party acquires directly or indirectly the beneficial ownership of any voting security of such Party, or if the percentage ownership of such Third Party in the voting securities of such Party is increased through stock redemption, cancellation, or other recapitalization, and immediately after such acquisition or increase such Third Party is, directly or indirectly, the beneficial owner of voting securities representing at least 50% of the total voting power of all of the then outstanding voting securities of such Party; (b) a merger, consolidation, recapitalization, or reorganization of such Party is consummated that would result in shareholders or equity holders of such Party that owned less than 50% of the outstanding voting securities of such Party immediately prior to such transaction, owning at least 50% of the outstanding voting securities of the surviving entity (or its parent entity) immediately following such transaction; or (c) there is a sale or transfer to a Third Party of all or substantially all of such Party's consolidated assets taken as a whole, through one or more related transactions.

1.47 "**Clinical Development**" means, with respect to a pharmaceutical or biologic product, Development activities conducted from and after (and including) the filing of an IND for such pharmaceutical or biologic product specifically in connection with (a) Clinical Trials and (b) regulatory activities related to Clinical Trials, including filing of MAAs and obtaining, supporting, or maintaining Regulatory Approvals for such pharmaceutical or biologic product following completion of a Pivotal Trial for such pharmaceutical or biologic product.

1.48 "**Clinical Supply Agreement**" has the meaning set forth in Section 7.1.1 (Development Supply).

1.49 "**Clinical Trial**" means any clinical trial in humans that is conducted in accordance with GCP and is designed to generate data in support or maintenance of an IND or MAA, or other similar marketing application, including any Phase I Clinical Trial, Phase II Clinical Trial, Phase III Clinical Trial, or any post-approval clinical trial in humans.

1.50 "**CMO**" means a contract manufacturing organization.

1.51 "**Collaboration Know-How**" means any Know-How developed or invented during the Term by a Party's or its Affiliates', licensees', Sublicensees', or Subcontractors' employees, agents, or independent contractors, or any Persons that are contractually required to assign or license such Know-How to a Party or any Affiliate of a Party, either alone or jointly with the other Party's or its Affiliates', licensees', Sublicensees', or Subcontractors' employees, agents, or independent contractors, or any Persons that are contractually required to assign or license such Know-How (or

patent Rights Covering such Know-How) to the other Party or any Affiliate of the other Party, in each case, in the performance of activities under this Agreement during the Term.

1.52 "**Collaboration Patent Rights**" means any Patent Rights that (a) (i) claim any Invention included in the Collaboration Know-How or (ii) disclose any Collaboration Know-How and (b) have a priority date that is after the Effective Date.

1.53 "**Collaboration Technology**" means Collaboration Know-How and Collaboration Patent Rights.

1.54 "**Combination Product**" means a Licensed Product that includes (a) BLU-701 or BLU-945, or both, on the one hand; and (b) another Active Ingredient, on the other hand, sold for a single price.

1.55 "**Combination Regimen**" means any product or treatment regimen that comprises, or is a combination of (a) a Licensed Product containing a Blueprint Compound, and (b) any other product containing an Active Ingredient other than such Blueprint Compound, where (a) and (b) are labeled for use together either simultaneously or in a separate or sequential administration, whether or not sold for a single price.

1.56 "**Commercial Supply Agreement**" has the meaning set forth in Section 7.1.2 (Commercial Supply).

1.57 "**Commercialization**" means any and all activities directed to the marketing, promotion, distribution, pricing, reimbursement, offering for sale, and sale of a pharmaceutical or biologic product and interacting with Regulatory Authorities following receipt of Regulatory Approval in the applicable country or region for such pharmaceutical or biologic product regarding the foregoing, including seeking and maintaining any required Reimbursement Approval, but excluding activities directed to Manufacturing, Development, or Medical Affairs. "**Commercialize**," "**Commercializing**," and "**Commercialized**" will be construed accordingly.

1.58 "**Commercialization Plan**" means, with respect to a Licensed Product, the written [****] strategic and tactical plans for the Commercialization activities for such Licensed Product to be conducted in the Territory that will be prepared and updated by Zai as provided in Section 9.2 (Commercialization Plans).

1.59 "**Commercially Reasonable Efforts**" means, with respect to the Exploitation of a Blueprint Compound or a Licensed Product by a Party, those efforts and resources, including reasonably necessary personnel, equivalent to the efforts that a reasonable international biopharmaceutical company or a pharmaceutical company[****] based on conditions then prevailing and taking into account all relevant factors [****]. Commercially Reasonable Efforts requires, with respect to an obligation, that the Party: (a) promptly assign responsibility for such obligation to specific employees who are held accountable for progress and monitor such progress on an on-going basis, (b) set and seek to achieve specific and meaningful objectives for carrying out such obligation, and (c) make and implement decisions and allocate resources designed to advance progress with respect to such objectives. [****]

1.60 [****]

1.61 "**Companion Diagnostics**" has the meaning set forth in Section 5.18 (Development of Companion Diagnostics).

1.62 "**Competitive Activities**" has the meaning set forth in Section 2.8.1 (Exclusivity Covenant).

1.63 "**Competitive Product**" means [****] other than a Licensed Product, that [****].

1.64 "**Confidential Information**" means (a) Know-How and any technical, scientific, trade, research, manufacturing, business, financial, marketing, product, supplier, intellectual property, and other non-public or proprietary data or information (including unpublished patent applications) that may be disclosed by one Party or its Affiliates to the other Party or its Affiliates pursuant to this Agreement (including information disclosed prior to the Effective Date pursuant to the Confidentiality Agreement), regardless of whether such information is specifically marked or designated as confidential and regardless of whether such information is in written, oral, electronic, or other form, and (b) the terms of this Agreement. Information of a Disclosing Party will not be Confidential Information of such Disclosing Party to the extent that the Receiving Party can demonstrate through competent evidence that such information:

(a) is known by the Receiving Party or any of its Affiliates without an obligation of confidentiality at the time of its receipt from the Disclosing Party, and not through a prior disclosure by or on behalf of the Disclosing Party, as documented by the Receiving Party's business records;

(b) is generally available to the public before its receipt from the Disclosing Party;

(c) became generally available to the public or otherwise part of the public domain after its disclosure by the Disclosing Party and other than through any act or omission of the Receiving Party or any of its Affiliates or discloses in breach of this Agreement;

(d) is subsequently disclosed to the Receiving Party or any of its Affiliates without obligation of confidentiality by a Third Party who may rightfully do so and is not under a conflicting obligation of confidentiality to the Disclosing Party; or

(e) is developed by the Receiving Party or any of its Affiliates independently and without use of or reference to any Confidential Information received from the Disclosing Party, as documented by the Receiving Party's business records.

No combination of features or disclosures will be deemed to fall within the foregoing exclusions merely because individual features are published or available to the general public or in the rightful possession of the Receiving Party unless the combination itself and principle of operation are published or available to the general public or in the rightful possession of the Receiving Party.

1.65 "**Confidentiality Agreement**" means the Confidential Disclosure Agreement dated [****] by and between the Parties.

1.66 "**Continuing Know-How Transfer**" has the meaning set forth in Section 4.3 (Continuing Know-How Transfer).

1.67 "**Control**" or "**Controlled**" means the possession by a Party (whether by ownership, license, or otherwise other than pursuant to this Agreement) of, (a) with respect to any tangible Know-How, the legal authority or right to physical possession of such tangible Know-How, with the right to provide such tangible Know-How to the other Party on the terms set forth herein, or (b) with respect to Patent Rights, Regulatory Approvals, Regulatory Submissions, intangible Know-How, or other intellectual property rights, the legal authority or right to grant a license, sublicense, access, or right to reference or use (as applicable) to the other Party under such Patent Rights, Regulatory Approvals, Regulatory Submissions, intangible Know-How, or other intellectual property rights on

the terms set forth herein, in each case ((a) and (b)), without breaching or otherwise violating the terms of any arrangement or agreement with a Third Party in existence as of the time such Party or its Affiliates would first be required hereunder to grant the other Party such access, right to use, licenses, or sublicense and without being required to make any payment to any Third Party other than payment obligations related to Blueprint In-Licensed Rights or Zai In-Licensed Rights acquired or licensed in accordance with Section 2.6 (Third Party In-Licenses) under which the other Party elects to take a sublicense and agrees to reimburse the contracting Party as set forth in Section 2.6 (Third Party In-Licenses). Notwithstanding the foregoing, a Party and its Affiliates will not be deemed to "Control" any Patent Right or Know-How that, prior to the consummation of a Change of Control of such Party, is owned or in-licensed by a Third Party that becomes an Affiliate of such acquired Party after the Effective Date as a result of such Change of Control unless (i) prior to the consummation of such Change of Control, such acquired Party or any of its Affiliates also Controlled such Patent Right or Know-How, or (ii) after the consummation of such Change of Control, such acquired Party or any of its Affiliates determines to use or uses any such Patent Rights or Know-How in the performance of its obligations or exercise of its rights under this Agreement, in each of which cases ((i) and (ii)), such Patent Rights or Know-How will be "Controlled" by such Party for purposes of this Agreement.

1.68 "**Controlling Party**" has the meaning set forth in Section 14.3.2(a)(ii) (Enforcement Rights; Zai First Right).

1.69 "**Cover**" means, with respect to a particular subject matter at issue and a relevant Patent Right, that the manufacture, use, sale, offer for sale, or importation of such subject matter would fall within the scope of a claim in such Patent Right.

1.70 [****]

1.71 "**CRO**" means a contract research organization.

1.72 "**Data Breach**" has the meaning set forth in Section 12.5.2.

1.73 "**Debarred/Excluded**" means any Person becoming debarred or suspended under 21 U.S.C. §335(a) or (b), the subject of a conviction described in Section 306 of the FD&C Act, excluded, or having previously been excluded, from a federal or governmental health care program, debarred from federal contracting, convicted of or pled *nolo contendere* to any felony, or to any federal or state legal violation (including misdemeanors) relating to prescription drug products or fraud, the subject to OFAC sanctions or on the OFAC list of specially designated nationals, or the subject of any similar sanction of any Governmental Authority in the Territory.

1.74 "**Deficient Site**" has the meaning set forth in Section 5.14.2 (Deficient Sublicensees or Sites and Replacement).

1.75 "**Development**" means all internal and external research, development, and regulatory activities related to pharmaceutical or biologic products, including (a) research, non-clinical testing, toxicology, testing and studies, non-clinical and preclinical activities, and Clinical Trials, (b) preparation, submission, review, and development of data or information (or reports relating thereto and analysis and review of such reports) for the purpose of reviewing the progress and status of the activities under subsection (a) or for the purposes of submission to a Regulatory Authority to obtain authorization to conduct Clinical Trials and to obtain, support, or maintain Regulatory Approval of a pharmaceutical or biologic product, but excluding activities directed to Manufacturing, Medical Affairs, or Commercialization, and (c) the design of future studies, non-

clinical and preclinical activities, and Clinical Trials. Development will include development and regulatory activities for additional forms, formulations, or indications for a pharmaceutical or biologic product after receipt of Regulatory Approval of such product (including label expansion), including Clinical Trials initiated following receipt of Regulatory Approval or any Clinical Trial to be conducted after receipt of Regulatory Approval that was mandated by the applicable Regulatory Authority as a condition of such Regulatory Approval with respect to an approved formulation or Indication (such as post-marketing studies, observational studies, implementation and management of registries and analysis thereof, in each case, if required by any Regulatory Authority in any region in the Territory to support or maintain Regulatory Approval for a pharmaceutical or biologic product in such region). "**Develop**," "**Developing**," and "**Developed**" will be construed accordingly.

1.76 "**Development Milestone Events**" has the meaning set forth in Section 10.2.1 (Development Milestone Events and Payments).

1.77 "**Development Milestone Payments**" has the meaning set forth in Section 10.2.1 (Development Milestone Events and Payments).

1.78 "**Development Subcontractor**" has the meaning set forth in Section 2.2.3 (Right to Subcontract).

1.79 "**Disclosing Party**" has the meaning set forth in Section 11.1.1 (Duty of Confidence).

1.80 "**Dispute**" has the meaning set forth in Section 16.1 (General).

1.81 "**Dollar**" means the U.S. dollar, and "$" will be interpreted accordingly.

1.82 "**Effective Date**" has the meaning set forth in the Preamble.

1.83 "**EGFR**" means epidermal growth factor receptor.

1.84 "**Examined Party**" has the meaning set forth in Section 10.11 (Financial Records and Audits).

1.85 "**Excess Enrollment Reimbursement**" has the meaning set forth in Section 5.2.3 (Enrollment of Additional Patients).

1.86 "**Executive Officers**" has the meaning set forth in Section 3.6.3 (Decisions of the JSC).

1.87 "**Exploit**" means to make, have made, use, offer to sell, sell, import, export, Develop, Manufacture, perform Medical Affairs activities, or Commercialize. "**Exploitation**" will be construed accordingly.

1.88 "**FD&C Act**" means the United States Federal Food, Drug and Cosmetic Act, as amended from time to time, together with any rules, regulations, and requirements promulgated thereunder (including all additions, supplements, extensions, and modifications thereto).

1.89 "**FDA**" means the United States Food and Drug Administration or any successor entity thereto having essentially the same function.

1.90 "**Field**" means the prevention, treatment, and diagnosis of any indications in humans.

1.91 "**First Commercial Sale**" means, with respect to any Licensed Product in any country or region, the first sale of such Licensed Product to a Third Party for distribution, use, or consumption in such

country or region after receiving all necessary Regulatory Approval and Reimbursement Approval (if required) to do so. First Commercial Sale excludes [****].

1.92 "**FTE**" means the equivalent of the work of one duly qualified employee of a Party full time for one year (consisting of a total of [****] per year) carrying out Development, Manufacturing, Medical Affairs activities, or other scientific or technical work under this Agreement. Overtime and work on weekends, holidays, and the like, in each case, will not be counted with any multiplier (*e.g.*, time-and-a-half or double time) toward the number of hours that are used to calculate the FTE contribution. The portion of an FTE billable by a Party for one individual during a given accounting period will be determined by dividing the number of hours worked directly by such individual on the work to be conducted under this Agreement during such accounting period and the number of FTE hours applicable for such accounting period based on [****] per Calendar Year.

1.93 "**FTE Rate**" means the amount for an FTE per Calendar Year, which for the Calendar Year ending on December 31, 2021 will be [****].

1.94 "**Fully Burdened Manufacturing Cost**" means, with respect to any Blueprint Compound, Licensed Product, or any Zai Product (or component thereof), in each case, supplied by or on behalf of the applicable Party to the other Party or its Affiliates hereunder:

(a) if and to the extent such Blueprint Compound, Licensed Product, or Zai Product (or any precursor or intermediate thereof), as applicable, is Manufactured by a Third Party manufacturer, (i) the actual Third Party costs of such Manufacturing incurred by the supplying Party, including the costs [****]; and

(b) if and to the extent such Blueprint Compound, Licensed Product, or Zai Product (or any precursor or intermediate thereof), as applicable, is Manufactured by a Party or its Affiliate, the actual, fully burdened costs [****], including the cost of [****] Such fully burdened costs will be calculated in accordance with applicable Accounting Standards, consistently applied.

1.95 "**GAAP**" means United States generally accepted accounting principles, consistently applied.

1.96 "**GCP**" means all applicable good clinical practice standards for the design, conduct, performance, monitoring, auditing, recording, analyses and reporting of Clinical Trials, including, as applicable (a) as set forth in the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use Harmonized Tripartite Guideline for Good Clinical Practice (CPMP/ICH/135/95) (the "**ICH Guidelines**") and any other guidelines for good clinical practice for trials on medicinal products in the Territory, (b) the Declaration of Helsinki (2004) as last amended at the 52nd World Medical Association in October 2000 and any further amendments or clarifications thereto, (c) U.S. Code of Federal Regulations Title 21, Parts 50 (Protection of Human Subjects), 56 (Institutional Review Boards), and 312 (Investigational New Drug Application), as may be amended from time to time, and (d) the equivalent Applicable Law in the region in the Territory, each as may be amended and applicable from time to time and in each case, that provide for, among other things, assurance that the clinical data and reported results are credible and accurate and protect the rights, integrity, and confidentiality of trial subjects.

1.97 [****]

1.98 "**Global Brand Elements**" has the meaning set forth in Section 14.9.1 (Global Brand Elements).

1.99 "**Global Brand Strategy**" has the meaning set forth in Section 9.2 (Commercialization Plan).

1.100 "**Global Clinical Trial**" means a Clinical Trial for a Licensed Product the data from which, at the time of commencement, is intended to be used to obtain Regulatory Approval both inside the Territory and in any of the following: [****].

1.101 "**Global Development Plan**" has the meaning set forth in Section 5.1 (Global Development Plan).

1.102 "**GLP**" means all applicable good laboratory practice standards, including, as applicable, as set forth in the then-current good laboratory practice standards promulgated or endorsed by the U.S. Food and Drug Administration, as defined in 21 C.F.R. Part 58, and the equivalent Applicable Law in the region in the Territory, each as may be amended and applicable from time to time.

1.103 "**Governmental Authority**" means any federal, national, state, provincial, or local government, or political subdivision thereof, or any multinational organization or any authority, agency, regulatory body, or commission entitled to exercise any administrative, executive, judicial, legislative, police, regulatory or taxing authority or power, or any court or tribunal (or any department, bureau or division of any of the foregoing, or any governmental arbitrator or arbitral body). Governmental Authorities include all Regulatory Authorities.

1.104 [****]

1.105 "**ICC**" has the meaning set forth in Section 16.3.1 (Rules).

1.106 "**ICH Guidelines**" has the meaning set forth in Section 1.96 (GCP).

1.107 "**IDL**" has the meaning set forth in Section 1.131 (Marketing Authorization Application or MAA).

1.108 "**IFRS**" means International Financial Reporting Standards, consistently applied.

1.109 "**IND**" means an Investigational New Drug application required pursuant to 21 C.F.R. Part 312 or any comparable filings outside of the U.S. required to commence human clinical trials in such country or region (such as an application for a Clinical Trial Authorization in the Territory), and all supplements or amendments that may be filed with respect to the foregoing.

1.110 "**Indemnified Party**" has the meaning set forth in Section 13.3 (Indemnification Procedure).

1.111 "**Indemnifying Party**" has the meaning set forth in Section 13.3 (Indemnification Procedure).

1.112 "**Indication**" means [****] that a Licensed Product is [****] in the indication section of the Approved Labeling for such Licensed Product, or that is the subject of a Clinical Trial and where it is [****]

1.113 "**Initial Know-How Transfer**" has the meaning set forth in Section 4.1 (Initial Know-How Transfer).

1.114 "**Invention**" means any process, method, composition, article of manufacture, discovery, or finding that is conceived or reduced to practice (whether or not patentable).

1.115 "**Joint Collaboration Know-How**" means (a) Blueprint/Zai Combination Know-How, and (b) other Collaboration Know-How, excluding any Assigned Collaboration Know-How, developed or invented jointly by a Party's or its Affiliates', licensees', Sublicensees', or Subcontractors'

employees, agents, or independent contractors, or any Persons that are contractually required to assign or license such Collaboration Know-How to such Party or any Affiliate of such Party, on the one hand, and the other Party's or its Affiliates', licensees', Sublicensees', or Subcontractors' employees, agents, or independent contractors, or any Persons that are contractually required to assign or license such Collaboration Know-How to such Party or any Affiliate of such Party, on the other hand, in the performance of activities under this Agreement during the Term.

1.116 "**Joint Collaboration Patent Rights**" means all Collaboration Patent Rights that Cover Joint Collaboration Know-How, including Blueprint/Zai Combination Patent Rights.

1.117 "**Joint Collaboration Technology**" means the Joint Collaboration Know-How and the Joint Collaboration Patent Rights.

1.118 "**JPT**" has the meaning set forth in Section 3.3 (Joint Project Teams).

1.119 "**JPT Chairperson**" has the meaning set forth in Section 3.3.1 (Formation; Composition; Meetings).

1.120 "**JSC**" has the meaning set forth in Section 3.2.1 (Formation).

1.121 "**JSC Chairperson**" has the meaning set forth in Section 3.2.1 (Formation).

1.122 "**Know-How**" means any information and materials, including records, discoveries, improvements, modifications, processes, techniques, methods, assays, chemical or biological materials, designs, protocols, formulas, data (including physical data, chemical data, toxicology data, animal data, raw data, clinical data, and analytical and quality control data), dosage regimens, control assays, product specifications, marketing, pricing and distribution costs, Inventions, algorithms, technology, forecasts, profiles, strategies, plans, results in any form whatsoever, know-how and trade secrets (in each case, whether or not patentable, copyrightable or otherwise).

1.123 "**Knowledge**" means [****] of (a) with respect to Blueprint, [****] and (b) with respect to Zai, [****].

1.124 "**Licensed Product**" means any product containing a Blueprint Compound as an Active Ingredient, in any form, formulation, dosage form, or method of delivery[****]. [****]

1.125 "**Listing Patents**" has the meaning set forth in Section 14.6 (Patent Listings).

1.126 "**Local Manufacturing Approval**" means receipt of all approvals and authorizations necessary for Zai or its Affiliate or their respective CMOs to Manufacture a particular Licensed Product in a particular region in the Territory (including after validation and qualification of Zai's or such Affiliate's or CMO's applicable facilities in the Territory).

1.127 "**Losses**" means damages, debts, obligations, and other liabilities, losses, claims, taxes, interest obligations, deficiencies, judgments, assessments, fines, fees, penalties, or expenses (including amounts paid in settlement, interest, court costs, costs of investigators, reasonable fees and expenses of attorneys, accountants, financial advisors, consultants, and other experts, and other expenses of litigation).

1.128 "**Manufacture**" means activities directed to manufacturing, processing, packaging, labeling, filling, finishing, assembly, shipping, storage, or freight of any pharmaceutical or biologic product (or any

components or process steps involving any product or any companion diagnostic), placebo, or comparator agent, as the case may be, including quality assurance and stability testing, characterization testing, quality control release testing of drug substance and drug product, quality assurance batch record review and release of product, process development, qualification, and validation, scale-up, pre-clinical, clinical, and commercial manufacture and analytic development, and product characterization, but excluding activities directed to Development, Commercialization, or Medical Affairs. "**Manufacturing**" and "**Manufactured**" will be construed accordingly.

1.129 "**Manufacturing Technology Transfer**" means the transfer of the Blueprint Manufacturing Know-How related to a Blueprint Compound and Licensed Products containing such Blueprint Compound in accordance with the Manufacturing Technology Transfer Plan for such Blueprint Compound, which includes the provision of any technical assistance to enable the Manufacture of such Licensed Products [****].

1.130 "**Manufacturing Technology Transfer Plan**" means, for each Blueprint Compound, the plan for the transfer to Zai and its designees of Blueprint Manufacturing Know-How for the Licensed Products that include such Blueprint Compound, which plan, among other things, will set forth [****].

1.131 "**Marketing Authorization Application**" or "**MAA**" means any new drug application, biologics license application, or other marketing authorization application, in each case, filed with the applicable Regulatory Authority in a country or other regulatory jurisdiction, which application is required to commercially market or sell a pharmaceutical or biologic product in such country or jurisdiction (and any amendments thereto). In the context of imported drugs, MAA is also known as the Import Drug License ("**IDL**") application.

1.132 "**Medical Affairs**" means activities conducted by a Party's medical affairs departments (or, if a Party does not have a medical affairs department, the equivalent function thereof), including communications with key opinion leaders, medical education, symposia, advisory boards (to the extent related to medical affairs or clinical guidance), activities performed in connection with patient registries, and other medical programs and communications, including educational grants, research grants (including conducting investigator-initiated studies), and charitable donations to the extent related to medical affairs and not to other activities that do not involve the promotion, marketing, sale, or other Commercialization of the Licensed Products and are not conducted by a Party's medical affairs (or equivalent) departments.

1.133 "**Medical Affairs Plan**" means, with respect to a Licensed Product, [****] for the Medical Affairs activities for such Licensed Product to be conducted in the Territory, which plan will include medical information that Zai will provide in the Territory, including [****] that will be prepared and updated by Zai as provided in Section 8.1 (Medical Affairs Plans).

1.134 "**Milestone Events**" has the meaning set forth in Section 10.2.3(a) (Notification of Milestone Events).

1.135 "**Milestone Payments**" has the meaning set forth in Section 10.2.3(a) (Notification of Milestone Events).

1.136 "**Net Sales**" means with respect to a Licensed Product, the gross amount [****] by Zai and its Affiliates and Sublicensees (each of the foregoing, a "**Seller**") to independent, unrelated persons (including Third Party Distributors) ("**Buyers**") in *bona fide* arm's length transactions with respect

to such Licensed Product, less the following deductions, in each case, to the extent [****] in connection with such Licensed Product:

(a) [****]

(b) [****]

(c) [****]

(d) [****]

(e) [****]

(f) [****].

If Seller receives non-cash consideration for a Licensed Product sold to a Buyer during the Term, then the Net Sales amount for such Licensed Product will be calculated based on [****].

No deduction will be made for any item of cost incurred by any Seller in Developing or Commercializing Licensed Products except as permitted pursuant to clauses (a) to (f) of the foregoing sentence; *provided* that Licensed Products transferred to Buyers in reasonable quantities in connection with Clinical Trials, compassionate use or named-patient use, in each case, will give rise to Net Sales only to the extent [****]. If a single item falls into more than one of the categories set forth in clauses (a)-(f) above, then such item may not be deducted more than once.

All deductions in clauses (a) through (f) above will be fairly and equitably allocated between such Licensed Product and other products of Zai and its Affiliates and Sublicensees such that such Licensed Product does not bear a disproportionate portion of such deductions. Calculations of Net Sales will be consistently applied across all products of Seller and will be consistent between periods.

Such amounts will be determined from the books and records of Seller, and will be calculated in accordance with applicable Accounting Standards.

Transfers or sales between Zai and its Affiliates and Sublicensees will be disregarded for purposes of calculating Net Sales, except if such purchaser is an end user.

[****]

If a Licensed Product is a Combination Product, [****].

If a Licensed Product containing the Blueprint Compound as the sole Active Ingredient is sold as part of an Combination Product and is sold separately in finished form, but the other Active Ingredients included in the Combination Product are not sold separately in finished form, [****].

If a Licensed Product containing the Blueprint Compound as the sole Active Ingredient is sold as part of a Combination Product and is not sold separately in finished form, but the other Active Ingredients included in the Combination Product are sold separately in finished form, [****].

If Net Sales of the Licensed Product when included in an Combination Product cannot be determined using the methods above (as neither the Licensed Product containing the applicable

Blueprint Compound as the sole Active Ingredient nor the other Active Ingredients are sold separately), [****]. At least [****] prior to the anticipated First Commercial Sale of any such Combination Product in a region in the Territory, Zai will propose such good faith estimate to Blueprint, and Blueprint will [****] consider such proposal, and the Parties will seek to reach agreement on such allocation. If the Parties are unable to reach such agreement within [****] after Zai provides such proposal, then the issue will be resolved in accordance with Article 16 (Dispute Resolution).

1.137 "**New Affiliate**" has the meaning set forth in Section 2.8.3 (New Affiliate Exception).

1.138 "**New Combination**" has the meaning set forth in Section 5.9 (New Development Proposed by Zai).

1.139 "**New Development Activities**" has the meaning set forth in Section 5.9 (New Development Proposed by Zai).

1.140 "**New Development Proposal**" has the meaning set forth in Section 5.9 (New Development Proposed by Zai).

1.141 "**New Indication**" has the meaning set forth in Section 5.9 (New Development Proposed by Zai).

1.142 [****]

1.143 "**New Territory-Specific Development Activities**" has the meaning set forth in Section 5.9.1(a) (JSC Approval).

1.144 "**NMPA**" means the National Medical Products Administration of the PRC, and local counterparts thereto, and any successor agency or authority thereto having substantially the same function.

1.145 "**Non-Clinical Development**" means all Development excluding Clinical Development.

1.146 "**Non-Funding Party**" has the meaning set forth in Section 5.8.1(a) (JSC Approval).

1.147 "**NSCLC**" means non-small cell lung cancer.

1.148 "**OFAC**" means the Office of Foreign Assets Control of the United States Department of the Treasury or any successor agency thereto.

1.149 "**Other Extensions**" has the meaning set forth in Section 14.7 (Patent Term Extensions).

1.150 "**Party**" or "**Parties**" has the meaning set forth in the Preamble.

1.151 "**Patent Challenge**" has the meaning set forth in Section 15.2.3 (Termination for Patent Challenge).

1.152 "**Patent Prosecution**" means activities directed to (a) preparing, filing, or prosecuting applications (of all types) for any Patent Right, (b) maintaining any Patent Right, or (c) deciding whether to abandon or maintain any Patent Right.

1.153 "**Patent Rights**" means (a) all patents and patent applications in any country or region, (b) all patent applications filed either from such patents or patent applications or from an application claiming priority from any of these, including divisionals, continuations, continuations-in-part, provisionals, converted provisionals, and continued prosecution applications, (c) any and all patents that have

issued or in the future issue from the foregoing patent applications, and (d) any and all substitutions, renewals, registrations, confirmations, extensions, or restorations, including revalidations, reissues, and re-examinations (including any supplementary protection certificates and the like) of the foregoing patents or patent applications.

1.154 "**Patent Term Adjustment**" has the meaning set forth in Section 14.7 (Patent Term Extensions).

1.155 "**Patent Term Extension**" has the meaning set forth in Section 14.7 (Patent Term Extensions).

1.156 "**Patient Commitment**" has the meaning set forth in Section 5.2.1 (Enrollment in Committed Trials).

1.157 "**Paying Party**" has the meaning set forth in Section 10.12.2 (Tax Cooperation).

1.158 "**Permitted Zai Non-Clinical Development**" has the meaning set forth in Section 5.7 (Non-Clinical and Preclinical Studies).

1.159 "**Person**" means any corporation, limited or general partnership, limited liability company, joint venture, joint stock company, trust, unincorporated association, governmental body, authority, bureau, or agency, or any other entity or body, or an individual.

1.160 "**Personal Information**" means information related to a reasonably identifiable natural person.

1.161 "**Phase I Clinical Trial**" means a clinical trial in humans that is generally consistent with 21 C.F.R. § 312.21(a), as amended (or its successor regulation), or, with respect to any other country or region, the equivalent of such a clinical trial in such other country or region.

1.162 "**Phase II Clinical Trial**" means a clinical trial in humans that is generally consistent with 21 C.F.R. § 312.21(b), as amended (or its successor regulation), or, with respect to any other country or region, the equivalent of such a clinical trial in such other country or region.

1.163 "**Phase III Clinical Trial**" means a clinical trial in humans of a pharmaceutical or biologic product (including any Combination Regimen) that is generally consistent with 21 C.F.R. § 312.21(c), as amended (or its successor regulation), or, with respect to any other country or region, the equivalent of such a clinical trial in such other country or region.

1.164 "**Pivotal Trial**" means any (a) [****] or (b) [****] in humans of a pharmaceutical or biologic product (including any Combination Regimen), the results of which, together with prior data and information concerning such product, are [****] in any particular jurisdiction and that is intended to support, or otherwise supports, the filing of an MAA in such jurisdiction (including any bridging study).

1.165 "**POC Trial**" means a clinical trial [****] in humans of a pharmaceutical or biologic product (including any Combination Regimen) performed to [****] of such product and that [****].

1.166 "**PRC**" means the People's Republic of China, which, for purposes of this Agreement, does not include Hong Kong Special Administrative Region, Macau Special Administrative Region, or Taiwan.

1.167 "**PRC Submission Estimated Timeline**" means, for each Licensed Product, a written timeline setting forth the estimated dates of achievement of key regulatory milestones and submission to

applicable Regulatory Authorities in the PRC of key Regulatory Submissions (including each MAA) for such Licensed Product.

1.168 "**Preapproved Subcontractor**" means any Subcontractor that the JSC has approved as a Subcontractor that Zai may engage to perform its obligations or exercise its rights under this Agreement as further described in Section 2.2.3 (Right to Subcontract).

1.169 "**Privacy Laws**" has the meaning set forth in Section 12.5.2.

1.170 "**Product Infringement**" has the meaning set forth in Section 14.3.1 (Patent Enforcement; Notice).

1.171 "**Product Marks**" has the meaning set forth in Section 14.9.1 (Global Brand Elements).

1.172 "**Proposed Blueprint/Zai Combination**" has the meaning set forth in Section 5.8.1 (Proposed Blueprint/Zai Combinations).

1.173 "**Prosecuting Party**" has the meaning set forth under Section 14.2.3(a) (Blueprint/Zai Combination Technology).

1.174 "**Public Official**" means (a) any officer, employee or representative of any regional, federal, state, provincial, county or municipal government or government department, agency or other division; (b) any officer, employee or representative of any commercial enterprise that is owned or controlled by a government, including any state-owned or controlled veterinary, laboratory or medical facility; (c) any officer, employee or representative of any public international organization, such as the International Monetary Fund, the United Nations or the World Bank; and (d) any person acting in an official capacity for any government or government entity, enterprise, or organization identified above.

1.175 "**Publication**" has the meaning set forth in Section 11.5 (Publications).

1.176 "**Receiving Party**" has the meaning set forth in Section 11.1.1 (Duty of Confidence).

1.177 "**Recipient**" has the meaning set forth in Section 10.12.2 (Tax Cooperation).

1.178 "**Regulatory Approval**" means, with respect to a particular country or other regulatory jurisdiction, any approval of an MAA or other approval, product, or establishment license, registration, permit, or authorization of any Regulatory Authority necessary for the commercial marketing or sale of a pharmaceutical or biologic product in such country or other regulatory jurisdiction, excluding, in each case, Reimbursement Approval.

1.179 "**Regulatory Authority**" means any applicable Governmental Authority with jurisdiction or authority over the Development, Manufacture, Commercialization, or other Exploitation (including Regulatory Approval or Reimbursement Approval) of pharmaceutical or biologic products in a particular country or other regulatory jurisdiction, including the NMPA, and any corresponding national or regional regulatory authorities.

1.180 "**Regulatory Exclusivity**" means any exclusive marketing rights or data protection or other exclusivity rights conferred by any Regulatory Authority with respect to a pharmaceutical or biologic product in a particular country or other regulatory jurisdiction that prohibits a Person from Commercializing [****].

1.181 [****]

1.182 "**Regulatory Submissions**" means any filing, application, or submission with any Regulatory Authority in support of Developing, Manufacturing, or Commercializing a pharmaceutical or biologic product (including to obtain, support, or maintain Regulatory Approval from that Regulatory Authority), and all correspondence or communication with or from the relevant Regulatory Authority, as well as minutes of any material meetings, telephone conferences, or discussions with the relevant Regulatory Authority. Regulatory Submissions include all INDs, MAAs, and other applications for Regulatory Approval and their equivalents.

1.183 "**Reimbursement Approval**" means an approval, agreement, determination, or other decision by the applicable Governmental Authority that establishes prices charged to end-users for pharmaceutical or biologic products at which a particular pharmaceutical or biologic product will be reimbursed by the Regulatory Authorities or other applicable Governmental Authorities in the Territory.

1.184 "**Replacement Site**" has the meaning set forth in Section 5.14.2 (Deficient Sublicensees or Sites and Replacement).

1.185 "**Review Period**" has the meaning set forth in Section 11.5 (Publications).

1.186 "**Royalty Estimate**" has the meaning set forth in Section 10.3.4 (Royalty Reports and Payments).

1.187 "**Royalty Patent Rights**" means the Blueprint Patent Rights, Blueprint Manufacturing Patent Rights, and the Joint Collaboration Patent Rights.

1.188 "**Royalty Payments**" has the meaning set forth in Section 10.3.1 (Royalty Rates).

1.189 "**Royalty Report**" has the meaning set forth in Section 10.3.4 (Royalty Reports and Payments).

1.190 "**Royalty Term**" has the meaning set forth in Section 10.3.2 (Royalty Term).

1.191 "**Rules**" has the meaning set forth in Section 16.3.1 (Arbitration; Rules).

1.192 "**Safety Agreement**" has the meaning set forth in Section 6.5.1 (Adverse Events Reporting; Safety Agreements).

1.193 "**Sales Milestone Events**" has the meaning set forth in Section 10.2.2 (Sales Milestone Events and Payments).

1.194 "**Sales Milestone Payments**" has the meaning set forth in Section 10.2.2 (Sales Milestone Events and Payments).

1.195 "**Scientific Officers**" has the meaning set forth in Section 2.8.2 (Competitive Product Disputes).

1.196 "**Seller**" has the meaning set forth in Section 1.136 (Net Sales).

1.197 "**Shared Services Costs**" means [****] **1.197** [****].

1.198 [****] has the meaning set forth in Section 5.2.2 [****].

1.199 "**Subcontractor**" means a Third Party contractor engaged by a Party to perform certain obligations or exercise certain rights of such Party under this Agreement on a fee-for-service basis (including CROs and CMOs).

1.200 "**Sublicensee**" means any Person, excluding any Subcontractor or Third Party Distributor, (a) with respect to Zai, to whom Zai grants a sublicense of, or other authorization or permission granted under, the rights granted to Zai in Section 2.1 (License Grants to Zai), and (b) with respect to Blueprint, to whom Blueprint grants a sublicense of, or other authorization or permission granted under, the rights granted to Blueprint in Section 2.3 (License Grants to Blueprint).

1.201 "**Tax**" or "**Taxes**" means any present or future taxes, levies, imposts, duties, charges, assessments or fees of any nature (including any interest thereon), including value add taxes ("**VAT**").

1.202 "**Technology Transfer**" has the meaning set forth in Section 4.3 (Continuing Know-How Transfer).

1.203 "**Term**" has the meaning set forth in Section 15.1 (Term).

1.204 "**Territory**" means the PRC, Hong Kong Special Administrative Region, Macau Special Administrative Region, and Taiwan, each of which will be deemed a separate region for purposes of this Agreement.

1.205 "**Territory Sponsor**" means, with respect to a Territory-Specific Clinical Trial or a Global Clinical Trial for a Licensed Product to be conducted at sites in the Territory, the Party that holds the IND from the applicable Regulatory Authority in the Territory for such Clinical Trial in its name.

1.206 "**Territory-Specific Clinical Trial**" means a Clinical Trial for a Licensed Product, the data from which at the time of commencement is intended to be used to obtain, support, or maintain Regulatory Approval in the Territory but not to obtain, support, or maintain Regulatory Approval in any of the following: [****].

1.207 "**Territory-Specific Development Plans**" has the meaning set forth in Section 5.4 (Territory-Specific Development Plans).

1.208 "**Third Party**" means any Person other than a Party or an Affiliate of a Party.

1.209 "**Third Party Claims**" means collectively, any and all Third Party demands, claims, actions, suits, and proceedings (whether criminal or civil, in contract, tort, or otherwise).

1.210 "**Third Party Distributor**" means any Third Party that purchases Licensed Product from Zai or its Affiliates, or Sublicensees, takes title to such Licensed Product, and distributes such Licensed Product directly to customers, but does not Develop or Manufacture any Blueprint Compound or Licensed Product and does not make any royalty, profit-share, or other payment to Zai or its Affiliates or Sublicensees, other than payment for the purchase of Licensed Products for resale.

1.211 "**Third Party IP Agreement**" means any agreement with a Third Party entered into by Blueprint or Zai respect to a grant of rights under any Blueprint Identified Rights or Zai Identified Rights.

1.212 "**United States**" or "**U.S.**" means the United States of America and its territories and possessions.

1.213 "**Upfront Payment**" has the meaning set forth in Section 10.1 (Upfront Payment).

1.214 "**Valid Claim**" means with respect to a particular country or region, a claim in any (a) unexpired and issued Patent Right that has not been irretrievably lapsed or been abandoned, disclaimed, permanently revoked, dedicated to the public, or held invalid, unenforceable, or not patentable by a final non-appealable decision of a court of competent jurisdiction or Governmental Authority in such country or region, or (b) pending patent application that has been pending for [****]; *provided* that, if a claim ceases to be a Valid Claim by reason of foregoing subclause (b), then such claim would again be deemed a Valid Claim in the event such claim subsequently issues prior to the end of the then-current Royalty Term in such country or region.

1.215 "**VAT**" has the meaning set forth in Section 1.201 (Tax).

1.216 "**VAT Credit**" has the meaning set forth in Section 10.13 (VAT Credits).

1.217 "**Working Group**" has the meaning set forth in Section 3.4 (Working Groups).

1.218 "**Zai**" has the meaning set forth in the Preamble.

1.219 "**Zai Collaboration Know-How**" means Collaboration Know-How, other than Blueprint/Zai Combination Know-How or Assigned Collaboration Know-How, developed or invented solely by Zai's or its Affiliates', licensees', Sublicensees', or Subcontractors' employees, agents, or independent contractors, or any Persons that are contractually required to assign or license such Collaboration Know-How (or Patent Rights Covering such Know-How) to Zai or any Affiliate of Zai, in each case, in the performance of activities under this Agreement during the Term.

1.220 "**Zai Collaboration Patent Rights**" means all Collaboration Patent Rights that Cover Zai Collaboration Know-How. For clarity, Zai Collaboration Patent Rights do not include any Blueprint/Zai Combination Patent Rights or Assigned Collaboration Patent Rights.

1.221 "**Zai Collaboration Technology**" means Zai Collaboration Know-How and Zai Collaboration Patent Rights.

1.222 "**Zai Identified General Rights**" has the meaning set forth in Section 2.6.2 (Zai Identified Rights).

1.223 "**Zai Identified Rights**" has the meaning set forth in Section 2.6.2 (Zai Identified Rights).

1.224 "**Zai Indemnitee(s)**" has the meaning set forth in Section 13.2 (By Blueprint).

1.225 "**Zai In-Licensed Rights**" has the meaning set forth in Section 2.6.2 (Zai Identified Rights).

1.226 "**Zai Know-How**" means, subject to Section 2.6.6 (Right to Decline Zai In-Licensed Rights), all Know-How (excluding Zai's interest in Blueprint/Zai Combination Know-How and other Joint Collaboration Know-How) that is (a) Controlled by Zai or any of its Affiliates as of the Effective Date or during the Term, and (b) used by either Party in the Exploitation of a Blueprint Compound or a Licensed Product, including all Zai Collaboration Know-How.

1.227 "**Zai Patent Rights**" means, subject to Section 2.6.6 (Right to Decline Zai In-Licensed Rights), all Patent Rights (excluding Zai's interest in Blueprint/Zai Combination Patent Rights and other Joint Collaboration Patent Rights) that are (a) Controlled by Zai or any of its Affiliates as of the Effective Date or during the Term; and (b) practiced by either Party in the Exploitation of a Blueprint Compound or a Licensed Product, including all Zai Collaboration Patent Rights.

1.228 "**Zai Product**" means any pharmaceutical or biologic product with respect to which Zai or any of its Affiliates has exclusive rights to Exploit inside the Territory or outside of the Territory, including all forms, modifications, and variants thereof that are Controlled by Zai, in each case, at the time that the JSC agrees in writing to include a Blueprint/Zai Combination containing such Zai Product under this Agreement pursuant to Section 5.8.1 (Proposed Blueprint/Zai Combinations) or Section 5.9 (New Development Proposed by Zai).

1.229 "**Zai Publication**" has the meaning set forth in Section 11.5.1.

1.230 "**Zai Specifications**" has the meaning set forth in Section 7.2.3 (Specifications).

1.231 "**Zai Technology**" means Zai Know-How, Zai Patent Rights, and Zai's interest in the Joint Collaboration Technology.

1.232 "**Zai Third Party IP Agreement**" has the meaning set forth in Section 2.6.6(b) (Right to Decline Zai In-Licensed Rights).

Article 2
LICENSES

2.1 License Grants to Zai.

2.1.1 **In the Territory**. Subject to the terms of this Agreement, Blueprint hereby grants to Zai (a) an exclusive, royalty-bearing license, with the right to grant sublicenses solely in accordance with Section 2.2 (Sublicensing and Subcontractors), under the Blueprint Technology to Exploit (other than to conduct or have conducted Non-Clinical Development, or Manufacture or have Manufactured) the Blueprint Compounds and the Licensed Products in the Field in the Territory in accordance with the Territory-Specific Development Plans, Global Development Plans, the Medical Affairs Plans, and the Commercialization Plans or as otherwise expressly permitted by this Agreement and (b) a non-exclusive, royalty-bearing license, with the right to grant sublicenses solely in accordance with Section 2.2 (Sublicensing and Subcontractors), under the Blueprint Technology to [****] in the Field in the Territory. Zai will not practice the Blueprint Technology licensed to Zai under this Section 2.1.1 (In the Territory) except as expressly set forth in the Territory-Specific Development Plans, Global Development Plan, Medical Affairs Plans, and Commercialization Plans or to conduct other activities expressly permitted under this Agreement. Notwithstanding any provision to the contrary set forth in this Agreement, [****].

2.1.2 **Manufacturing License**. Subject to the terms of this Agreement, effective upon the commencement of the Manufacturing Technology Transfer to Zai for the Manufacture of the Licensed Products in accordance with Section 7.2.2 (Clinical and Commercial Supply), Blueprint hereby grants to Zai [****] in accordance with and subject to the terms of this Agreement, including pursuant to Section 7.2 (Supply by Zai). Zai will not practice the Blueprint Manufacturing Technology licensed to Zai under this Section 2.1.2 (Manufacturing License) until the commencement of the Manufacturing Technology Transfer to Zai for the Manufacture of the Licensed Products in accordance with Section 7.2.2 (Clinical and Commercial Supply).

2.2 Sublicensing and Subcontractors.

2.2.1 **Right to Sublicense**. Subject to the terms of this Agreement, Zai will have the right to grant sublicenses of the rights granted under Section 2.1 (License Grants to Zai) to (a) its Affiliates, *provided* that any such sublicense will automatically terminate if such Person ceases to be an Affiliate of Zai, (b) Development Subcontractors and Third Party Distributors in accordance with this Section 2.2 (Sublicensing and Subcontractors), and (c) subject to Blueprint's prior written approval, not to be unreasonably withheld, conditioned, or delayed, Third Parties (other than Development Subcontractors and Third Party Distributors). Notwithstanding the foregoing, Zai will not grant a sublicense to a Third Party of all or substantially all of Zai's rights or obligations under this Agreement with respect to one or more regions within the Territory without Blueprint's prior written consent, which consent Blueprint may withhold, condition, or delay in its sole discretion. Each Sublicensee will hold its rights contingent on the rights licensed to Zai under the terms of this Agreement. Any termination of the licenses granted to Zai under Section 2.1 (License Grants to Zai) as a result of a termination of this Agreement with respect to one or more Licensed Products or in its entirety will, subject to Section 15.3.11 (Sublicense Survival), cause the Sublicensees to automatically lose the same rights under any sublicense.

2.2.2 **Terms of Sublicenses to Third Parties**. Zai will provide prior written notice to Blueprint identifying its intention to grant a sublicense under Section 2.2.1 (Right to Sublicense) to any Third Party (other than a sublicense granted by Zai to a Development Subcontractor or Third Party Distributor; *provided* that such engagement is otherwise in accordance with Section 2.2.3 (Right to Subcontract)), the purpose of such sublicense, and the identity of the Third Party to whom Zai intends to grant such sublicense. Each sublicense to a Third Party will be granted under a written agreement that is consistent with the terms of this Agreement and that (a) requires each such Third Party Sublicensee to which Zai grants a sublicense of the rights granted to Zai under Section 2.1 (License Grants to Zai) to comply with the terms of this Agreement that are applicable to such sublicense (including obligations of confidentiality and non-use at least as stringent as those set forth Article 11 (Confidentiality; Publication), as applicable, the Milestone Event and Royalty Payment reporting obligations set forth under Section 10.2 (Milestone Payments) and Section 10.3 (Royalty Payments to Blueprint), the record keeping and audit requirements set forth under Section 5.14 (Clinical Trial Audit Rights), Section 10.11 (Financial Records and Audits), and the intellectual property provisions set forth in Article 14 (Intellectual Property)), and (b) precludes the granting of further sublicenses in contravention with the terms of this Agreement. Without limiting the generality of the foregoing, each sublicense agreement with such a Third Party entered into after the Effective Date must include (i) [****], (ii) [****], and (iii) [****].

2.2.3 **Right to Subcontract**. Zai will not propose the engagement of any Subcontractor that is Debarred/Excluded. Zai may engage (a) Subcontractors solely to perform Zai's Development activities with respect to Licensed Products under this Agreement on Zai's behalf (each a "**Development Subcontractor**") or (b) Third Party Distributors to distribute Licensed Products in the Territory on behalf of Zai, in either case, without Blueprint's prior written consent, but subject to the requirements set forth in the first, the second to last, and the last sentence of this Section 2.2.3 (Right to Subcontract), Section 2.2.4 (Notices of Sublicensing and Subcontractors), Section 2.2.5 (Zai Audits of Sublicensees and Subcontractors), and Section 2.2.6 (Responsibility for Sublicensees and Subcontractors). Prior to Zai's engagement of the first Subcontractor (other than a Development Subcontractor or Third Party Distributor), Zai will provide to the JSC to review, discuss, and determine whether to approve as Preapproved Subcontractors a list

of Subcontractors that Zai may engage to perform its obligations and exercise its rights under this Agreement. In addition, during the term, Zai may propose additional Subcontractors to be approved by the JSC as Preapproved Subcontractors and following the approval by the JSC of any such additional Subcontractors, such Subcontractors will be Preapproved Subcontractors. Zai may engage any such Preapproved Subcontractor to perform Zai's obligations and exercise of Zai's rights under this Agreement. In addition, if Zai wishes to engage a Subcontractor (other than a Development Subcontractor or Third Party Distributor) that is not a Preapproved Subcontractor to perform its obligations or exercise its rights under this Agreement related to the (i) Manufacture of a Licensed Product following completion of the Manufacturing Technology Transfer, or (ii) the Commercialization of such Licensed Product in a region in the Territory, then, in each case ((i) and (ii)), Zai will provide written notice to Blueprint at least [****] before engaging any such Subcontractor identifying Zai's intention to engage such Subcontractor, the purpose of engaging such Subcontractor, and the identity of such Subcontractor. Within [****] after the receipt of such written notice, Blueprint may provide written notice of its veto of Zai's engagement of such proposed Subcontractor and in such case, Zai will not engage such Subcontractor to perform its obligations or exercise its rights under this Agreement, *provided* that Blueprint will not unreasonably veto such engagement. If Blueprint does not provide written notice to Zai of Blueprint's veto of Zai's engagement of a particular proposed Subcontractor within [****] after Blueprint's receipt of such notice, then Zai may engage such proposed Subcontractor to perform its obligations or exercise its rights under this Agreement (subject to the terms set forth herein). Any agreement pursuant to which Zai engages any Subcontractor (including any Development Subcontractor or Third Party Distributor) must be consistent with the terms of this Agreement, including containing obligations of confidentiality and non-use at least as stringent as those set forth Article 11 (Confidentiality; Publication), and terms that are consistent with the intellectual property provisions set forth in Article 14 (Intellectual Property). Without limiting the generality of the foregoing, unless otherwise agreed by the Parties, each agreement pursuant to which Zai engages a Subcontractor (including any Development Subcontractor or Third Party Distributor) to Exploit Licensed Products hereunder must include [****].

2.2.4 **Notice of Sublicenses and Subcontracts**. Zai will provide Blueprint with a true and complete copy of each sublicense or subcontracting agreement (including all schedules, exhibits, and appendices thereto) with any Third Party (including any Development Subcontractor or Third Party Distributor) within [****] after it becomes effective[****] Any sublicense granted under this Agreement must either be in English or [****].

2.2.5 **Zai Audits of Sublicensees and Subcontractors**. Zai will provide Blueprint with copies of all quality oversight or audit reports from audits that Zai (or its agent) has conducted on any Sublicensees or Subcontractors that Zai engages to perform its obligations or exercise its rights under this Agreement with respect to any Licensed Product, as well as all corrective action plans resulting from any such audits, in each case, to the extent such reports and plans are relevant to such Sublicensees or Subcontractors' performance of such obligations or exercise of such rights no later than [****].

2.2.6 **Responsibility for Sublicensees and Subcontractors**. Zai will require that all Sublicensees and Subcontractors perform the activities that they are sublicensed or engaged to perform (as applicable) in accordance with GLP, cGMP, and GCP, as applicable, and otherwise in compliance with Applicable Law. Notwithstanding any sublicense or subcontracting, Zai will remain primarily liable to Blueprint for the

performance of all of its obligations under, and Zai's compliance with all provisions of, this Agreement. Zai will be fully responsible and liable for any breach of the terms of this Agreement by any of its Sublicensees or Subcontractors to the same extent as if Zai itself has committed any such breach and will terminate the agreement with any Sublicensee or Subcontractor [****] if such Sublicensee or Subcontractor is in breach of this Agreement and neither Zai nor such Subcontractor cures such breach in a timely manner [****].

2.3 License Grants to Blueprint.

2.3.1 **Development Activities**. Subject to the terms of this Agreement, Zai hereby grants to Blueprint a worldwide, non-exclusive, royalty-free license, with the right to grant sublicenses through multiple tiers, under the Zai Technology to perform the Development activities for the Blueprint Compounds and the Licensed Products in the Field for which it is responsible under a Global Development Plan, including any Global Clinical Trial for a Licensed Product (including a POC Trial or other Development of any Blueprint/Zai Combination approved by the JSC pursuant to Section 5.8.1 (Proposed Combinations)).

2.3.2 **Outside of the Territory**. Subject to the terms of this Agreement, Zai hereby grants to Blueprint a perpetual, irrevocable, royalty-free license, with the right to grant sublicenses through multiple tiers, under the Zai Technology to Exploit the Blueprint Compounds and the Licensed Products in the Field outside of the Territory. Such license under this Section 2.3.2 (Outside of the Territory) will be (a) exclusive under the Zai Collaboration Technology and Zai's interest in the Joint Collaboration Technology and (b) non-exclusive under all other Zai Technology.

2.4 Retained Rights. Nothing in this Agreement will be interpreted to grant a Party any rights under any intellectual property rights owned or Controlled by the other Party, including Blueprint Technology, Blueprint Manufacturing Technology, Joint Collaboration Technology, or Zai Technology, in each case, that are not expressly granted herein, whether by implication, estoppel, or otherwise. Any rights not expressly granted to Blueprint by Zai under this Agreement are hereby retained by Zai. Any rights not expressly granted to Zai by Blueprint under this Agreement are hereby retained by Blueprint. In addition, Blueprint expressly retains (a) the exclusive right under the Blueprint Technology (on behalf of itself and its licensees and Sublicensees, other than Zai, Zai's Affiliates and Zai's Sublicensees) to conduct Non-Clinical Development involving Blueprint Compounds or Licensed Products anywhere in the world (including in the Territory[****]), (b) the right under the Blueprint Technology to perform Development activities for the Blueprint Compounds and the Licensed Products in the Territory in accordance with this Agreement, including to conduct Development activities under a Global Development Plan as provided hereunder (including in the event that Zai declines, through the JSC, to participate in a Global Clinical Trial proposed by Blueprint under Section 5.11 (New Development Proposed by Blueprint) or fails to satisfy the Patient Commitment with respect to one or more Committed Trials), (c) the right under the Blueprint Technology (on behalf of itself and its licensees and Sublicensees, other than Zai, Zai's Affiliates and Zai's Sublicensees) to Manufacture Licensed Products in the Territory itself or through its Affiliates or Third Parties (i) for use by Zai and its authorized Sublicensees in the Territory or (ii) for use by Blueprint, or its licensees, Sublicensees, Affiliates or Third Parties outside of the Territory, (d) the right to perform Blueprint's other obligations under this Agreement, (e) in the event that Zai does not participate in a Global Clinical Trial for one or more Licensed Products in one or more Indications or with respect to one or more Combination Products or Combination Regimens, the non-exclusive right to Develop Blueprint Compounds and Licensed Products through the use of clinical trial sites, CROs, and other Third Parties in the Territory in connection with the performance of such Global Clinical Trials, and (f) the exclusive right to

Exploit the Blueprint Compounds and Licensed Products outside of the Territory. Zai will not practice the Blueprint Technology and Blueprint will not practice the Zai Technology, in each case, other than as expressly licensed and permitted under this Agreement or otherwise agreed by the Parties in writing.

2.5 Combination Products Rights. Notwithstanding any other provision of this Agreement, for purposes of the license grants under Section 2.1 (License Grants to Zai) or Section 2.3 (License Grants to Blueprint), with respect to any Licensed Product that is a Combination Product or Combination Regimen, such license will only include rights with respect to any Blueprint Compound component of such Combination Product or Combination Regimen and not any other Active Ingredient Controlled by, as applicable, the Party granting such license (*e.g.*, with respect to Zai, any Zai Product or with respect to Blueprint, a compound Controlled by Blueprint other than BLU-701 or BLU-945) or any of its Affiliates except in the event that [****].

2.6 Third Party In-Licenses.

2.6.1 **Blueprint Identified Rights**. Blueprint will remain solely responsible for the payment of all royalties, license fees, milestone payments, and other payment obligations under all agreements entered into by Blueprint prior to the Effective Date. If, after the Effective Date during the Term, Blueprint intends to obtain Control of any Know-How or Patent Rights from a Third Party (whether by acquisition or license) that may be necessary or useful to Exploit one or more Blueprint Compounds or Licensed Products in the Field anywhere in the world (other than a Change of Control of Blueprint or as a result of the acquisition by Blueprint of a Third Party by merger, acquisition, or similar transaction or series of related transactions) (such Know-How and Patent Rights, "**Blueprint Identified Rights**"), then Blueprint will notify Zai in writing of such Blueprint Identified Rights and Section 2.6.3 (Third Party IP Agreements) will apply.

2.6.2 **Zai Identified Rights**. If Zai determines that a license under any Know-How or Patent Rights controlled by a Third Party is [****] ("**Zai Identified Rights**"), then Zai will [****]. Blueprint will have the first right to acquire rights to any such Zai Identified Rights from such Third Party (whether by acquisition or license)[****]. If [****], then Blueprint will notify Zai of such intention within [****] and the terms of Section 2.6.3 (Third Party IP Agreements) will apply. If (a) Blueprint [****] within such [****] period or otherwise [****], or (b) [****], then Zai will have the right to acquire rights under such Zai Identified Rights from such Third Party solely for the Territory or any region therein and any such right obtained by Zai will be referred to as "**Zai In-Licensed Rights**."

2.6.3 **Blueprint In-Licensed Rights**. Prior to executing a Third Party IP Agreement with a Third Party to acquire or license any Blueprint Identified Rights or Zai Identified Rights (together, "**Blueprint In-Licensed Rights**"), Blueprint will (a) provide Zai an opportunity to review and comment on [****], including any [****] (b) take Zai's comments into consideration [****] prior to finalizing such Third Party IP Agreement, and (c) ensure that such Third Party IP Agreement includes [****]. Upon execution of such Third Party IP Agreement, Blueprint will notify Zai in writing and will provide [****].

2.6.4 **Responsibility for Costs of Blueprint In-Licensed Rights**. Subject to Zai's right to decline a license or sublicense of Blueprint In-Licensed Rights within [****] in accordance with the terms of Section 2.6.5 (Right to Decline Blueprint In-Licensed Rights), following Blueprint's execution of the applicable Third Party IP Agreement (a) such Blueprint In-Licensed Rights will be included in the Blueprint Know-How or the

Blueprint Patent Rights (as applicable) and licensed or sublicensed (as applicable) to Zai under the licenses granted in Section 2.1 (License Grants to Zai), subject to the terms of this Agreement and the applicable Third Party IP Agreement, and (b) Zai will reimburse Blueprint (i) [****] of any such payments under the applicable Third Party IP Agreement that [****] pertain to, or arise [****] as a result of, the Exploitation of the Blueprint Compounds or the Licensed Products in the Territory (for example, [****]) by Zai or its Affiliates or Sublicensees, and (ii) with respect to any [****] payments payable in consideration for any Blueprint In-Licensed Rights that pertain to, or arise as a result of, the Exploitation of the Blueprint Compounds or the Licensed Products both inside and outside of the Territory or are non-Territory-specific (for example, [****]), [****]. Blueprint will bear [****] of amounts payable in consideration for any Blueprint In-Licensed Rights that pertain to any product other than a Blueprint Compound or Licensed Product or that [****] pertain to, or arise [****] as a result of, the Exploitation of the Blueprint Compounds or the Licensed Products outside of the Territory (for example, [****]).

2.6.5 **Right to Decline Blueprint In-Licensed Rights**. Zai will have the right to decline a license or sublicense (as applicable) from Blueprint under Blueprint In-Licensed Rights under a Third Party IP Agreement by providing written notice to Blueprint [****]. Upon Blueprint's [****] receipt of such notice declining such a license or sublicense (as applicable) under any Blueprint In-Licensed Rights, Blueprint will not be deemed to Control such Blueprint In-Licensed Rights, the definitions of Blueprint Patent Rights and Blueprint Know-How will exclude such Blueprint In-Licensed Rights, as applicable, and such Blueprint In-Licensed Rights will not be included in the scope of the rights granted to Zai under Section 2.1 (License Grants to Zai).

2.6.6 **Right to Decline Zai In-Licensed Rights; Responsibility for Costs**.

(a) **Zai In-Licensed Rights**. Prior to executing a Third Party IP Agreement with a Third Party to acquire or license any Zai In-Licensed Rights, Zai will (i) provide Blueprint an opportunity to review and comment on [****], including any [****], (ii) take Blueprint's comments into consideration [****] prior to finalizing such Third Party IP Agreement, and (iii) ensure that such Third Party IP Agreement includes [****]. Upon execution of such Third Party IP Agreement, Zai will notify Blueprint in writing and will provide [****].

(b) **Right to Decline Zai In-Licensed Rights**. Blueprint will have the right to decline a license or sublicense (as applicable) from Zai under Zai In-Licensed Rights by providing written notice to Zai [****] (the "**Zai Third Party IP Agreement**") [****]. Upon Zai's [****] receipt of such notice declining such a license or sublicense (as applicable) under any Zai In-Licensed Rights, Zai will not be deemed to Control such Zai In-Licensed Rights, the definitions of Zai Patent Rights and Zai Know-How will exclude such Zai In-Licensed Rights, as applicable, and such Zai In-Licensed Rights will not be included in the scope of the rights granted to Blueprint under Section 2.3 (License Grants to Blueprint).

(c) **Responsibility for Costs of Zai In-Licensed Rights**. Subject to Blueprint's right to decline a license or sublicense of Zai In-Licensed Rights in accordance with the terms of Section 2.6.6(b) (Right to Decline Zai In-Licensed Rights), following Zai's execution of the applicable Zai Third Party IP Agreement: (i) such Zai In-Licensed Rights will be included in the Zai Know-How or the Zai Patent Rights (as applicable) and licensed or sublicensed (as applicable) to Blueprint under the licenses granted in Section 2.3 (License

Grants to Blueprint), subject to the terms of this Agreement and the applicable Zai Third Party IP Agreement, and (ii) Blueprint will reimburse Zai (A) [****] of any such payments under the applicable Zai Third Party IP Agreement that [****]pertain to, or arise [****] as a result of, the Exploitation of the Blueprint Compounds or the Licensed Products outside the Territory (for example, [****] by Blueprint, its Affiliates or (sub)licensees, and (B) with respect to [****] payments payable in consideration for any Zai In-Licensed Rights that pertain to, or arise as a result of, the Exploitation of the Blueprint Compounds or the Licensed Products both inside and outside of the Territory or are non-Territory-specific (for example, [****]), a [****]. Zai will bear [****]of amounts payable in consideration for any Zai In-Licensed Rights that pertain to any product other than a Blueprint Compound or Licensed Product or that [****] pertain to, or arise [****] as a result of, the Exploitation of the Blueprint Compounds or the Licensed Products in the Territory (for example, [****]).

2.7 [****]

2.8 Exclusivity.

2.8.1 **Exclusivity Covenant**. Subject to Section 2.8.3 (New Affiliate Exception), during the Term neither Party will, and will ensure that its Affiliates and Sublicensees do not, independently or for or with any Third Party, [****] unless agreed in writing by the Parties (the "**Competitive Activities**").

2.8.2 **Competitive Product Disputes**. If a Party disputes whether a pharmaceutical or biologic product is a Competitive Product, then the Parties will refer the matter to the head of Research & Development of Zai and Blueprint (or, if a Party does not have a head of Research & Development, its most senior employee having the equivalent responsibilities) or their designees (the "**Scientific Officers**"). The Scientific Officers will meet [****] to discuss and resolve the matter within [****] after referral of such matter to such Scientific Officers. If the Scientific Officers cannot agree on a resolution to the matter within such [****] period, then the Parties will refer such matter for resolution to an independent Third Party expert agreed upon by the Parties within [****] after the Scientific Officers failed to resolve such matter. Such independent Third Party expert will be [****], and unless otherwise agreed in writing by the Parties, must not [****]. Such expert will make its determination as to whether the applicable pharmaceutical or biologic product is a Competitive Product [****]. The Party bringing a dispute pursuant to this Section 2.8.2 (Competitive Product Disputes) will [****] engage such expert and the Parties will share the out-of-pocket costs incurred in connection with the engagement of such expert [****]. Within [****] of the engagement of such expert by the disputing Party, such expert will deliver a written decision to the Parties on the matter as to whether such product is a Competitive Product (including a detailed report as to such expert's rationale for such decision), and such decision will be binding on the Parties.

2.8.3 **New Affiliate Exception**. Notwithstanding Section 2.8.1 (Exclusivity Covenant), if (1) a Third Party becomes an Affiliate of a Party during the Term through merger, acquisition, consolidation, Change of Control, or other similar transaction (any such Third Party, a "**New Affiliate**") and (2) such New Affiliate, as of the execution date of the definitive agreement with respect to such transaction, is engaged in Competitive Activities with respect to one or more Competitive Products, then:

(a) If such transaction results in a Change of Control of a Party, then such New Affiliate of such Party (the "**Acquiror**") and such Party and their respective Affiliates may continue to perform such Competitive Activities after such Change of Control and such Party will not be in violation of its exclusivity obligations set forth in Section 2.8.1 (Exclusivity Covenant), as long as (i) no Confidential Information of the other Party or Blueprint Technology (if the acquired Party is Zai) or Zai Technology (if the acquired Party is Blueprint) is used by or on behalf of such Party, its Acquiror and their respective Affiliates in connection with any such Competitive Activities, and (ii) such Party, its Acquiror and their respective Affiliates institute commercially reasonable [****] safeguards to ensure the requirements set forth in the foregoing clause (i) are met, including by creating "firewalls" between the personnel working on such Competitive Activities and the personnel teams charged with working on the Blueprint Compounds and Licensed Products hereunder or having access to data from activities performed under this Agreement or to the Confidential Information of the other Party.

(b) If such transaction does not result in a Change of Control of a Party, then such Party (i) will provide to the other Party [****], (ii) unless the Parties agree otherwise in writing, such Party and its New Affiliate (an "**Acquiree**") will take one of the following actions set forth below in clauses (A) or (B) and (iii) no later than [****] following the date of consummation of the relevant acquisition transaction, such Party will notify the other Party of which of the actions in the following clauses (A) or (B), it will pursue: (A) divest, or cause its Acquiree to divest, whether by license or otherwise, its interest in the program of applicable Competitive Activities; or (B) terminate any further Competitive Activities. If such Party notifies the other Party in writing that it intends to divest the program of applicable Competitive Activities or terminate the performance of the applicable Competitive Activities, then such Party or its Acquiree will effect the consummation of such divestiture within [****] (or such other period as may be required to comply with Applicable Law), or effect such termination of the program of applicable Competitive Activities within [****], in each case, after the closing of the relevant transaction and will confirm to the other Party in writing when it completes such divestiture pursuant to clause (A) or termination pursuant to clause (B). Such Party will keep the other Party reasonably informed of its efforts and progress in effecting such divesture or termination until such Party or its Acquiree completes the same. During such [****] or [****] period, as applicable, such Party and its Acquiree's and their respective Affiliates' conduct of such Competitive Activities will not constitute a breach by such Party of its exclusivity obligations set forth in Section 2.8.1 (Exclusivity Covenant), as long as during such period, (I) no Confidential Information of the other Party or Blueprint Technology (if the acquiring Party is Zai) or Zai Technology (if the acquiring Party is Blueprint) is used by or on behalf of such acquiring Party, its Acquiree, and their respective Affiliates in connection with any such Competitive Activities, and (II) such acquiring Party, its Acquiree and their respective Affiliates institute commercially reasonable [****] safeguards to ensure the requirements set forth in the foregoing clause (I) are met, including by creating "firewalls" between the personnel working under such Competitive Activities and the personnel teams charged with working on the Blueprint Compounds and Licensed Products hereunder or having access to data from activities performed under this Agreement or Confidential Information of the other Party.

Article 3
GOVERNANCE

3.1 Alliance Managers. Each Party will appoint an individual to act as its alliance manager under this Agreement as soon as practicable after the Effective Date (each an "**Alliance Manager**"). The Alliance Managers will: (a) serve as the primary points of contact between the Parties for the purpose of providing the other Party with information on the progress of a Party's activities under this Agreement; (b) be responsible for facilitating the flow of information and otherwise promoting communication, coordination, and collaboration between the Parties, all of which communications between the Parties will be in English; (c) facilitate the prompt resolution of any disputes; and (d) attend JSC, JPT, and Working Group meetings, in each case, as a non-voting member. An Alliance Manager may also bring any matter to the attention of the JSC, a JPT, or applicable Working Group if such Alliance Manager reasonably believes that such matter warrants such attention. Each Party will use reasonable efforts to keep an appropriate level of continuity but may replace its Alliance Manager at any time upon written notice to the other Party.

3.2 Joint Steering Committee.

3.2.1 **Formation**. No later than [****] after the Effective Date, the Parties will establish a joint steering committee (the "**JSC**") to monitor and coordinate the Exploitation of the Blueprint Compounds and the Licensed Products in the Territory. The JSC will be composed of [****] representatives from each Party (unless otherwise agreed by the Parties) who are fluent in English and who have the appropriate and direct knowledge and expertise and requisite decision-making authority. Each Party may replace any of its representatives on the JSC and appoint a person to fill the vacancy arising from each such replacement. A Party that replaces a representative will notify the other Party at least [****] prior to the next scheduled meeting of the JSC. Both Parties will use reasonable efforts to keep an appropriate level of continuity in representation. Representatives may be represented at any meeting by another person designated by the absent representative. The JSC will be chaired by one of the representatives ("**JSC Chairperson**") and will rotate between the Parties every 12 months during the Term. The initial JSC Chairperson of the JSC will be a representative of Zai for the period ending [****], and a Blueprint representative will become the JSC Chairperson of the JSC for the next [****] period during the Term. The role of the JSC Chairperson will be to convene and preside at meetings of the JSC and to ensure that the Alliance Managers prepare minutes, but the JSC Chairperson will have no additional powers or rights beyond those held by the other JSC representatives. Each Party's representatives on the JSC will inform and coordinate within their respective organization to enable each Party to fulfill its obligations as agreed upon between the Parties under this Agreement, including within the time frames set forth hereunder.

3.2.2 **Meeting Agendas**. Each Party will disclose to the other Party the proposed agenda items along with appropriate information at least [****] in advance of each meeting of the JSC; *provided* that under exigent circumstances requiring JSC input, a Party may provide its agenda items to the other Party within a shorter period of time in advance of a meeting, or may propose that there not be a specific agenda for a particular meeting, so long as such other Party consents to such later addition of such agenda items or the absence of a specific agenda for such JSC meeting.

3.2.3 **Meetings**. The JSC will hold meetings at such times as it elects to do so, but will meet no less frequently than quarterly, unless otherwise agreed by the Parties. All meetings

will be conducted in English. The JSC may meet in person or by means of teleconference, internet teleconference, videoconference, or other similar communication method; *provided* that, [****] meeting each Calendar Year will be conducted in person at a location selected alternatively by Blueprint and Zai or such other location as the Parties may agree. Each Party will be responsible for all of its own costs and expenses of participating in any JSC meeting. The Alliance Managers will jointly prepare and circulate minutes for each JSC meeting within [****] after each such meeting and will ensure that such minutes are reviewed and approved by their respective companies within [****] thereafter.

3.2.4 **JSC Roles and Responsibilities**. The responsibilities of the JSC will be to:

(a) provide a forum for the discussion of the Parties' activities under this Agreement;

(b) review, discuss, and determine whether to approve the initial list of Preapproved Subcontractors and any updates thereto, as described in Section 2.2.3 (Right to Subcontract);

(c) oversee the JPTs and establish and oversee Working Groups as necessary or advisable to further the purpose of this Agreement and settle any disputes that arise within any JPT or Working Groups, as described in Section 3.6.2 (Resolution of JPT and Working Group Disputes);

(d) oversee the implementation of, and the coordination between the Parties of activities to be performed under, the Clinical Supply Agreement, the Commercial Supply Agreement, the Safety Agreements, and any other written agreement between the Parties with respect to the subject matter hereof;

(e) review, discuss, and determine whether to approve each Manufacturing Technology Transfer Plan, as described in Section 4.2 (Manufacturing Technology Transfer);

(f) review, discuss, and determine whether to approve any change in the scope of Manufacturing activities to be transferred to Zai in connection with the Manufacturing Technology Transfer for any Blueprint Compound and any updates or amendments thereto, as described in Section 4.2 (Manufacturing Technology Transfer);

(g) review, discuss, and determine whether to approve the [****] PRC Submission Estimated Timeline for each Licensed Product and each update thereto for each Licensed Product, in each case, as described in Section 5.6.2 (Amendments and Obligations);

(h) review, discuss, and determine whether to approve the initial Territory-Specific Development Plan for each Licensed Product and each update thereto, in each case, as described in Section 5.4 (Territory-Specific Development Plans);

(i) review and discuss the initial Global Development Plan for each Licensed Product and each update thereto for any Licensed Product, in each case, as described in Section 5.1 (Global Development Plan);

(j) review, discuss, and determine whether to approve allocation to Zai of any new or additional activities under the Global Development Plan, including any additional Committed Trials proposed by Blueprint, as described in Section 5.1 (Global Development Plan);

(k) review, discuss, and determine whether to approve for Development under this Agreement [****];

(l) review, discuss, and determine whether to approve any New Development Proposal, and review, discuss, and determine whether to approve any New Territory-Specific Development Activities, in each case, as described in Section 5.9 (New Development Proposed by Zai);

(m) review, discuss, and determine whether to approve the regulatory strategy for the Territory with respect to each Licensed Product and each update thereto, as described in Section 6.1 (Regulatory Strategy);

(n) review and discuss Zai's plan for undertaking additional regulatory activities for any Licensed Product delegated by Blueprint or the JSC to Zai, as described in Section 6.2.1 (Obtaining and Maintaining Regulatory Approvals);

(o) review, discuss, and determine matters that may have a material adverse impact upon the regulatory status of the Licensed Products pursuant to Section 6.7 (No Harmful Actions);

(p) discuss and determine whether to approve [****];

(q) review, discuss, and determine whether to approve each Medical Affairs Plan and each update thereto, as described in Section 8.1 (Medical Affairs Plans);

(r) review, discuss, and determine whether to approve each Commercialization Plan and each update thereto, as described in Section 9.2 (Commercialization Plans);

(s) determine whether a Product Mark is not appropriate for the Territory due to linguistic reasons or market research showing that such Product Mark is not appropriate, and review and comment on any alternative Product Marks selected by Zai, in each case, as described in Section 14.9.2 (Product Marks in the Territory);

(t) review, discuss, and determine whether to approve any brand strategy for a Licensed Product that is specific to the Territory (or any region therein) and that is inconsistent with the Global Brand Strategy for such Licensed Product, as described in Section 9.2 (Commercialization Plans);

(u) review, discuss, and determine whether to approve any alternative Licensed Product-specific trademark selected by Zai in accordance with Section 14.9.2 (Product Marks in the Territory); and

(v) perform such other functions as expressly set forth in this Agreement or allocated to the JSC by the Parties' written agreement.

3.3 Joint Project Teams.

3.3.1 **Formation; Composition; Meetings**. No later than [****], the Parties will form one or more joint project teams to coordinate and oversee the day-to-day performance of the activities and obligations of the Parties under this Agreement related to the Exploitation of each Blueprint Compound and the corresponding Licensed Products (each, a "**JPT**"). Each JPT will be composed of representatives from each Party who have direct knowledge and expertise in each of the following functional areas (as applicable depending on the stage of the applicable Licensed Products): clinical, clinical operations, pharmaceutical and biologic product development (including Companion Diagnostics, to the extent applicable), regulatory, safety, manufacturing, intellectual property, marketing, and commercial, in each case, as such functional areas relate to products similar to the applicable Licensed Product. Initially, only one JPT will be formed for all Licensed Products, but the JPT may during the Term elect to form separate JPTs for one or more Licensed Products. Each Party may replace any of its representatives on a JPT and appoint a person to fill the vacancy arising from each such replacement. A Party that replaces a representative will notify the other Party at least [****] prior to the next scheduled meeting of the applicable JPT. An individual may serve on more than one JPT and each Party will use reasonable efforts to keep an appropriate level of continuity in representation. Representatives may be represented at any meeting by another person designated by the absent representative. Each Party's representatives on the JPT will inform and coordinate within their respective organization to enable each Party to fulfill its obligations within the time frames as agreed upon between the Parties under this Agreement. Each JPT will be chaired by one of the representatives ("**JPT Chairperson**") and will rotate between the Parties every [****] during the Term. The initial JPT Chairperson of each JPT will be a representative of Blueprint for the period [****] and a Zai representative will become the JPT Chairperson of each JPT for the next [****] period during the Term. Each JPT will meet as frequently as, and will operate as, the JSC may determine [****]. The role of the JPT Chairperson will be to convene and preside at meetings of the applicable JPT and to ensure that the Alliance Managers prepare minutes, but the JPT Chairperson will have no additional powers or rights beyond those held by the other JPT representatives. The JPTs may meet in person or by means of teleconference, Internet conference, videoconference, or other similar communications method, and the JPT for each Blueprint Compound and corresponding Licensed Products may hold meetings at the same time as one or more other JPTs if agreed by the Parties. All meetings of each JPT will be held in English. Each JPT and its activities will be subject to the oversight of, and will report to, the JSC. In no event will the authority of any JPT exceed the authority of the JSC. Each Party will be responsible for all of its own costs and expenses of participating in the JPTs. The Alliance Managers will jointly prepare and circulate minutes for each JPT meeting within [****] after each such meeting and will ensure that such minutes are reviewed and approved by their respective companies within [****] thereafter.

3.3.2 **JPT Roles and Responsibilities**. The responsibilities of the JPT will be to:

(a) oversee the day-to-day performance of the activities and obligations of each Party under this Agreement related to the Exploitation of each Blueprint Compound and Licensed Product;

(b) discuss and develop the Manufacturing Technology Transfer Plan for each Blueprint Compound, as described in Section 4.2 (Manufacturing Technology Transfer);

(c) review and discuss updates of any Blueprint Know-How related to any Blueprint Compound or Licensed Product developed by Blueprint or its Affiliates or licensees since the previous meeting, as described in Section 4.3 (Continuing Know-How Transfer);

(d) review, discuss, and submit to the JSC the [****] PRC Submission Estimated Timeline for each Licensed Product and each update thereto for each Licensed Product, as described in Section 5.6.2 (Amendments and Obligations);

(e) review, discuss, provide comments on, and submit to the JSC the Territory-Specific Development Plan for each Licensed Product, and each update thereto, as described in Section 5.4 (Territory-Specific Development Plans);

(f) review, discuss, and determine whether to approve the inclusion of any Non-Clinical Development in the Territory-Specific Development Plan for a Licensed Product, as described in Section 5.7 (Non-Clinical and Preclinical Studies);

(g) review and discuss the Global Development Plan for each Licensed Product, and each update thereto, as described in Section 5.1 (Global Development Plans);

(h) discuss, develop, and submit to the JSC the Global Development Plan for any Proposed Blueprint/Zai Combination, as described in Section 5.8.1 (Proposed Blueprint/Zai Combinations);

(i) review, discuss, provide comments on, and submit to the JSC any update to the Territory-Specific Development Plan for any Licensed Product that includes any New Territory-Specific Development Activities that have been approved by the JSC, as described in Section 5.9.1(a) (JSC Approval);

(j) discuss, develop, and submit to the JSC the regulatory strategy for the Territory for each Licensed Product, as described in Section 6.1 (Regulatory Strategy);

(k) review and monitor the Parties' compliance with the Safety Agreements, as described in Section 6.5.1 (Safety Agreements);

(l) review and monitor the Parties' compliance with and performance under the Clinical Supply Agreement, the Commercial Supply Agreement, and any other written agreement between the Parties with respect to the subject matter hereof, and review and discuss Manufacturing of the Licensed Products by each Party for the Territory;

(m) review, discuss, and comment on the Medical Affairs Plan for each Licensed Product and each update thereto, as described in Section 8.1 (Medical Affairs Plans);

(n) review and discuss each report provided by Zai of the Medical Affairs activities performed by or on behalf of Zai in the Territory for each Licensed Product, as described in Section 8.3 (Medical Affairs Reports);

(o) review, discuss, and comment on the Commercialization Plan for each Licensed Product and each update thereto, as described in Section 9.2 (Commercialization Plans);

(p) review and discuss each report provided by Zai of the Commercialization activities performed by or on behalf of Zai in the Territory for each Licensed Product, as described in Section 9.4 (Commercialization Reports);

(q) coordinate activities between the Parties with respect to certain Commercialization and Medical Affairs activities for the Licensed Products inside and outside of the Territory, as described in Section 8.4 (Coordination of Medical Affairs Activities) and Section 9.5 (Coordination of Commercialization Activities; Blueprint Support), respectively;

(r) raise matters for which the JPT is responsible to the JSC for discussion or resolution as appropriate; and

(s) perform such other functions as expressly set forth in this Agreement or allocated to JPT by the Parties' written agreement or by the JSC.

3.4 Working Groups. From time to time, the JSC may establish joint working groups (each, a "**Working Group**") on an "as-needed" basis to oversee specific functional areas or activities and coordinate the day-to-day performance of such activities under this Agreement, which establishment of Working Groups will be reflected in the minutes of the meetings of the JSC. Each such Working Group will have at least two representatives of each Party and will be otherwise constituted, will meet as frequently as, and will operate as the JSC may determine. Working Groups may meet in person or by means of teleconference, Internet conference, videoconference, or other similar communications method. Each Working Group and its activities will be subject to the oversight of, and will report to, the JSC. In no event will the authority of any Working Group exceed the authority of the JSC. Each Party will be responsible for all of its own costs and expenses of participating in any Working Group. The Alliance Managers will jointly prepare and circulate minutes for each Working Group meeting within [****] after each such meeting and will ensure that such minutes are reviewed and approved by their respective companies within [****] thereafter.

3.5 Non-Member Attendance. Each Party may from time to time invite a reasonable number of participants, in addition to its representatives, to attend a meeting of the JSC (in a non-voting capacity), a JPT, or any Working Group if such participants have expertise that is relevant to the planned agenda for such JSC, JPT, or Working Group meeting; *provided that* if either Party intends to have any Third Party (including any consultant) attend such a meeting, then such Party will provide prior written notice to the other Party reasonably in advance of such meeting and will ensure that such Third Party is bound by obligations of confidentiality and non-use at least as stringent as those set forth in Article 11 (Confidentiality; Publication). Notwithstanding anything to the contrary set forth in this Agreement, if the other Party objects in good faith to the participation of such Third Party in such meeting due to a *bona fide* concern regarding competitively sensitive information that is reasonably likely to be discussed at such meeting *(i.e.*, a consultant that also provides services to a Third Party with a Competitive Product), then such Third Party will not be

permitted to participate in such meeting (or the portion thereof during which such competitively sensitive information is reasonably likely to be discussed).

3.6 Decision-Making.

3.6.1 **General Process**. The JSC, the JPTs, and any Working Group will only have the powers expressly assigned to it in this Article 3 (Governance) and elsewhere in this Agreement and will not have the authority to: (a) modify or amend the terms of this Agreement; or (b) waive either Party's compliance with the terms of this Agreement. All decisions of the JSC, a JPT, and any Working Group will be made by unanimous vote, with each Party's representatives having one vote (*i.e.*, one vote per Party). No action taken at any meeting of the JSC or any JPT or Working Group will be effective unless there is a quorum at such meeting, and at all such meetings, a quorum will be reached if two voting representatives of each Party are present or participating in such meeting. [****]

3.6.2 **Resolution of JPT and Working Group Disputes**. The JSC will [****] to resolve all disputes that arise within a JPT or any Working Group within [****] after any such matter is brought to the JSC for resolution.

3.6.3 **Decisions of the JSC**. The JSC [****] to promptly resolve any such matter for which it has authority. If [****] the JSC is unable to resolve any such matter referred to it by the JPT or any Working Group or any matter that is within the scope of the JSC's authority or any other disagreement between the Parties that may be referred to the JSC, in each case, within a period of [****], then a Party may refer such matter for resolution in accordance with 3.7.1 (Referral to Executive Officers) to the Chief Executive Officer of Blueprint (or an executive officer of Blueprint designated by the Chief Executive Officer of Blueprint who has the power and authority to resolve such matter) and the Chief Executive Officer of Zai (or an executive officer of Zai designated by the Chief Executive Officer of Zai who has the power and authority to resolve such matter) (collectively, the "**Executive Officers**").

3.7 Resolution of JSC Disputes.

3.7.1 **Referral to Executive Officers**. If a Party makes an election under Section 3.6.3 (Decisions of the JSC) to refer a matter on which the JSC cannot reach a consensus decision for resolution by the Executive Officers, then the JSC will submit in writing the respective positions of the Parties to their respective Executive Officers. The Executive Officers will [****] to resolve any such matter so referred to them [****], and any final decision that the Executive Officers agree to in writing will be conclusive and binding on the Parties.

3.7.2 **Final Decision-Making Authority**. If the Executive Officers are unable to reach agreement on any such matter referred to them [****] after such matter is so referred (or such longer period as the Executive Officers may agree upon), then:

(a) **No Change; Status Quo**. Neither Party will have final decision-making authority [****] and all such matters set forth in the foregoing [****] must be decided by unanimous agreement of the Parties in order to take any action or adopt any change from the then-current *status quo*.

(b) **Zai Decisions**. Except for any decision listed in Section 3.7.2(a) (No Change; Status Quo), Zai will have final decision-making authority with respect to [****]; *provided* that:

(i) [****]; and

(ii) [****].

(c) **Blueprint Decisions**. Except for any decision listed in Section 3.7.2(a) (No Change; Status Quo), Blueprint will have final decision-making authority with respect to [****] *provided* that [****].

3.7.3 **Limitations on Decision-Making**. Notwithstanding any provision to the contrary set forth in this Agreement, without the other Party's prior written consent, no decision of the JSC or a Party's Executive Officer (in the exercise of a Party's final decision-making authority on any such matters), in each case, may make a decision that could reasonably be expected to (a) result in a [****] in the other Party's obligations, costs, or expenses under this Agreement, or any Global Development Plan or Territory-Specific Development Plan, unless, in each case, such actions are necessary for Blueprint to comply with Applicable Law as the Territory Sponsor or as the owner and holder of any Regulatory Submission, Regulatory Approval, or Reimbursement Approval, as applicable, for a Licensed Product in the Territory, (b) require the other Party to take any action that such other Party [****] would (i) require such other Party to violate any Applicable Law, the requirements of any Regulatory Authority, or any agreement with any Third Party entered into by such other Party or (ii) require such other Party to infringe or misappropriate any intellectual property rights of any Third Party, (c) conflict with, amend, interpret, modify, or waive compliance under this Agreement, or (d) impose any obligation on either Party that would be in violation of such Party's written standard operating procedures, written business policies, or written compliance policies or procedures.

3.8 Discontinuation of JSC. The JSC will continue to exist until the first to occur of (a) the Parties agreeing to disband the JSC, or (b) Blueprint providing written notice to Zai of its intention to disband and no longer participate in the JSC. Once the JSC is disbanded, the JSC will have no further obligations under this Agreement and, thereafter, the Alliance Managers will be the points of contact for the exchange of information between the Parties under this Agreement and any references in this Agreement to decisions of the JSC will automatically become references to decisions by and between the Parties in writing, subject to the other terms of this Agreement and consistent with the terms of Section 3.7.2 (Final Decision-Making Authority).

Article 4
TECHNOLOGY TRANSFERS

4.1 Initial Know-How Transfer. [****] Blueprint will provide and transfer to Zai copies of Blueprint Know-How (other than Blueprint Manufacturing Know-How, the transfer of which will be performed pursuant to Section 4.2 (Manufacturing Technology Transfer)) that exists on the Effective Date to the extent not previously provided to Zai, including data and results required for Zai to file an IND for the Licensed Products, in each case, in the Territory (the "**Initial Know-How Transfer**"). Blueprint may make such Blueprint Know-How available in such reasonable form as Blueprint determines, including, if Blueprint so elects, in the form such Blueprint Know-How is maintained by Blueprint.

4.2 Manufacturing Technology Transfer.

4.2.1 **Initiation of Manufacturing Technology Transfer**. In addition to the Blueprint Know-How provided to Zai pursuant to the Initial Know-How Transfer, unless otherwise agreed by the Parties, on a Blueprint Compound-by-Blueprint Compound basis, upon [****] commencing [****] and ending no later than [****], Blueprint and Zai will jointly develop a draft Manufacturing Technology Transfer Plan for such Licensed Products containing such Blueprint Compound. Notwithstanding the foregoing, Blueprint will have the right to elect to initiate a Manufacturing Technology Transfer with respect to a Blueprint Compound at any time during the Term by developing a draft Manufacturing Technology Transfer Plan for Licensed Products containing such Blueprint Compound.

4.2.2 **Approval of Manufacturing Technology Transfer Plans**. Following development thereof, either Party will submit each Manufacturing Technology Transfer Plan to the JPT to review and discuss, and thereafter to the JSC to review, discuss, and determine whether to approve no later than [****] following either Party's submission to the JPT of each such plan. Blueprint or Zai may propose updates or amendments to any Manufacturing Technology Transfer Plan from time to time, and such updates or amendments will become effective upon approval thereof by the JSC.

4.2.3 **Manufacturing Transfer Plan Requirements**. Unless otherwise agreed by the JSC, each initial Manufacturing Technology Transfer Plan will contemplate the transfer to Zai of, at minimum, all Manufacturing steps that are necessary for Zai to obtain all applicable Regulatory Approvals (including Local Manufacturing Approvals) required to market and sell a locally-Manufactured version of such Licensed Product in the PRC in the name of Zai or its Affiliate. If transfer of the Manufacture [****] of a Blueprint Compound is not [****] for Zai to obtain all applicable Regulatory Approvals (including Local Manufacturing Approvals) required to market and sell a locally-Manufactured version of such Licensed Product in the PRC in the name of Zai or its Affiliate, and Manufacture [****] is not otherwise transferred to Zai under the initial Manufacturing Technology Transfer Plan for such Blueprint Compound, then, if requested by Zai and agreed to by Blueprint, Blueprint will prepare and submit to the JSC for approval, a Manufacturing Technology Transfer Plan for the transfer of Manufacture to Zai [****] of such Blueprint Compound.

4.2.4 **Performance of Manufacturing Technology Transfers**. If the Manufacturing Technology Transfer Plan for a Blueprint Compound contemplates the Manufacturing of the applicable Licensed Product from [****], then Blueprint will supply to Zai each of such [****] in accordance with Article 7 (Manufacturing). [****] Blueprint will perform (or cause one or more applicable Third Parties (including any CMO engaged by Blueprint to Manufacture such Licensed Product) to perform) a Manufacturing Technology Transfer for such Licensed Products containing such Blueprint Compound in accordance with such plan. The Parties will [****] complete the Manufacturing Technology Transfer for Licensed Products containing each Blueprint Compound [****] following the approval of the applicable Manufacturing Technology Transfer Plan pursuant to the applicable Manufacturing Technology Transfer Plan, but in any event [****]. Without limiting the foregoing, the Parties will [****] to complete a Manufacturing Technology Transfer with respect to each Licensed Product [****]. Thereafter during the Term, Blueprint (a) will provide Blueprint Manufacturing Know-How as part of the Continuing Know-How Transfer in accordance with Section 4.3 (Continuing Know-How Transfer) and (b) may transfer additional Manufacturing steps with respect to a Blueprint Compound to Zai by

proposing another Manufacturing Technology Transfer Plan (or an amendment or update to a prior Manufacturing Technology Transfer Plan) to the JSC.

4.3 **Continuing Know-How Transfer**. Following the applicable Manufacturing Technology Transfer for each Blueprint Compound and the Licensed Products containing such Blueprint Compound and the Initial Know-How Transfer for each Licensed Product, Blueprint will provide to the JPT in advance of its meeting [****] a summary of any additional Blueprint Manufacturing Know-How and other Blueprint Know-How, in each case, developed by Blueprint or its Affiliates or licensees since the previous quarterly summary that was provided to the JPT. Upon Zai's reasonable request during the Term, Blueprint will (a) make available to Zai all Blueprint Manufacturing Know-How and other Blueprint Know-How, in each case, in Blueprint's possession and not previously provided to Zai hereunder and that is necessary or reasonably useful for Zai's Exploitation of any Blueprint Compound or Licensed Product (as applicable) in accordance with this Agreement, (b) provide a schedule of applicable Blueprint Manufacturing Patent Rights following delivery of a Manufacturing Technology Transfer Plan, (c) transfer any such Blueprint Know-How or Blueprint Manufacturing Know-How, or provide such schedule, to Zai no later than [****] after Zai's request therefor, and (d) [****] after the Initial Know-How Transfer or Manufacturing Technology Transfer for a Blueprint Compound or Licensed Product (as applicable), provide Zai with reasonable access to Blueprint personnel involved in the Development or Manufacture of such Blueprint Compound or Licensed Product (as applicable) (and the corresponding Blueprint Compound), either in-person at Blueprint's facility or by teleconference (the "**Continuing Know-How Transfer**," and together with the Initial Know-How Transfer and the Manufacturing Technology Transfer, the "**Technology Transfers**"). Zai may only use the Blueprint Know-How to perform its obligations or exercise its rights under this Agreement and in accordance with the terms hereof. Notwithstanding anything to the contrary set forth in this Agreement, the terms of this Section 4.3 (Continuing Know-How Transfer) will not apply to any data or results of any Global Clinical Trial (including a Global Clinical Trial for a Licensed Product in a New Indication or for a Combination Product or Combination Regimen) unless [****]

4.4 **Conduct of Technology Transfer**. Blueprint personnel will not be obligated to travel to Zai's (or its designee's) facilities in connection with the performance of any Technology Transfer. Any materials provided by Blueprint to Zai in connection with the transfer of Blueprint Know-How (including pursuant to any Technology Transfer) will remain the sole property of Blueprint.

4.5 **Technology Transfer Costs**. Blueprint will provide consultation and assistance with qualified personnel in connection with the Technology Transfer for each Blueprint Compound and the Licensed Products containing such Blueprint Compound as reasonably requested by Zai, subject to personnel availability. Blueprint will be responsible for the internal costs of up to [****] of such consultation and assistance for each Blueprint Compound. Zai will reimburse Blueprint for (a) internal costs (at the FTE Rate) in excess of [****] of such consultation and assistance for each Blueprint Compound and (b) all out-of-pocket costs, in each case ((a) and (b)), reasonably incurred by or on behalf of Blueprint in connection with such assistance within [****] after receiving Blueprint's invoice therefor.

Article 5
DEVELOPMENT PROGRAM

5.1 **Global Development Plan**. The global Development of Licensed Products that involves activities both inside and outside of the Territory will be conducted pursuant to a written Development plan (as updated from time to time in accordance with this Section 5.1 (Global Development Plan), the "**Global Development Plan**"). The initial Global Development Plan has been agreed by the Parties

in writing on or prior to the Effective Date and is attached hereto as **Schedule 5.1** (Global Development Plan). [****] With respect to the Licensed Products, the Global Development Plan will be consistent with the overall global development synopsis for each such Licensed Product provided by Blueprint to Zai prior to the Effective Date, and will include, as applicable to each Licensed Product, all Global Clinical Trials (including Clinical Trials that Blueprint has determined will include trial sites both inside and outside of the Territory) for the Licensed Products. Zai will support the global Development of each Licensed Product by conducting certain Development activities in the Territory as set forth in, and in accordance with, the Global Development Plan, including by satisfying the enrollment requirements for the Committed Trials as required under Section 5.2 (Enrollment in Global Clinical Trials). The Global Development Plan will include for each Licensed Product [****]. From time to time, Blueprint (or the JPT, with respect to any Blueprint/Zai Combination) may make and implement updates to the then-current Global Development Plan for one or more Licensed Products, including to contemplate the conduct of the Development of any Licensed Product for a New Indication or a new Combination Product or Combination Regimen. To the extent such amendments (i) are [****], and (ii) include activities to be conducted in the Territory, Blueprint will submit such proposed updates to the JSC for review and discussion before adopting such updates, *provided, however*, that if the updates to the Global Development Plan include [****] in the Territory, including any additional proposed Committed Trials, then such update must be approved by the JSC.

5.2 Enrollment in Committed Trials.

5.2.1 **Enrollment in Committed Trials**. Zai will, in accordance with the Global Development Plan for each Licensed Product, enroll and treat [****].

5.2.2 **Failure to Satisfy Patient Commitments**. On a Committed Trial-by-Committed Trial basis, unless the Parties otherwise agree in writing, if Zai fails to enroll the Patient Commitment in such Committed Trial, other than due to [****] then Zai will reimburse Blueprint for [****]. Zai will pay each Shortfall Reimbursement to Blueprint within [****] after receiving Blueprint's invoice therefor. For example, [****].

5.2.3 **Enrollment of Additional Patients in Committed Trials**. If requested by Blueprint for one or more Committed Trials and agreed to by Zai, then Zai will enroll and treat additional patients in each such Committed Trial in excess of the Patient Commitment and Blueprint will reimburse Zai for [****]. Blueprint will pay each Excess Enrollment Reimbursement to Zai within [****] after receiving Zai's invoice therefor. For example, [****]

5.2.4 **Data Access Criteria**. Subject to the terms of this Agreement, Blueprint and Zai will share in a timely fashion and allow the other Party to utilize data generated from each Party's on-going and future Clinical Trials and Regulatory Submissions for all Indications for the Licensed Products, including as set forth in Section 4.3 (Ongoing Know-How Transfer), Section 5.16 (Development Reports), Section 5.17 (Data Exchange and Use), and Section 6.4 (Right of Reference). [****] If Zai does not satisfy the criteria set forth in the foregoing clause (a) or (b), then Zai will not have any rights with respect to any data or results generated from such Global Clinical Trial for such Licensed Product, including pursuant to Section 4.3 (Ongoing Know-How Transfer), Section 5.17 (Data Exchange and Use) or pursuant to Section 6.4 (Right of Reference), except as necessary for Zai to comply with Applicable Law or safety reporting requirements of the applicable Regulatory Authorities in the Territory [****].

5.3 **Zai Decision to Use a CRO**. If Zai decides to engage a Development Subcontractor to perform one or more Clinical Trials with respect to Licensed Products in the Territory assigned to Zai under the Global Development Plan on Zai's behalf, then, if applicable, Zai will [****] engaging a local Affiliate of the same contract research organization that Blueprint has engaged or plans to engage, in each case, to perform such Clinical Trials outside of the Territory (including if such Clinical Trial is a Committed Trials).

5.4 **Territory-Specific Development Plans**. Except for the activities allocated to Zai under the Global Development Plan for a Licensed Product pursuant to Section 5.1 (Global Development Plan), all Development of each Licensed Product in the Territory under this Agreement will be conducted pursuant to a written development plan for each such Licensed Product (each, as updated from time to time in accordance with this Section 5.4 (Territory-Specific Development Plans) and Section 3.2 (Joint Steering Committee), a "**Territory-Specific Development Plan**"). At least [****] prior to Zai's planned initiation of any Development activities for a Licensed Product in the Territory that are not contemplated under the Global Development Plan, Zai will provide the applicable JPT with an initial draft of the Territory-Specific Development Plan for such Licensed Product for the JPT's review and comment. Each such Territory-Specific Development Plan will contain [****] (a) [****], (b) all major Clinical Development activities for such Licensed Product and all Territory-Specific Clinical Trials and the trial design thereof, in each case, to be conducted solely in furtherance of obtaining Regulatory Approval of such Licensed Product in the Territory (and not outside of the Territory) for the upcoming [****] period, (c) [****] timelines for achieving such activities described in (a) and (b), and (d) [****] key elements involved in obtaining Regulatory Approval of such Licensed Product from all applicable Regulatory Authorities throughout the Territory and the regulatory strategy for each Licensed Product for the Territory approved by the JSC pursuant to Section 6.1 (Regulatory Strategy). Each Territory-Specific Development Plan will include all Clinical Development required to obtain and maintain Regulatory Approval for the applicable Licensed Product in each region of the Territory. Zai will take the applicable JPT's comments [****] and incorporate such comments where appropriate prior to finalizing the initial Territory-Specific Development Plan for each Licensed Product. From time to time thereafter, [****] to include any New Territory-Specific Development Activities, Zai will propose updates to each Territory-Specific Development Plan in consultation with Blueprint through the applicable JPT and submit each initial Territory-Specific Development Plan and each such proposed updated Territory-Specific Development Plan to the JSC. The JSC will review, discuss, and determine whether to approve the initial Territory-Specific Development Plan for each Licensed Product and each update thereto. Once approved by the JSC, each update to a Territory-Specific Development Plan for a Licensed Product will become effective and supersede the then-current Territory-Specific Development Plan for such Licensed Product.

5.5 **Development Diligence**. Subject to the terms of this Agreement, Zai will be responsible for and will use Commercially Reasonable Efforts to Develop and obtain Regulatory Approval, and, if applicable, Reimbursement Approval, for [****] each Licensed Product that is the subject of a Territory-Specific Development Plan or Global Development Plan in the Field in the Territory. Without limiting the generality of the foregoing, Zai will use Commercially Reasonable Efforts to [****].

5.6 **PRC Submission Estimated Timeline**.

5.6.1 **Other Licensed Products**. [****] the Parties have finalized the PRC Submission Estimated Timeline [****], in each case, such PRC Submission Estimated Timeline is included in the initial Global Development Plan. In addition, the JPT will develop a PRC Submission Estimated Timeline for any additional Licensed Products at the appropriate

time. The JPT will submit each such PRC Submission Estimated Timeline to the JSC to review, discuss, and determine whether to approve.

5.6.2 **Amendments and Obligations**. The JPT will update, and will provide to the JSC to review, discuss, and determine whether to approve, the PRC Submission Estimated Timeline for each Licensed Product annually to include in detail the anticipated key regulatory activities for such Licensed Product [****] in the Territory and the dates on which such activities are estimated to occur. Without limiting the obligations set forth in Section 5.5 (Development Diligence), Zai will use Commercially Reasonable Efforts to: (a) make all Regulatory Submissions to the NMPA pursuant to and in accordance with Section 6.2.1 (Obtaining and Maintaining Regulatory Approvals) for each Licensed Product and in accordance with the applicable PRC Submission Estimated Timeline (as may be amended by the JSC from time to time) [****] and (b) promptly obtain all approvals from the applicable Regulatory Authorities required to dose the first patient with each Licensed Product in Clinical Trials in the Territory.

5.7 Non-Clinical and Preclinical Studies. Blueprint will be responsible for [****] Non-Clinical Development for all Licensed Products, other than specific Non-Clinical Development for any Licensed Product that (a) is required specifically in support of [****] for such Licensed Product in the Territory, which additional Non-Clinical Development will, subject to approval by the JPT [****] be included under the Territory-Specific Development Plan for such Licensed Product or (b) that the JPT otherwise agrees to include in a Territory-Specific Development Plan, and in each case ((a) or (b)), for which Zai will be responsible (such Non-Clinical Development, "**Permitted Zai Non-Clinical Development**"). Notwithstanding any provision to the contrary set forth in this Agreement, in no event will the JPT be permitted to withhold consent to Zai's performance of any specific Non-Clinical Development in the Territory that is required specifically in support of [****] for such Licensed Product in the Territory, unless[****]. Blueprint will provide support and cooperation as reasonably requested by Zai in connection with any such Permitted Zai Non-Clinical Development. In addition, Zai will provide support and cooperation as reasonably requested by Blueprint in connection with any Non-Clinical Development for any Blueprint/Zai Combination that is required to support [****] for such product outside of the Territory. The Party generating data and results (or on whose behalf such data and results are generated) in the course of conducting such Non-Clinical Development for any Licensed Product will provide such data and results to the other Party in accordance with Section 5.17 (Data Exchange and Use).

5.8 Proposed Blueprint/Zai Combination Products.

5.8.1 **Proposed Combinations**. If the JPT wishes to include, under the Global Development Plan, Development of any Blueprint/Zai Combination (each, a "**Proposed Blueprint/Zai Combination**"), then the JPT will develop a Global Development Plan for such Proposed Blueprint/Zai Combination, which plan will include the conduct of a POC Trial for such Proposed Blueprint/Zai Combination and a regulatory strategy for the applicable Proposed Blueprint/Zai Combination and the conduct those Clinical Trials contemplated in such Global Development Plan. Thereafter, the JPT will submit such plans, along with details regarding the scope of intellectual property rights relating to the applicable Active Ingredient Controlled by Zai or its Affiliates that will be licensed or sublicensed (as applicable) to Blueprint (where any license for Blueprint to obtain any right to any Zai Product beyond the conduct of Clinical Trials in accordance with this Section 5.8.1 (Proposed Combinations) will only be as contemplated under an agreement or amendment to this Agreement entered into by the Parties pursuant to Section 5.8.2 (Further

Exploitation of Proposed Blueprint/Zai Combinations)), to the JSC for its review, discussion, and approval.

(a) **JSC Approval**. If the JSC approves the Development under this Agreement of the applicable Proposed Blueprint/Zai Combination under the Global Development Plan, then [****].

(b) **No JSC Approval**. If the JSC does not approve the Development under this Agreement of a Proposed Blueprint/Zai Combination, then such Proposed Blueprint/Zai Combination will not be a Blueprint/Zai Combination for purposes of this Agreement and the Parties may not Exploit such Proposed Blueprint/Zai Combination under this Agreement unless and until the JSC approves the Development such Proposed Blueprint/Zai Combination hereunder.

5.8.2 **Further Exploitation of Proposed Blueprint/Zai Combinations**. If the JSC determines to approve the conduct of a Pivotal Trial as a Global Clinical Trial for any Blueprint/Zai Combination that was a Proposed Blueprint/Zai Combination approved by the JSC pursuant to Section 5.8.1 (Proposed Blueprint/Zai Combinations), then:

(a) the JSC will determine which Party will conduct such Pivotal Trial as a Global Clinical Trial;

(b) following completion [****];

(c) (i) Zai will not be required to grant any license to Blueprint to seek Regulatory Approval for, or Commercialize the Zai Product included in such Blueprint/Zai Combination, and (ii) Blueprint will not be required to grant any license to Zai to seek Regulatory Approval for, or Commercialize, the Blueprint Compound included in such Blueprint/Zai Combination, in each case ((i) and (ii)), unless the Parties reach agreement on the terms and conditions for such commercial arrangement under this Section 5.8.2 (Further Exploitation of Proposed Blueprint/Zai Combinations);

(d) notwithstanding any provision to the contrary set forth in this Agreement, no license will be deemed to have been granted to Blueprint or its Affiliates or (sub)licensees to Exploit any Zai Product, except that the license grant to Blueprint under Section 2.3 (License Grants to Blueprint) will include the right to Develop Blueprint/Zai Combinations solely through POC Trials if approved by the JSC pursuant to Section 5.8.1 (Proposed Combinations);

(e) the Parties will [****] reach agreement on such commercial arrangement prior to commencement of such Pivotal Trial or any further Development of such Blueprint/Zai Combination after completion of the POC Trial for such Blueprint/Zai Combination; and

(f) neither Party will conduct further Development or other Exploitation of the applicable Blueprint/Zai Combination inside or outside of the Territory, unless and until the Parties enter into a written agreement setting forth such terms as described above in Section 5.8.2(a) through Section 5.8.2(c).

5.9 **New Development Proposed by Zai**. Notwithstanding Zai's final decision-making authority with respect to Development activities for a Licensed Product that are Territory-specific as set forth in Section 3.7.2(b) (Zai Decisions), if [****], then, in either case ((a) or (b)), Zai will present to the JSC to review, discuss, and determine whether to approve, a proposal to add such Development activities for such New Indication or such New Combination to the Territory-Specific Development Plan for the applicable Licensed Product, including the regions in the Territory in which such activities would be conducted (a "**New Development Proposal**"). Each New Development Proposal will describe [****] the applicable Non-Clinical Development and Clinical Trials that Zai desires to conduct with respect to such New Indication or such New Combination, including [****] (the "**New Development Activities**"), as well as [****] anticipated to result from such New Development Activities, and [****].

5.9.1 **JSC Decision Regarding New Development Activities**. The JSC will review, discuss, and determine whether to approve a New Development Proposal within [****] after receipt thereof from Zai.

(a) **JSC Approval**. If the JSC approves a New Development Proposal, then upon such an approval, (i) the New Development Activities set forth in such New Development Proposal will be "**New Territory-Specific Development Activities**" for purposes of this Agreement, and (ii) the JPT will update the Territory-Specific Development Plan for such Licensed Product to include such New Territory-Specific Development Activities for those regions in the Territory agreed by the JSC, including the proposed timelines, in each case, for such New Development Activities set forth in such New Development Proposal (as may be amended by the JSC upon such approval). Any New Territory-Specific Development Activities included in a Territory-Specific Development Plan pursuant to this Section 5.9.1(a) (JSC Approval) will be Development activities for all purposes under Section 5.5 (Development Diligence).

(b) **No JSC Approval**. If the JSC fails to approve a New Development Proposal, then upon such a failure, the New Development Activities proposed in the New Development Proposal will not be included in any Territory-Specific Development Plan and Zai will not perform any such New Development Activities.

5.10 **Standard of Conduct**. Each Party will perform, and will cause its Affiliates, sublicensees (or Sublicensees, as applicable), and subcontractors (or Subcontractors, as applicable) to perform, all Development activities for the Licensed Products under this Agreement (including under each Territory-Specific Development Plan and each Global Development Plan and any New Territory-Specific Development Activities) in good scientific manner, in a timely, professional manner, and in compliance with the applicable Territory-Specific Development Plan or Global Development Plan, as applicable, in accordance with GLP, cGMP, and GCP, as applicable, and in compliance with Applicable Law and with applicable FDA and EMA requirements to the extent necessary for the submission of data generated from such activities in Regulatory Submissions in the U.S. and the European Union. In addition, each Party will conduct its obligations with respect to any Global Clinical Trial under a Global Development Plan or (with respect to Zai) Territory-Specific Clinical Trial under a Territory-Specific Development Plan (as applicable) in strict adherence with the study design set forth in the applicable protocol therefor and as set forth in such Global Development Plan or such Territory-Specific Development Plan, each as may be amended from time to time, and will comply with each statistical analysis plan implemented by the other Party (as applicable) in connection therewith. Zai will not perform any Development of Blueprint Compounds or Licensed

Products except for those activities set forth in a Territory-Specific Development Plan or set forth in, and allocated to Zai under, a Global Development Plan.

5.11 New Development Proposed by Blueprint. At anytime during the Term, Blueprint may propose additional Committed Trials in addition to those identified on **Schedule 1.60** (Committed Trials) by adding additional Global Clinical Trials for Licensed Products in New Indications or as new Combination Products or Combination Regimens (beyond the Indications, Combination Products, and Combination Regimens contemplated by the then-current Committed Trials) to the Global Development Plan in accordance with Section 5.1 (Global Development Plan).

5.11.1 **Zai Election Not to Sponsor**. If the JSC does not approve the allocation of responsibility to Zai to serve as the Territory Sponsor or regulatory agent in the Territory for, or to otherwise implement in the Territory, such additional Global Clinical Trials added to the Global Development Plan by Blueprint for a Licensed Product for any New Indication or new Combination Product or Combination Regimen (beyond the Indications, Combination Products, and Combination Regimens contemplated by the then-current Committed Trials), then:

(a) **Not A Committed Trial**. The proposed Global Clinical Trial will not be considered a Committed Trial under this Agreement and Zai will not be obligated to implement such Global Clinical Trials in the Territory;

(b) **Right to Develop**. Notwithstanding any provision to the contrary set forth in this Agreement (including the terms of Section 2.1 (License Grant to Zai)), Blueprint will have the right to implement such Global Clinical Trials for such Licensed Product for such New Indication or for such new Combination Product or Combination Regimen globally (including in the Territory) [****]; and

(c) **Zai Assistance**. Zai will provide reasonable assistance to Blueprint to recruit and enroll patients from the Territory for such Global Clinical Trials [****].

5.11.2 **Patient Commitment for Data Access**. If Zai wishes to be granted rights with respect to any data or results generated in such Global Clinical Trials for such Licensed Product for such New Indication or for such new Combination Product or Combination Regimen added to the Global Development Plan by Blueprint (beyond the Indications, Combination Products, and Combination Regimens contemplated by the then-current Committed Trials), including pursuant to Section 4.3 (Continuing Know-How Transfer), Section 5.17 (Data Exchange and Use) or Section 6.4 (Right of Reference), then: (a) each Global Clinical Trial for such Licensed Product for such New Indication or such new Combination Product or Combination Regimen will be considered a Committed Trial for all purposes under this Agreement, (b) Zai will be obligated to satisfy the Patient Commitment with respect to all Global Clinical Trials for such Licensed Product for such New Indication or such new Combination Product or Combination Regimen, and (c) the terms of Section 5.2 (Enrollment in Global Clinical Trials) will apply to all Global Clinical Trials for such Licensed Product for such New Indication or for such new Combination Product or Combination Regimen.

5.12 Development of Co-Formulated Products. Unless otherwise agreed by the Parties, in the course of performing their obligations and exercising their rights under this Agreement, neither Party will (independently or for or with any Third Party) Develop any co-formulated pharmaceutical or biologic product that includes a Blueprint Compound together with any Zai Product.

5.13 Responsibility for Development Costs.

5.13.1 **Territory-Specific Development Costs**. Except as otherwise set forth in this Agreement, [****].

5.13.2 **Global Development Costs**. Except as otherwise set forth in this Agreement, and otherwise subject to Section 5.1 (Global Development Plan), Zai will be responsible for and will pay (a) all Third Party out-of-pocket costs [****] (b) all other costs and expenses [****], (c) costs of [****], and (d) the internal costs (at the FTE Rate) of Blueprint personnel incurred [****]. Blueprint will invoice Zai quarterly for the foregoing costs incurred by or on behalf of Blueprint in such Calendar Quarter, and Zai will pay the undisputed invoiced amounts within [****] after the date of any such invoice.

5.13.3 **Shared Services**. Zai will be responsible for and will pay [****] of the Shared Services Costs incurred by Blueprint in connection with any Committed Trials. Blueprint will invoice Zai quarterly for the foregoing costs incurred by or on behalf of Blueprint in each Calendar Quarter, and Zai will pay the undisputed invoiced amounts within [****] after the date of any such invoice. Blueprint will be responsible for and will pay [****] of the Shared Services Costs incurred by Zai in the performance of any Committed Trials, if any. Zai will invoice Blueprint quarterly for the foregoing costs incurred by or on behalf of Zai in each Calendar Quarter, and Blueprint will pay the undisputed invoiced amounts within [****] after the date of any such invoice.

5.14 Clinical Trial Audit Rights.

5.14.1 **Conduct of Audits**. Upon reasonable notification by Blueprint [****], Blueprint or its representatives may conduct an audit of Zai, its Affiliates, or any Sublicensees, Subcontractors, and all Clinical Trial sites engaged by Zai or its Affiliates or Sublicensees to perform Zai's obligations under any Global Development Plan or Territory-Specific Development Plan, in each case, to ensure that the applicable Global Clinical Trials and Territory-Specific Clinical Trials are conducted in compliance with the applicable Global Development Plan or Territory-Specific Development Plan, GCP, and Applicable Law and meet Blueprint's global Clinical Trial standards provided by Blueprint from time to time during the Term. [****] Blueprint will provide Zai with a written summary of Blueprint's findings of any deficiencies or other areas of remediation that Blueprint identifies during any such audit. Zai will use Commercially Reasonable Efforts to remediate any such deficiencies within [****] following Zai's receipt of such report[****]. Without limiting the foregoing, Zai will have the right to be present at any such audit conducted by Blueprint pursuant to this Section 5.14.1 (Conduct of Audits) of any Sublicensees, Subcontractors, or Clinical Trial sites.

5.14.2 **Deficient Sites and Replacement**. With respect to any Global Clinical Trial or Territory-Specific Clinical Trial, if either Party reasonably determines that any deficiencies with respect to a Clinical Trial site identified pursuant to Section 5.14.1 (Conduct of Audits) (each, a "**Deficient Site**") may cause a Regulatory Authority to reject or otherwise deem deficient the Clinical Trial data from the conduct of any such Global Clinical Trial or Territory-Specific Clinical Trial (as applicable) at such Deficient Site, then such Party will notify the other Party of such Deficient Site and the Parties will discuss and attempt to agree upon a remediation plan for such Deficient Site. If the Parties cannot agree to such a remediation plan for a Deficient Site that is participating in a Global Clinical Trial, then Zai will promptly remove such Deficient Site from the applicable Global Clinical

Trial or Territory-Specific Clinical Trial and replace such Deficient Site with a new Clinical Trial site (a "**Replacement Site**") within the Territory[****] (unless not permitted by Applicable Law or for ethical reasons). Any such Replacement Site will be compliant in all respects with Applicable Law and Blueprint's global Clinical Trial standards.

5.14.3 **Zai Audits**. Zai will provide Blueprint with copies of all quality oversight or audit reports prepared in connection with any audit that Zai or its Affiliates or Sublicensees conduct of any Sublicensee, Subcontractor, or Clinical Trial site that Zai or its Affiliates or Sublicensees have engaged or are evaluating to potentially engage to fulfill Zai's obligations under a Global Development Plan or a Territory-Specific Development Plan no later than [****] after receiving or preparing any such report (as applicable), including English translations thereof. If Blueprint believes in good faith that any such quality oversight or audit report may be necessary in connection with obtaining, supporting, or maintaining one or more Regulatory Approvals for a Licensed Product or for other communications with Regulatory Authorities outside of the Territory, then upon Blueprint's request, Zai will provide a certified translation thereof [****].

5.15 Development Records. Zai will, and will cause its Affiliates, Sublicensees, and Subcontractors to, maintain reasonably complete, current, and accurate records of all Development activities conducted by or on behalf of Zai, and its Affiliates, Sublicensees, and Subcontractors, respectively, pursuant to this Agreement and all data and other information resulting from such activities consistent with its usual practices, in validated computer systems that are compliant with 21 C.F.R. §11 and in accordance with Applicable Law of both the United States and the Territory. [****] Zai will maintain all such records relating to the Development of Licensed Products for a period of [****]. Such records will fully and properly reflect all work done and results achieved in the performance of the Development activities for the Licensed Products in good scientific manner appropriate for regulatory and patent purposes. Zai will document all Non-Clinical Development and Clinical Trials in formal written study reports in accordance with GLP, cGMP, and GCP, as applicable, and in compliance with Applicable Law. Upon Blueprint's reasonable request, not more frequently than [****] during which Zai or its Affiliates, Sublicensees, or Subcontractors are performing or having performed Development activities for any Licensed Product, Zai will, and will cause its Affiliates, Sublicensees, and Subcontractors to, allow Blueprint to access, review, and copy such records (including access to relevant databases). Blueprint will have the right to use the data and results generated by or on behalf of Zai and its Affiliates, Sublicensees, and Subcontractors hereunder to Exploit the Blueprint Compounds and Licensed Products outside of the Territory and to perform Development activities under a Global Development Plan that are allocated to Blueprint thereunder. Each Party will ensure that all records or other documents that it transmits to the other Party electronically under this Agreement are transmitted over secure systems that include adequate encryption safeguards to prevent unauthorized access and maintain data security.

5.16 Development Reports. No later than [****] during which Zai is performing, or having performed, Development activities for any Licensed Product, Zai will provide Blueprint[****] with [****] written reports [****] the Development activities performed during the period since the preceding report, the Development activities in process, and the future activities that Zai or its Sublicensees or Subcontractors expect to initiate, including a summary of the data, timelines, and results of such Development activities. Such reports will be in English. Zai will also establish a secure link that includes adequate encryption safeguards to provide Blueprint with electronic access to, and secure file transfer of, such information. Without limiting the foregoing, such reports will contain sufficient detail to enable Blueprint to assess Zai's compliance with its Development diligence

obligations set forth in Section 5.5 (Development Diligence). Zai will [****] respond to Blueprint's [****] requests from time to time for additional information regarding significant Development activities for any Licensed Product performed by or on behalf of Zai or its Affiliates, Sublicensees, or Subcontractors. The Parties will discuss the status, progress, and results of all Development activities at each JSC meeting. Such reports will be the Confidential Information of Zai and subject to the terms of Article 11 (Confidentiality; Publication).

5.17 Data Exchange and Use. Subject to Section 5.2.4 (Data Access Criteria) and Section 5.8.1(a) (JSC Approval), in addition to its adverse event and safety data reporting obligations set forth in Section 6.5 (Adverse Events Reporting), each Party will [****] provide the other Party with copies of all data and results and all supporting documentation (*e.g.*, protocols, investigator's brochures, case report forms, and analysis plans) Controlled by such Party that are generated by or on behalf of such Party or its Affiliates, Sublicensees, or Subcontractors, if applicable, in the Development of each Licensed Product or any Companion Diagnostic, *provided*, *however*, that Blueprint may decline to receive copies of data and results of Development of a Blueprint/Zai Combination Product or other Combination Product or Combination Regimen. Zai will have the right to use and reference such data and results provided by Blueprint for the purpose of obtaining, supporting, and maintaining Local Manufacturing Approvals, Regulatory Approvals, and any Reimbursement Approval, as applicable, of the Licensed Products and Companion Diagnostics in the Territory, without additional consideration. Blueprint and its designees will have the right to use and reference such data and results provided by Zai for the purpose of obtaining, supporting, or maintaining Regulatory Approval or any Reimbursement Approval, as applicable, of any Licensed Product or Companion Diagnostic (a) outside of the Territory during the Term, or (b) anywhere in the world following termination of this Agreement, in each case ((a) and (b)), without additional consideration.

5.18 Development of Companion Diagnostics. In connection with the Development or Commercialization of any Licensed Product for which the JSC has approved a Territory-Specific Development Plan (as applicable) contemplating the Development of one or more companion diagnostic products to be used in connection with such Licensed Product (each a "**Companion Diagnostic**"), Zai may elect to Develop one or more Companion Diagnostics solely in the Territory. Unless otherwise allocated to Zai under a Global Development Plan for a Licensed Product, Blueprint will be responsible for Developing Companion Diagnostics for Licensed Products if such Companion Diagnostics are to be used with one or more Licensed Products inside and outside of the Territory. If JSC determines that Zai will Develop a Companion Diagnostic for use with the Commercialization of any Licensed Product in the Territory, then Zai will be responsible [****]. Without limiting Zai's reimbursement obligations under Section 5.13 (Responsibility for Development Costs) (which obligations pertain to the Development of each Licensed Product, including the cost to purchase Companion Diagnostics [****] to screen patients in connection with the Development of such Licensed Products), Blueprint will be responsible for [****] Notwithstanding Blueprint's responsibility for [****] if Zai wishes to use any Companion Diagnostic Developed by Blueprint in connection with Zai's Commercialization of any Licensed Product in the Territory, then Zai will reimburse Blueprint for: (a) [****] that are related to the Development of Companion Diagnostics for use with a Licensed Product solely in the Territory [****] and (b) with respect to [****] that are related to the Development of Companion Diagnostics for use [****] the Territory [****].

Article 6
REGULATORY

6.1 Regulatory Strategy. [****] the JPT will discuss and develop a regulatory strategy for the Territory for each Licensed Product and will submit the same to the JSC to review, discuss, and determine whether to approve. From time to time the JPT may update the regulatory strategy for the Territory for any Licensed Product and submit the same to the JSC to review, discuss, and determine whether to approve. Once approved by the JSC, each update to a regulatory strategy for such a Licensed Product will become effective and supersede the then-current regulatory strategy for the Territory for such Licensed Product and such approved regulatory strategy will be included in the Territory-Specific Development Plan. The Parties will reasonably coordinate with respect to the implementation of the regulatory strategy for each Licensed Product in the Territory.

6.2 Zai's Regulatory Responsibilities.

6.2.1 **Obtaining and Maintaining Regulatory Approvals**. Each Party will keep the other Party informed of regulatory developments related to the Licensed Products in each region in the Territory and will promptly notify the other Party in writing of any decision by any Regulatory Authority in the Territory regarding any Licensed Product.

(a) **In the PRC**. Prior to [****], Zai or one of its Affiliates will be responsible for undertaking all regulatory activities and interactions with Regulatory Authorities in the PRC for such Licensed Product in Blueprint's name as the express and authorized regulatory agent of record for Blueprint in the Territory and will take such actions on behalf of and for the benefit of Blueprint in the PRC in accordance with the applicable regulatory strategy approved by the JSC (including performing any and all regulatory activities assigned to Zai in this Agreement or by the JSC during the Term in connection with the Development or Commercialization of a Licensed Product in the Territory). Following [****] Zai or one of its Affiliates will be responsible for all regulatory activities and interactions with Regulatory Authorities in the PRC leading up to and including obtaining (to the extent not already obtained) and thereafter maintaining, Local Manufacturing Approvals, Regulatory Approvals, and any Reimbursement Approvals, as applicable, for such Licensed Product in the PRC in Zai's or its Affiliate's own name in accordance with the applicable regulatory strategy approved by the JSC. Prior to undertaking any such activities and interactions relating to obtaining and maintaining Local Manufacturing Approvals, Regulatory Approvals, or Reimbursement Approvals for any Licensed Product in the PRC, whether prior to or after [****] for the applicable Licensed Product, Zai will submit a [****] plan for undertaking the same to the JSC for review and discussion. Following [****] Zai or one of its Affiliates will continue to be responsible for all regulatory activities and interactions with Regulatory Authorities in the PRC with respect to any imported version of such Licensed Product as the express and authorized regulatory agent of record for Blueprint in the PRC and will continue to take such actions with respect to the imported Licensed Product on behalf of and for the benefit of Blueprint in the PRC in accordance with the applicable regulatory strategy approved by the JSC.

(b) **Obtaining and Maintaining Regulatory Approvals outside the PRC**. Zai will be responsible for all regulatory activities with respect to Licensed Products leading up to and including obtaining, and thereafter maintaining, Regulatory Approvals and any Reimbursement Approvals in all regions of the Territory other than the

PRC in its own name or in the name of its Affiliate, Sublicensee, or Third Party Distributor, in each case, in accordance with the regulatory strategy approved by the JSC.

6.2.2 **Consultation with NMPA**. If Blueprint determines in its reasonable discretion that a consultation meeting with the NMPA may be necessary to conduct any Development of Licensed Products in the Territory contemplated under this Agreement, then at Blueprint's reasonable request, Zai will request a consultation meeting with the NMPA to discuss such Development in advance of commencing such Development. In such event, the Parties will coordinate with each other regarding the contents of any materials to be shared with the NMPA in connection with such meeting.

6.2.3 **Review of Regulatory Submissions**. Zai will provide to Blueprint for review and comment drafts of all Regulatory Submissions in the Territory for the Licensed Products. Zai will incorporate any [****] comments received from Blueprint on such Regulatory Submissions. In addition, each Party will notify the other Party of any Regulatory Submissions for the Licensed Products and any comments or other correspondences related thereto submitted to or received from any Regulatory Authority in the Territory and will provide the other Party with copies thereof as soon as reasonably practicable, but in all events within [****] after submission or receipt thereof (or such longer time period as may be necessary to obtain translations thereof). If any such Regulatory Submission, comment, or correspondence is not in English, then Zai will provide Blueprint with a certified English translation [****] after receipt of such Regulatory Submission, comment, or correspondence[****]. Blueprint will have the right to review and comment on all such Regulatory Submissions, and Zai will [****] and incorporate such comments [****]

6.2.4 **Notice of Meetings**. Each Party will provide the other Party with notice of any meeting or discussion with any Regulatory Authority in the Territory related to any Licensed Product no later than [****] after receiving notice thereof [****] Zai will lead any such meeting or discussion and Blueprint or its designee will have the right, but not the obligation, to attend and participate in any such meeting or discussion unless prohibited or restricted by Applicable Law or Regulatory Authority. At Zai's request, Blueprint will reasonably cooperate with Zai in preparing for any such meeting or discussion. If Blueprint elects not to attend such meeting or discussion, then Zai will provide to Blueprint a written summary thereof in English [****] following such meeting or discussion.

6.2.5 **Zai Responsibility for Costs and Expenses**. Zai will be responsible for all costs and expenses incurred in connection with the performance of all regulatory activities leading up to and including obtaining and thereafter maintaining, Local Manufacturing Approvals, Regulatory Approvals, and any Reimbursement Approvals, as applicable, for each Licensed Product from Regulatory Authorities in the Territory.

6.3 Blueprint's Regulatory Responsibilities. Other than with respect to a locally-Manufactured version of a Licensed Product following [****] therefor (if applicable), Blueprint will own and hold all Regulatory Submissions, Regulatory Approvals, and Reimbursement Approvals, as applicable, for all Licensed Products in the PRC, and upon Zai's reasonable request Blueprint will provide Zai with access to and copies of the applicable Regulatory Submissions, Regulatory Approvals, and Reimbursement Approvals for such Licensed Products in the PRC. Following [****] with respect a locally-Manufactured version of a Licensed Product, Zai will own and hold the Local Manufacturing Approvals, Regulatory Submissions, Regulatory Approvals, and

Reimbursement Approvals, as applicable, for such locally-Manufactured version of such Licensed Product (and any Combination Regimen of which such Licensed Product is a part) in the PRC, and upon Blueprint's reasonable request Zai will provide Blueprint with access to and copies of the applicable Local Manufacturing Approvals, Regulatory Submissions, Regulatory Approvals, and Reimbursement Approvals for such locally-Manufactured version of such Licensed Product (and each Combination Regimen of which it is a part) in the PRC. For clarity, following [****], Blueprint will continue to own and hold the IDL and other Regulatory Submissions, Regulatory Approvals, and other approvals and authorizations in the PRC, as applicable, with respect to imported Licensed Products. Subject to Section 5.2.4 (Data Access Criteria) and Section 5.8.1(a) (JSC Approval), Blueprint will reasonably cooperate with Zai in obtaining any Regulatory Approvals and any Reimbursement Approvals, as applicable, for each Licensed Product in the Territory by providing access to Regulatory Approvals, Regulatory Submissions, clinical data, and other data, information, and documentation for the Licensed Products, both inside and outside of the Territory, in each case, to the extent Controlled by Blueprint. Zai [****] in connection with providing any such access or further assistance to Zai.

6.4 Right of Reference. Subject to Section 5.2.4 (Data Access Criteria) and Section 5.8.1(a) (JSC Approval), each Party will grant, and hereby does grant, to the other Party and its Affiliates, licensees, and Sublicensees a right of reference to all Regulatory Submissions pertaining to the Licensed Products in the Field submitted by or on behalf of such Party or its Affiliates, including any Zai Product as necessary in relation to any Blueprint/Zai Combination. Subject to Section 5.8.1(b) (No JSC Approval), Section 5.8.2 (Further Exploitation of Proposed Additional Blueprint/Zai Combinations that are Blueprint/Zai Combinations), and Section 5.11 (New Development Proposed by Blueprint), Zai and its Affiliates and Sublicensees may use such right of reference to Blueprint's Regulatory Submissions solely for the purpose of seeking, obtaining, supporting, and maintaining Local Manufacturing Approvals, Regulatory Approvals, and any Reimbursement Approvals, as applicable, for the applicable Licensed Product in the Field in the Territory, as Blueprint's authorized regulatory agent of record, or on its own behalf for a locally-Manufactured version of a Licensed Product following [****] for such Licensed Product. Subject to Section 5.8.1(b) (No JSC Approval) and Section 5.8.2 (Further Exploitation of Proposed Additional Blueprint/Zai Combinations that are Blueprint/Zai Combinations), Blueprint and its Affiliates, licensees, and Sublicensees may use such right of reference to Zai's Regulatory Submissions, if any, solely for the purpose of seeking, obtaining, supporting, and maintaining Regulatory Approval and any Reimbursement Approvals of Licensed Products outside of the Territory. Each Party will bear its own costs and expenses associated with providing the other Party with the right of reference pursuant to this Section 6.4 (Right of Reference). Each Party will take such actions as may be reasonably requested by the other Party to give effect to the intent of this Section 6.4 (Right of Reference) and to give the other Party the benefit of the granting Party's Regulatory Submissions in the other Party's territory as provided herein. Such actions may include (a) providing to the other Party copies of correspondence and communications received from the applicable Regulatory Authorities related to such Party's application for Regulatory Approval of the Licensed Products in the Territory or outside of the Territory, as applicable, or (b) providing the other Party with any underlying raw data or information submitted by the granting Party to the Regulatory Authority with respect to any Regulatory Submissions Controlled by such granting Party or its Affiliates that relates to any Licensed Product.

6.5 Adverse Events Reporting.

6.5.1 **Safety Agreements**. [****] the Parties will enter into one or more written agreements setting forth worldwide safety and pharmacovigilance procedures for the Parties with respect to each Licensed Product (each a "**Safety Agreement**"). Each Safety Agreement

will describe the obligations of both Parties with respect to the coordination of collection, investigation, reporting, and exchange of information between the Parties concerning any adverse event experienced by a subject or, in the case of non-clinical studies, an animal in a toxicology study, and the seriousness thereof, whether or not determined to be attributable to any Blueprint Compound or Licensed Product, including any such information received by either Party from a Third Party (subject to receipt of any required consents from such Third Party) and will be sufficient to permit each Party and its Affiliates, licensees, or Sublicensees (as applicable) to comply with its legal obligations with respect thereto, including each Party's obligations as the owner or holder of Regulatory Approvals and Regulatory Submissions for such Licensed Product in the Territory or outside the Territory, as applicable. Each Safety Agreement will also detail each Party's responsibilities with respect to recalls and withdrawals of the applicable Licensed Product inside and outside of the Territory. If required by changes in Applicable Law, then the Parties will make appropriate updates to the applicable Safety Agreements. Each Party will comply with its respective obligations under each Safety Agreement and cause its Affiliates, licensees, and Sublicensees to comply with such obligations. Each Party will notify the other Party of any new planned Clinical Trials for any Licensed Product and the Parties will update the Safety Agreement to the extent necessary to comply with any applicable requirements set forth under Applicable Law or of any Regulatory Authorities related to adverse event reporting, drug safety, patient safety, pharmacovigilance, and risk management. Notwithstanding anything to the contrary in this Agreement or the Safety Agreement, each Party and its Affiliates, licensees, and Sublicensees will have the right to disclose information related to the safety of one or more Blueprint Compounds or Licensed Products to the extent that such disclosure is required for such Party to comply with its obligations under Applicable Law or the safety requirements of the applicable Regulatory Authorities. To the extent that there is a conflict between the terms of this Agreement and the terms of any Safety Agreement, the terms of the applicable Safety Agreement will govern with respect to the subject matter set forth therein.

6.5.2 **Safety Databases**. Zai will maintain a safety database in English for Clinical Trials for the Licensed Products conducted in the Territory under a Territory-Specific Development Plan[****]. During such time that Blueprint is the holder of Regulatory Approvals and Regulatory Submissions for a Licensed Product in the Territory, Zai will be responsible for, on Blueprint's behalf: (a) reporting to the applicable Regulatory Authorities in the Territory all quality complaints, adverse events, and safety data related to such Licensed Product for all Territory-Specific Clinical Trials or Global Clinical Trials conducted in the Territory; and (b) responding to safety issues and to all requests of Regulatory Authorities related to such Licensed Product in the Territory. Zai will provide Blueprint (i) secure, real-time access to Zai's safety database for the Licensed Products in the Territory, and (ii) upon Blueprint's request, query results from Zai's worldwide safety database for each Zai Product solely for the purpose of Developing Blueprint/Zai Combinations. Blueprint will maintain a global safety database for Global Clinical Trials for the Licensed Products conducted under each Global Development Plan [****].

6.5.3 **Notification Obligations**. Without limiting the provisions of Section 6.5.1 (Safety Agreements), Zai will be responsible for complying with all Applicable Law governing adverse events (including the reporting thereof) in the Territory and will comply fully with all applicable adverse event reporting recommendations and requirements in all regions in the Territory where Zai intends to Commercialize the applicable Licensed Product. Zai will notify Blueprint on a timely basis of any adverse events related to one or more

Licensed Products occurring in the Territory. Zai will submit copies of reports of adverse events related to the Licensed Products to Blueprint simultaneously with submission thereof to the applicable Regulatory Authorities in the Territory, including any single case reports, together with an appropriate medical evaluation, as well as aggregate data, such as Periodic Safety Update Reports (PSURs) required by authorities. Each Party will notify the other in a timely manner and in any event [****] (or such shorter period as may be required for a Party to comply with its obligations under Applicable Law) of receiving any (a) serious adverse event reports from Clinical Trials for a Licensed Product that the applicable Party is monitoring, (b) notice from a Regulatory Authority, independent review committee, data safety monitoring board, or another similar clinical trial or post-marketing monitoring body alleging significant concern regarding a patient safety issue related to a Licensed Product, or (c) other material information relevant to the safety or efficacy of any Licensed Product.

6.6 **Regulatory Audits**. In addition to its rights to conduct audits pursuant to Section 5.14 (Clinical Trial Audit Rights), upon reasonable notification, Blueprint or its representatives will be entitled to conduct audits of safety and regulatory systems, procedures, or practices of Zai or its Affiliates, Sublicensees, or Subcontractors (including Clinical Trial sites) relating to any Licensed Product. With respect to any inspection of Zai or its Affiliates, Sublicensees or Subcontractors (including Clinical Trial sites) by any Governmental Authority relating to any Licensed Product, Zai will notify Blueprint of such inspection (a) no later than [****] after Zai receives notice of such inspection [****] or (b) within [****] after the completion of any such inspection of which Zai did not receive prior notice. Zai will promptly provide Blueprint with all information related to any such inspection. To the extent permitted by Applicable Law, Zai will also permit Governmental Authorities outside of the Territory to conduct inspections of Zai or its Affiliates, Sublicensees, or Subcontractors (including Clinical Trial sites) relating to any Licensed Product, and will ensure that all such Affiliates, Sublicensees, and Subcontractors permit such inspections. Blueprint will have the right, but not the obligation (unless required by Applicable Law or any Governmental Authority), to be present at any such inspection. Following any such regulatory inspection related to one or more Licensed Products, Zai will provide Blueprint with (i) an unredacted copy of any findings, notice, or report provided by any Governmental Authority related to such inspection (to the extent related to a Licensed Product) within [****] of Zai receiving the same, and (ii) an English translation of any findings, notice, or report of a Governmental Authority related to such inspection (to the extent related to a Licensed Product) within [****] after receiving the same [****].

6.7 **No Harmful Actions**. If either Party believes that the other Party is taking or intends to take any action with respect to a Licensed Product in such other Party's territory that could [****] of any Licensed Product in such Party's territory, then such Party will have the right to bring the matter to the attention of the JSC and the JSC will [****]. Without limiting the foregoing, unless the Parties otherwise agree (or unless otherwise set forth in this Agreement or in the applicable Global Development Plan), neither Party will communicate with any Regulatory Authority having jurisdiction outside of its respective territory with respect to any Licensed Product, unless for the purpose of seeking Regulatory Approval or so ordered by such Regulatory Authority, in which case, such Party will immediately notify the other Party of such order.

6.8 **Notice of Regulatory Action**. If any Regulatory Authority takes or gives notice of its intent to take any regulatory action with respect to any activity of Zai relating to any Licensed Product, then Zai will notify Blueprint of such contact, inspection, notice, or action within [****] after receipt of such notice (or, if action is taken without notice, within [****] of Zai becoming aware of such action). If any Regulatory Authority takes or gives notice of its intent to take any regulatory action with respect to any activity of Blueprint relating to any Licensed Product that is reasonably likely

to have a material adverse impact on Zai's activities with respect to the Licensed Product in the Territory, then Blueprint will notify Zai of such contact, inspection, notice, or action within [****] after receipt of such notice (or, if action is taken without notice, within [****] of Blueprint becoming aware of such action), *provided* that, except to the extent disclosure is required pursuant to Applicable Law, Blueprint will not be required to disclose any information that is subject to a confidentiality restriction and will not be required to delay any response or action as a result of such notification requirement. Blueprint will have the final decision-making authority with respect to [****], but and will consider Zai's reasonable comments to such responses. Zai will have the final decision-making authority with respect to [****], but will incorporate Blueprint's reasonable comments to any such responses. [****] Upon Zai's request, Blueprint will provide an update on material regulatory actions taken with respect to the Licensed Products outside the Territory at regularly scheduled meetings of the JSC.

6.9 Notice of Other Actions. In addition, each Party will promptly notify the other of any information that it receives regarding any threatened or pending action, inspection, or communication by or from a Third Party that would reasonably be expected to materially affect the Development of the Licensed Products.

Article 7
MANUFACTURING

7.1 Supply by Blueprint.

7.1.1 **Development Supply**. [****] the Parties will enter into a clinical supply agreement for the supply to Zai of Licensed Products containing each Blueprint Compound (together with the corresponding quality agreement, each a "**Clinical Supply Agreement**") pursuant to which Zai will purchase from Blueprint its requirements of each such Licensed Product [****] as necessary for Zai to fulfill its obligations under this Agreement related to the Development of Licensed Products. [****] Pursuant to each Clinical Supply Agreement:

(a) **Sole Supply**. Blueprint will, subject to Section 7.2 (Supply by Zai) and any right for Zai to procure its own supply as set forth in such Clinical Supply Agreement, have the sole right to, either by itself or through a CMO, Manufacture and supply to Zai all Blueprint Compounds and Licensed Products containing such Blueprint Compounds, required by Zai for Development use in the Territory as set forth in a Territory-Specific Development Plan and to perform Zai's Development responsibilities under a Global Development Plan [****].

(b) **Supply Price**. Blueprint will supply the Blueprint Compounds and Licensed Products to Zai pursuant to this Section 7.1.1 (Development Supply) at a transfer price equal to [****], and Zai will pay such invoice, based on a payment schedule to be set forth in the Clinical Supply Agreement and in accordance with Section 7.1.3 (Shipment and Delivery).

7.1.2 **Commercial Supply**. [****] the Parties will enter into a commercial supply agreement (together with the corresponding quality agreement, the "**Commercial Supply Agreement**"), for the supply to Zai of (a) the [****] of each Licensed Product or such other form of such Licensed Product as the JSC may agree, in either case, until [****], and (b) until [****] Licensed Product, pursuant to which Zai will purchase from Blueprint its requirements of the same as necessary for Zai to fulfill its obligations under this

Agreement related to the Manufacture and Commercialization of each Licensed Product in the Territory. Notwithstanding the entrance into any Commercial Supply Agreement, [****]. The Parties may also elect to amend the terms of a Commercial Supply Agreement into which the Parties have entered to contemplate the commercial supply to Zai of one or more additional Licensed Products in lieu of entering into a separate Commercial Supply Agreement for such Licensed Product. [****] Pursuant to all Commercial Supply Agreements for Licensed Products in the Territory:

(a) **Sole Supply**. Subject to Section 7.2 (Supply by Zai) and any right for Zai to procure its own supply as set forth in such Commercial Supply Agreement, Blueprint will have the sole right to, either by itself or through an Affiliate, CMO, or licensee, Manufacture and supply to Zai all such Licensed Products as required by Zai for Commercialization in the Territory in accordance with this Agreement. The Commercial Supply Agreement will [****].

(b) **Supply Price**. Blueprint will supply to Zai pursuant to this Section 7.1.2 (Commercial Supply) each Licensed Product (or Active Ingredient thereof, as applicable) at a transfer price equal to [****]. Blueprint will invoice Zai for such Licensed Products, and Zai will pay such invoice, based on a payment schedule to be set forth in the Commercial Supply Agreement and in accordance with Section 7.1.3 (Shipment and Delivery).

7.1.3 **Shipment and Delivery**. Delivery of all Blueprint Compounds and Licensed Products supplied by Blueprint under any Clinical Supply Agreement or Commercial Supply Agreement will take place [****].

7.2 Supply by Zai.

7.2.1 **Restriction on Manufacturing by Zai**. Zai will not Manufacture or have Manufactured any Blueprint Compound or any Licensed Product that contains such Blueprint Compound until the completion of a Manufacturing Technology Transfer for the applicable Blueprint Compound in accordance with Section 4.2 (Manufacturing Technology Transfer). Notwithstanding any provision to the contrary in this Agreement, unless otherwise subsequently agreed by Blueprint in a Clinical Supply Agreement or Commercial Supply Agreement, or otherwise in writing, in no event will Zai perform any step in the Manufacturing process for any Licensed Product [****].

7.2.2 **Clinical and Commercial Supply**. Following [****], Zai will Manufacture locally-Manufactured Licensed Products in the Territory for Development purposes or commercial use, as applicable, and will be responsible for all Manufacturing steps transferred to Zai under a Manufacturing Technology Transfer Plan, in each case, in the Territory [****]. Zai agrees that Zai's Manufacturing process with respect to each locally-Manufactured Licensed Product will at all times be in accordance with the Zai Specifications for such Licensed Product approved by Blueprint pursuant to Section 7.2.3 (Specifications) and cGMP and ICH Guidelines, and in compliance with Applicable Law.

7.2.3 **Specifications**. Unless the JSC determines that Zai will be granted rights only to package and label, but not otherwise Manufacture, a particular Licensed Product for Development or Commercialization purposes in the Territory, as part of the Manufacturing Technology Transfer for each Blueprint Compound and the Licensed Products containing such Blueprint Compound, Blueprint will provide Zai with Blueprint's written process and

quality specifications for the Manufacturing drug product of such Licensed Product (the "**Blueprint Specifications**"). Zai will prepare written process and quality specifications for the Manufacture of drug product of such Licensed Products applicable to Zai's Manufacturing facilities, systems, processes, and capabilities, including how the foregoing relate to drug substance, drug product, in-process intermediates, raw materials, and reference material (the "**Zai Specifications**"), which Zai Specifications will be consistent in all respects with the Blueprint Specifications for such Licensed Product, unless the requirements of any Regulatory Authority or Applicable Law in the Territory necessitate any deviations from such Blueprint Specifications. Zai will provide to Blueprint all such Zai Specifications (and any subsequent changes thereto) for Blueprint's review, comment and approval. In addition, Zai will promptly provide to Blueprint for its review and approval any changes to the Zai Specifications for any Licensed Product at any time following Blueprint's approval of the Zai Specifications for such Licensed Product, and will provide such proposed amendment to Blueprint for Blueprint's review, comment and approval in accordance with the procedure described below. [****] Blueprint will either (a) approve the Zai Specifications for such Licensed Product (or any changes thereto), or (b) provide Zai with a written response to the Zai Specifications for such Licensed Product (or such changes thereto) that includes a description of any deficiencies or limitations that Blueprint has identified with respect thereto, and the Parties will cooperate to develop a plan for remediation with respect to any such deficiencies or limitations within a reasonable period of time thereafter. Following Zai's remediation of all deficiencies, Zai will provide Blueprint with a revised draft of the Zai Specifications for the applicable Licensed Product (or any subsequent changes to any Zai Specifications) for Blueprint's review and approval. Thereafter, and on a continuing basis for so long as Zai Manufactures a particular Licensed Product, Zai will (i) Manufacture and require its Affiliates and CMOs to Manufacture such Licensed Product is at all times in accordance with the Blueprint-approved Zai Specifications for such Licensed Product and cGMP and ICH Guidelines, and (ii) complete any additional studies or testing required to maintain any qualifications and Regulatory Approvals (including manufacturing licenses) from any Regulatory Authorities or other Governmental Authorities necessary to continue to Manufacture such Licensed Product in the Territory and provide to Blueprint copies of reports from any such additional studies or testing in English[****].

7.2.4 **Second Source of Supply**. Blueprint will have the right at any time during the Term to request that Zai serve as a back-up supplier of one or more Licensed Products for use by Blueprint inside or outside of the Territory. Upon Blueprint's request, and Zai's agreement, following completion of the Manufacturing Technology Transfer with respect to a Blueprint Compound and the Licensed Products containing such Blueprint Compound, Zai will supply such Licensed Products to Blueprint for Blueprint's Exploitation of such Licensed Products outside of the Territory, as a second source of supply, at a price equal to [****].

7.3 Product Tracking in the Territory. Zai will, and will ensure that its Affiliates and Sublicensees, maintain adequate records to permit the Parties to trace the distribution, sale, and use of all Licensed Products to hospitals and pharmacies in the Territory.

Article 8
MEDICAL AFFAIRS

8.1 **Medical Affairs Plans**. [****] Zai will develop and provide an initial draft of the Medical Affairs Plan for such Licensed Product to the JPT for its review and discussion. The Medical Affairs Plan for a Licensed Product will contain a [****] of the major Medical Affairs activities to be undertaken for such Licensed Product in the Territory and the estimated timelines for performing such activities, including all key opinion leaders that Zai plans to engage. The JPT will have the right to comment on each such Medical Affairs Plan and each update thereto, and Zai will consider such comments [****] and incorporate such comments [****] prior to finalizing each such Medical Affairs Plan (or any update thereto). Thereafter, from time to time, [****] Zai will propose updates to the Medical Affairs Plan for each Licensed Product in consultation with the JPT to reflect changes in such plans, including to account for relevant factors that may influence such plan and the Medical Affairs activities set forth therein. Zai submit each initial Medical Affairs Plan and each such proposed updated Medical Affairs Plan to the JSC. The JSC will review, discuss, and determine whether to approve each initial Medical Affairs Plan for each Licensed Product and each update thereto. Once approved by the JSC, each update to a Medical Affairs Plan for a Licensed Product will become effective and supersede the then-current Medical Affairs Plan for such Licensed Product.

8.2 **Conduct of Medical Affairs Activities**. Zai will conduct all Medical Affairs activities for Licensed Products in the Territory in accordance with the applicable Medical Affairs Plan. Zai will not conduct any Medical Affairs activities with respect to Licensed Products except for those activities set forth in an applicable Medical Affairs Plan. Zai will, subject to Applicable Laws, conduct such activities in compliance with its internal policies on engaging and sponsoring healthcare providers.

8.3 **Medical Affairs Reports**. For each Calendar Year following the first Regulatory Approval for a Licensed Product in the Territory, [****] Zai will provide to Blueprint a report (by means of a slide presentation or otherwise) summarizing the Medical Affairs activities performed by or on behalf of Zai and its Affiliates and Sublicensees in the Territory for each Licensed Product in each region in the Territory since the prior report provided by Zai. Such reports will be Confidential Information of Zai and subject to the terms of Article 11 (Confidentiality; Publication). Zai will provide [****] updates [****] to any such report at each meeting of the JSC, JPT, and any Working Group established by the JSC to oversee Medical Affairs activities under this Agreement.

8.4 **Coordination of Medical Affairs Activities**. The Parties recognize that each Party may benefit from the coordination of certain Medical Affairs activities for the Licensed Products inside and outside of the Territory. Accordingly, the Parties will coordinate such activities through the JPT where appropriate, including to ensure that medical information provided by each Party in their respective territories is consistent inside and outside of the Territory. Upon Zai's request, Blueprint will provide an update on Blueprint's material planned key Medical Affairs activities with respect to the Licensed Products outside the Territory at regularly scheduled meetings of the JSC.

Article 9
COMMERCIALIZATION

9.1 **Commercialization Diligence Obligations**. Zai will be solely responsible for and will use Commercially Reasonable Efforts to Commercialize each Licensed Product in each region in the Territory after receiving Regulatory Approval and, if applicable, Reimbursement Approval for such Licensed Product in such region. Zai will conduct all Commercialization of each Licensed Product in the Territory in accordance with the Commercialization Plan for such Licensed Product, at its sole cost and expense. [****]

9.2 **Commercialization Plans**. [****] Zai will develop and provide an initial draft of the Commercialization Plan for such Licensed Product to the JPT for its review and discussion. The Commercialization Plan for a Licensed Product will contain [****] Commercialization activities to be undertaken (including [****]) for such Licensed Product in the Territory and the estimated timelines for achieving such activities. The JPT will have the right to comment on each such Commercialization Plan and Zai will consider such comments [****] and incorporate such comments [****] prior to finalizing each such Commercialization Plan. Thereafter, from time to time, [****] Zai will propose updates to the Commercialization Plan for each Licensed Product in consultation with the JPT to reflect changes in such plans, including those in response to changes in the marketplace, relative commercial success of the applicable Licensed Product, and other relevant factors that may influence such plan and the Commercialization activities set forth therein. Zai will submit each proposed updated Commercialization Plan for a Licensed Product to the JPT for review and discussion and will consider [****] and incorporate [****] any comments thereon provided by the JPT before finalizing any such update. Zai submit each initial Commercialization Plan and each such proposed updated Commercialization Plan to the JSC. The JSC will review, discuss, and determine whether to approve each initial Commercialization Plan for each Licensed Product and each update thereto. Once approved by the JSC, each update to a Commercialization Plan for a Licensed Product will become effective and supersede the then-current Commercialization Plan for such Licensed Product. Each Commercialization Plan for a Licensed Product (including each update thereto) must be consistent with Blueprint's global brand strategy and global key messaging, and Global Brand Elements for such Licensed Product (each, a "**Global Brand Strategy**"), if and as provided to Zai by Blueprint from time to time during the Term; *provided*, *however*, that if the JSC agrees upon brand strategy for a Licensed Product that is specific to the Territory (or any region therein) and that is inconsistent with the Global Brand Strategy for such Licensed Product (including any product positioning or messaging for the Territory or any region therein), then Zai will have the right to implement such Territory-specific brand strategy within the Territory and to incorporate such inconsistent strategies in the Commercialization Plan for such Licensed Product.

9.3 **Conduct of Commercialization Activities**. Zai will conduct all Commercialization of Licensed Products in the Territory in accordance with the applicable Commercialization Plan. Zai will not conduct any Commercialization activities with respect to Licensed Products except for those activities set forth in an applicable Commercialization Plan.

9.4 **Commercialization Reports**. For each Calendar Year following the first Regulatory Approval for a Licensed Product in the Territory, [****] Zai will provide to Blueprint a report [****] summarizing the Commercialization activities performed by or on behalf of Zai and its Affiliates and Sublicensees in the Territory for each Licensed Product in each region in the Territory since the prior report provided by Zai. Each such report will contain sufficient detail to enable Blueprint to assess Zai's compliance with its Commercialization diligence obligations set forth in Section 9.1 (Commercialization Diligence Obligations). Such reports will be Confidential Information of Zai and subject to the terms of Article 11 (Confidentiality; Publication). Zai will provide updates to any such report at each meeting of the JSC, JPT, and any Working Group established by the JSC to oversee Commercialization activities under this Agreement.

9.5 **Coordination of Commercialization Activities**. The Parties recognize that each Party may benefit from the coordination of certain Commercialization activities for the Licensed Products inside and outside of the Territory (other than pricing for the Licensed Products inside and outside of the Territory, the responsibilities for which are set forth in Section 9.6 (Pricing; Reimbursement Approvals)). Accordingly, the Parties will coordinate such activities through the JPT where appropriate, which coordination may include communications regarding product positioning.

9.6 **Pricing; Reimbursement Approvals**. Notwithstanding any provision to the contrary set forth in this Agreement, each Party will have the right to determine the price of the Licensed Products sold in its territory and neither Party will have the right to direct, control, or approve the pricing of the Licensed Products in the other Party's territory. Zai will keep Blueprint timely informed on (a) any [****] changes to the [****] pricing strategies with respect to any Licensed Product in the Territory, and (b) the status of any application for Reimbursement Approval for a Licensed Product in the Territory, including any discussion with any Regulatory Authority with respect thereto.

9.7 **Diversion**. Each Party agrees that it will not, and will ensure that its Affiliates and licensees and subcontractors (or Sublicensees and Subcontractors, as applicable) will not, either directly or indirectly, promote, market, distribute, import, sell, or have sold any Licensed Products to any Third Party or to any address or Internet Protocol address or the like outside of such Party's respective territory, including via the Internet or mail order. Neither Party will engage, and each Party will not permit its Affiliates or Sublicensees to engage, in any advertising or promotional activities relating to any Licensed Products for use directed primarily to customers or other buyers or users of the Licensed Products located in any country or jurisdiction outside of such Party's respective territory, or solicit orders from any prospective purchaser located in any country or jurisdiction outside of such Party's respective territory. If either Party or its respective Affiliates or licensees (or Sublicensees, as applicable) receives any order for any Licensed Products from a prospective purchaser located in a country or jurisdiction outside of such Party's respective territory, then such Party will immediately refer that order to the other Party and will not accept any such orders. Neither Party will, and neither Party will permit its Affiliates, licensees (or Sublicensees, as applicable), or subcontractors (or Subcontractors, as applicable) to, deliver or tender (or cause to be delivered or tendered) any Licensed Products to Third Parties for use outside of such Party's respective territory, except in accordance with a Global Development Plan or Territory-Specific Development Plan, or except in connection with a Manufacturing Technology Transfer pursuant to Section 4.2 (Manufacturing Technology Transfer) and Article 7 (Manufacturing). For purposes of this Section 9.7 (Diversion), (a) Zai's territory will be the Territory and (b) Blueprint's territory will be worldwide except for the Territory.

Article 10
PAYMENTS

10.1 **Upfront Payment**. Within [****] after the Effective Date, Zai will pay to Blueprint by wire transfer of immediately available funds a non-refundable, non-creditable upfront payment of $25,000,000 in U.S. Dollars (the "**Upfront Payment**").

10.2 **Milestone Payments**.

10.2.1 **Development Milestone Events and Payments**. No later than [****] after the earliest achievement of each development milestone event set forth below [****], Zai will pay to Blueprint the corresponding non-refundable, non-creditable development milestone payment set forth below (the development milestone events set forth in Table 10.2.1 the "**Development Milestone Events**" and the development milestone payments set forth in Table 10.2.1 the "**Development Milestone Payments**").

Table 10.2.1 – LICENSED PRODUCT DEVELOPMENT MILESTONES		
	Development Milestone Events For Licensed Products	***Development Milestone Event Payment (in U.S. Dollars)***
[****]	[****]	[****]
[****]	[****]	[****]
[****]	[****]	[****]
[****]	[****]	[****]
[****]	[****]	[****]

[****]

[****]

10.2.2 **Sales Milestone Events and Payments**. On a Licensed Product-by-Licensed Product basis, no later than [****] after the end of the first Calendar Quarter in which each sales milestone event set forth below for such Licensed Product is achieved, Zai will pay to Blueprint with respect to each Licensed Product the corresponding non-refundable, non-creditable sales milestone payment set forth below in Table 10.2.2 (the sales milestone events set forth in Table 10.2.2, the "**Sales Milestone Events**" and the sales milestone payments set forth in Table 10.2.2, the "**Sales Milestone Payments**"). If in a given Calendar Year more than one of the Sales Milestone Events set forth in Table 10.2.2 below is achieved with respect to a particular Licensed Product, then Zai will pay to Blueprint a separate Sales Milestone Payment with respect to each such Sales Milestone Payment that is achieved for the first time in such Calendar Year. For purposes of this Section 10.2.2 (Sales Milestone Events and Payments), (a) Licensed Products containing [****] and (b) Combination Products containing [****].

Table 10.2.2 –SALES MILESTONES FOR LICENSED PRODUCTS		
	Sales Milestone Event	***Sales Milestone Payment (in U.S. Dollars)***
[****]	[****]	[****]

[****]	[****]	[****]
[****]	[****]	[****]
[****]	[****]	[****]
[****]	[****]	[****]

[****]

10.2.3 **Milestone Conditions**.

(a) **Notification of Milestone Events**. Zai will promptly notify Blueprint in writing, but in no event later than (i) [****] after the achievement of each Development Milestone Event and (ii) [****]after the end of the Calendar Quarter in which each Sales Milestone Event is achieved (together with the Development Milestone Events, the "**Milestone Events**"). However, in no event will a failure by Zai to deliver such notice of achievement of a Milestone Event relieve Zai of its obligation to pay Blueprint the corresponding Development Milestone Payment or Sales Milestone Payment (collectively, the "**Milestone Payments**").

(b) **Skipped Milestone Events**. If Zai achieves any of the Development Milestone Events for a particular Licensed Product [****] but without the prior achievement of any corresponding earlier listed Development Milestone Events for such Licensed Product [****], then Zai will pay to Blueprint the applicable Milestone Payment to be made with respect to such earlier Development Milestone Events for such Licensed Product [****] at the same time as Zai pays the applicable Development Milestone Payment due upon achievement of such Development Milestone Event. For example, [****].

(c) **Maximum Milestone Payment Example.** For example: [****].

10.3 Royalty Payments to Blueprint.

10.3.1 **Royalty Rates**. Subject to the remainder of this Section 10.3 (Royalty Payments to Blueprint), Zai will make non-refundable royalty payments to Blueprint, on a Licensed Product-by-Licensed Product basis for Licensed Products sold in the Territory during the applicable Royalty Term, calculated by multiplying the applicable royalty rate set forth below in Table 10.3.1 by [****]. The royalty payments due with respect to Net Sales of each Licensed Product pursuant to this Section 10.3 (Royalty Payments to Blueprint), collectively the "**Royalty Payments**." For purposes of this Section 10.3 (Royalty Payments to Blueprint), (a) Licensed Products [****] and (b) Combination Products [****].

Table 10.3.1 – LICENSED PRODUCT ROYALTY PAYMENTS	
Portion of Aggregate Calendar Year Net Sales of the same Licensed Product in the Territory (in U.S. Dollars)	***Royalty Rate***
[****]	[****]
[****]	[****]
[****]	[****]
[****]	[****]

[****]

10.3.2 **Royalty Term**. Zai will pay to Blueprint the Royalty Payments on a Licensed Product-by-Licensed Product and region-by-region basis beginning on the date of the First Commercial Sale of such Licensed Product in such country or region and lasting until the later of: (a) [****] (b) [****] and (c) [****] ("**Royalty Term**").

10.3.3 **Royalty Reductions**.

(a) **Expiration of Valid Claims.** Subject to Section 10.3.3(c) (Cumulative Reductions Floor), on a Licensed Product-by-Licensed Product and region-by-region basis, if there is no Valid Claim of a Royalty Patent Right that Covers the Licensed Product [****] in such region, then, commencing [****] after the date on which this Section 10.3.3(a) (Expiration of Valid Claims) applies and for all [****] thereafter during which this Section 10.3.3(a) (Expiration of Valid Claims) applies, the applicable royalty rate that would otherwise be owed on such Net Sales of such Licensed Product in such region under Section 10.3.1 (Royalty Payments to Blueprint) will be [****]; *provided* that if such Licensed Product [****] subsequently becomes Covered by a Valid Claim within the Royalty Patent Rights in such region prior to [****], then the applicable royalty rate that would otherwise be owed on such Net Sales of such Licensed Product in such region will no longer be subject to the aforementioned reduction beginning at [****].

(b) **Offset For Third Party Licensing Payments**. Subject to Section 2.6 (Third Party In-Licenses) and Section 10.3.3(c) (Cumulative Reductions Floor), Zai will be entitled to, on a country-by-country basis, credit against the royalties due to Blueprint upon Net Sales of a Licensed Product in such country an amount equal to [****]of the total royalties paid by Zai to Third Parties with respect to license rights to Patent Rights, or Patent Rights together with Know-How, controlled by Third Parties that are necessary to avoid infringement of such Third Party rights in the Territory (i) [****] or (ii) [****].

(c) **Cumulative Reductions Floor**. In no event will the aggregate amount of Royalty Payments due to Blueprint for a Licensed Product in a region in the Territory in any given [****] during the Royalty Term for such Licensed Product in such region be reduced to less than [****] of the amount that otherwise would have been due and payable to Blueprint in such [****] for such Licensed Product in such region but

for the reductions set forth in Section 10.3.3(a) (Expiration of Valid Claims) and Section 10.3.3(b) (Offset For Third Party Licensing Payments).

10.3.4 **Royalty Reports and Payments**. Commencing with the [****] during which the First Commercial Sale of a Licensed Product is made anywhere in the Territory, [****] Zai will provide Blueprint with [****] the amount of royalties payable by Zai for the applicable [****], on a Licensed Product-by-Licensed Product and region-by-region basis (each, a "**Royalty Estimate**"). [****] Zai will provide Blueprint with a detailed report for the applicable [****], on a Licensed Product-by-Licensed Product and region-by-region basis (each, a "**Royalty Report**") containing: (a) the amount of gross sales and Net Sales of each Licensed Product sold by Zai and its Affiliates and Sublicensees in each region and all deductions used to determine such Net Sales of each such Licensed Products for such [****], (b) a calculation of the Royalty Payment due on such Net Sales of each Licensed Product in each region, including any royalty reduction made in accordance with Section 10.3.3(a) (Expiration of Valid Claims) and Section 10.3.3(b) (Offset For Third Party Licensing Payments), (c) the exchange rate used for converting any Net Sales recorded in a currency other than Dollars, (d) any withholding taxes required to be made from such Royalty Payments, and (e) the quantity and description of each Licensed Product sold by Zai or its Affiliate or Sublicensee in each region in the Territory during such [****] comprising such Net Sales, including detailed sales reports for each Licensed Product for [****] in each region in the Territory. Concurrent with the delivery of the applicable Royalty Report, [****], Zai will pay the amount of the Royalty Payments set forth in the applicable Royalty Report to Blueprint in Dollars. If requested by Blueprint, the Parties will seek to resolve any questions or issues related to a Royalty Report within [****] following receipt by Blueprint of each Royalty Report.

10.4 Payments to Third Parties Under Existing Agreements. Each Party will be solely responsible for any payments due to Third Parties under any agreement entered into by such Party prior to the Effective Date.

10.5 Other Amounts Payable. With respect to any amounts owed under this Agreement by one Party to the other for which no other invoicing and payment procedure is specified hereunder, within [****] after the end of each [****], each Party will provide an invoice, together with reasonable supporting documentation, to the other Party for such amounts owed in respect of such [****]. The owing Party will pay any undisputed amounts within [****] of receipt after the invoice, and any disputed amounts owed by a Party will be paid within [****] after resolution of the dispute. As used throughout this Agreement, a disputed amount owed by one Party to the other Party will be considered "undisputed" hereunder following a final, unappealable determination in accordance with Article 16 (Dispute Resolution) that such amount is owed.

10.6 No Refunds. Except as expressly provided herein or in the case of an overpayment of Royalty Payments [****], all payments under this Agreement will be irrevocable, non-refundable, and non-creditable.

10.7 Accounting Standards. If a Party changes its general accounting principles from the then-current standard (*e.g.*, from GAAP to IFRS) at any time during the Term, then at least [****] prior to adopting such change in principles, such Party will provide written notice to the other Party of such change.

10.8 Currency; Exchange Rate. All payments to be made by Zai to Blueprint or Blueprint to Zai under this Agreement will be made in Dollars by electronic funds transfer in immediately available funds

to a bank account designated in writing by Blueprint or Zai, as applicable. Conversion of Net Sales recorded in local currencies will be converted to Dollars at the exchange rate set forth in *Wall Street Journal* or any successor thereto for [****].

10.9 Blocked Payments. If by reason of Applicable Law in any country or region, it becomes impossible or illegal for a Party to transfer, or have transferred on its behalf, payments owed the other Party hereunder, then such Party will promptly notify the other Party of the conditions preventing such transfer and such payments will be deposited in local currency in the relevant country or region to the credit of the other Party in a recognized banking institution designated by the other Party or, if none is designated by the other Party within a period of [****], in a recognized banking institution selected by the transferring Party, as the case may be, and identified in a written notice given to the other Party.

10.10 Late Payments. Any payments or portions thereof due hereunder that are not paid on the date such payments are due under this Agreement will bear interest at a rate equal to the lesser of: (a) [****] as published by *The Wall Street Journal* or any successor thereto on the [****] in which such payments are overdue; or (b) the maximum rate permitted by Applicable Law; in each case, calculated on the number of days such payment is delinquent, compounded monthly.

10.11 Financial Records and Audits. Each Party will maintain complete and accurate records in sufficient detail to permit the other Party to confirm the accuracy of the amount of royalty payments and other amounts payable under this Agreement. Upon reasonable prior notice, such records will be open during regular business hours for a period of [****] from the creation of individual records for examination by an independent certified public accountant selected by the examining Party and reasonably acceptable to the other Party for the sole purpose of verifying for the examining Party the accuracy of the financial reports furnished by the other Party (the "**Examined Party**") pursuant to this Agreement or of any payments made, or required to be made, by such Examined Party pursuant to this Agreement; *provided that* such independent accounting firm is subject to written obligations of confidentiality and non-use applicable to each Party's Confidential Information that are at least as stringent as those set forth in Article 11 (Confidentiality; Publication). Such audit will not be (a) performed more frequently than [****] during the Term or [****] after the expiration or termination of this Agreement, (b) conducted for any Calendar Year [****] after the end of such year, or (c) repeated for any Calendar Year or with respect to the same set of records (unless a material discrepancy with respect to such records is discovered during a prior audit). Such auditor will not disclose the Examined Party's Confidential Information to the examining Party or to any Third Party, except to the extent such disclosure is necessary to verify the accuracy of the financial reports furnished by the Examined Party or the amount of payments by the Examined Party under this Agreement. The Examined Party will pay any amounts shown to be owed to the examining Party but unpaid within [****] after the accountant's report, *plus* interest (as set forth in Section 10.10 (Late Payments)) from the original due date. The examining Party will bear the full cost of such audit unless such audit reveals an underpayment by the Examined Party of [****], in which case the Examined Party will reimburse the examining Party for the reasonable audit fees for such examination.

10.12 Taxes.

10.12.1 **Taxes on Income**. Except as set forth in this Section 10.12 (Taxes) or Section 10.13 (VAT Credits), each Party will be solely responsible for the payment of any and all Taxes levied on account of all payments it receives under this Agreement.

10.12.2 **Tax Cooperation**. The Parties agree to cooperate with one another in accordance with Applicable Law and use reasonable efforts to minimize Tax withholding or similar obligations in respect of royalties, milestone payments, and other payments made by each Party to the other Party under this Agreement. To the extent either Party (the "**Paying Party**") is required to deduct and withhold Taxes on any payment to the other Party (the "**Recipient**"), the Paying Party will (a) pay the amount of such Taxes to the proper Governmental Authority in a timely manner, and (b) promptly transmit to the Recipient an official tax certificate or other evidence of such payment sufficient to enable the Recipient to claim such payment of Taxes on the Recipient's applicable tax returns. The Paying Party will provide the Recipient with advance notice prior to withholding any Taxes from payments payable to the Recipient and will, to the extent practicable, provide the Recipient with a commercially reasonable period of time to claim an exemption or reduction in otherwise applicable Taxes. The Recipient will provide the Paying Party any tax forms that may be reasonably necessary in order for the Paying Party to not withhold Tax or to withhold Tax at a reduced rate under an applicable bilateral income tax treaty, to the extent the Paying Party is legally able to do so. The Recipient will use reasonable efforts to provide any such tax forms to the Paying Party in advance of the due date. Each Party will provide the other with reasonable assistance to enable the recovery, as permitted by Applicable Law, of withholding Taxes or similar obligations resulting from payments made under this Agreement, such recovery to be for the benefit of the Paying Party if the Paying Party is the Party bearing such withholding Tax under this Section 10.12 (Taxes). In addition, the Parties will cooperate in accordance with Applicable Law to minimize indirect Taxes (such as VAT, sales tax, consumption tax, and other similar Taxes) in connection with this Agreement. In the event of any inconsistency between this Section 10.12 (Taxes) and Section 10.13 (VAT Credits), Section 10.13 (VAT Credits) will take precedence.

10.12.3 **Changes in Domicile**. Notwithstanding anything to the contrary in this Agreement, if the Paying Party assigns, transfers or otherwise disposes of some or all of its rights and obligations to any Person and if, as a result of such action, the withholding or deduction of Tax required by Applicable Law with respect to payments under this Agreement is increased, then any amount payable to the Recipient under this Agreement will be increased to take into account such withheld Taxes as may be necessary so that, after making all required withholdings (including withholdings on the withheld amounts), the Recipient receives an amount equal to the sum it would have received had no such withholding been made.

10.12.4 **Returns**. All transfer, documentary, sales, use, stamp, registration, and other such Taxes, and any conveyance fees, recording charges, and other fees and charges (including any penalties and interest) incurred in connection with consummation of the transactions contemplated hereby, if any, will be borne and paid by the Paying Party. The Paying Party will prepare and timely file all tax returns required to be filed in respect of any such Taxes. The Parties will reasonably cooperate in accordance with Applicable Law to minimize transfer Taxes in connection with this Agreement.

10.13 VAT Credits. All payments due to Blueprint from Zai pursuant to this Agreement will be paid without any deduction for any VAT that Zai may be required to pay to any tax authorities in the Territory. Blueprint will use Commercially Reasonable Efforts to assist Zai to minimize and obtain all available exemptions from such VAT or other taxes, but if applicable, Zai will pay any such VAT to the proper taxing authorities upon receipt of a valid VAT invoice (where such invoice is required under local VAT laws). If Zai is required to pay or Blueprint is required to report, any

such VAT, then [****]. Zai will promptly provide to Blueprint applicable receipts evidencing payment of such VAT and other documentation reasonably requested by Blueprint.

Article 11
CONFIDENTIALITY; PUBLICATION

11.1 Duty of Confidence. Subject to the other provisions of this Article 11 (Confidentiality; Publication):

11.1.1 except to the extent expressly authorized by this Agreement, all Confidential Information of a Party (the "**Disclosing Party**") will be maintained in confidence and otherwise safeguarded, and not published or otherwise disclosed, by the other Party (the "**Receiving Party**") and its Affiliates for the Term and for [****] thereafter;

11.1.2 the Receiving Party will treat all Confidential Information provided by the Disclosing Party with the same degree of care as the Receiving Party uses for its own similar information, but in no event less than a reasonable degree of care;

11.1.3 the Receiving Party may only use any Confidential Information of the Disclosing Party for the purposes of performing its obligations or exercising its rights under this Agreement;

11.1.4 a Receiving Party may disclose Confidential Information of the Disclosing Party to: (a) such Receiving Party's Affiliates, licensees and Sublicensees; and (b) employees, directors, officers, agents, contractors, consultants, attorneys, accountants, banks, investors, and advisors of the Receiving Party and its Affiliates, licensees, and Sublicensees, in each case ((a) and (b)), to the extent reasonably necessary for the purposes of, and for those matters undertaken pursuant to, this Agreement; *provided that* such Persons are bound by legally enforceable obligations of confidentiality and non-use with respect to the Disclosing Party's Confidential Information no less stringent than the confidentiality and non-use obligations set forth in this Agreement. Each Party will remain responsible for any failure by its Affiliates, licensees, and Sublicensees, and its and its Affiliates', licensees', and Sublicensees' respective employees, directors, officers, agents, consultants, attorneys, accountants, banks, investors, advisors, and contractors, in each case, to treat such Confidential Information as required under this Section 11.1 (Duty of Confidence) (as if such Affiliates, licensees, Sublicensees, employees, directors, officers agents, consultants, advisors, attorneys, accountants, banks, investors, and contractors were Parties directly bound to the requirements of this Section 11.1 (Duty of Confidence)); and

11.1.5 each Party will promptly notify the other Party of any misuse or unauthorized disclosure of the other Party's Confidential Information.

11.2 Confidential Information. The Blueprint Know-How and Blueprint Manufacturing Know-How will be the Confidential Information of Blueprint notwithstanding the fact that certain of such information may be developed or invented and disclosed to Blueprint by Zai. The Joint Collaboration Know-How and the terms of this Agreement will be the Confidential Information of each Party. The Zai Know-How will be the Confidential Information of Zai. Except as provided in Section 11.3 (Authorized Disclosures) and Section 11.7 (Publicity; Use of Names), neither Party nor its Affiliates may disclose the existence or the terms of this Agreement.

11.3 Authorized Disclosures.

11.3.1 **Permitted Circumstances**. Notwithstanding the obligations set forth in Section 11.1 (Duty of Confidence) and Section 11.6 (Publication and Listing of Clinical Trials), a Party may disclose the other Party's Confidential Information (including this Agreement and the terms herein) to the extent such disclosure is reasonably necessary in the following situations:

(a) (i) the Patent Prosecution, enforcement, and defense of Blueprint Patent Rights, Joint Collaboration Patent Rights, or Zai Collaboration Patent Rights, in each case, as contemplated by this Agreement; or (ii) regulatory filings and other filings with Governmental Authorities (including Regulatory Authorities), as necessary or reasonably useful for the Exploitation of a Licensed Product;

(b) disclosure of this Agreement, its terms, and the status and results of Exploitation of one or more Licensed Products to actual or *bona fide* [****] solely for the purpose of evaluating or carrying out an actual or potential investment, acquisition, (sub)license, debt transaction, or collaboration; *provided* that, in each such case, on the condition that such Persons are bound by obligations of confidentiality and non-use at least as stringent as those set forth Article 11 (Confidentiality; Publication) or otherwise customary for such type and scope of disclosure and that any such disclosure is limited to the maximum extent practicable for the particular context in which it is being disclosed;

(c) such disclosure is required to comply with Applicable Law (whether generally or in pursuit of an application for listing of securities) including the United States Securities and Exchange Commission, the Stock Exchange of Hong Kong Limited, or equivalent foreign agency or regulatory body, or otherwise required by judicial or administrative process, *provided* that in each such event, as promptly as reasonably practicable and to the extent not prohibited by Applicable Law or judicial or administrative process, such Party will notify the other Party of such required disclosure and provide a draft of the disclosure to the other Party reasonably in advance of such filing or disclosure for the other Party's review and comment. The non-disclosing Party will provide any comments as soon as practicable, and the disclosing Party will consider [****] comments provided by the non-disclosing Party; *provided* that [****]. Confidential Information that is disclosed in order to comply with Applicable Law or by judicial or administrative process pursuant to this Section 11.3.1(c), in each case, will remain otherwise subject to the confidentiality and non-use provisions of this Article 11 (Confidentiality; Publication) with respect to the Party disclosing such Confidential Information, and such Party will take all steps reasonably necessary, including seeking of confidential treatment or a protective order for a period of at least [****] (to the extent permitted by Applicable Law or Governmental Authority), to ensure the continued confidential treatment of such Confidential Information, and each Party will be responsible for its own legal and other external costs in connection with any such filing or disclosure pursuant to this Section 11.3.1(c) (Permitted Circumstances);

(d) to prosecute or defend litigation [****];

(e) to present, disclose, and discuss general information about the existence of the Agreement and the general progress of the Licensed Products at investor press conferences or similar events; or

(f) disclosure pursuant to Section 11.6 (Publication and Listing of Clinical Trials) and Section 11.7 (Publicity; Use of Name).

11.3.2 **Confidential Treatment**. Notwithstanding anything to the contrary set forth in this Agreement, if a Party is required or permitted to make a disclosure of the other Party's Confidential Information pursuant to Section 11.3.1 (Permitted Circumstances), then it will, to the extent not prohibited by Applicable Law or judicial or administrative process, except where impracticable, give reasonable advance notice to the other Party of such proposed disclosure and use reasonable efforts to secure confidential treatment of such information and will only disclose that portion of Confidential Information that is legally required to be disclosed as advised by its legal counsel. In any event, each Party agrees to take all reasonable action to avoid disclosure of Confidential Information of the other Party hereunder.

11.4 Tax Treatment. Nothing in Section 11.1 (Duty of Confidence) or 11.3 (Authorized Disclosures) will limit either Party in any way from disclosing to any Third Party such Party's U.S. or foreign income Tax treatment and the U.S. or foreign income Tax structure of the transactions relating to such Party that are based on or derived from this Agreement, or materials of any kind (including opinions or other Tax analyses) relating to such Tax treatment or Tax structure, except to the extent that nondisclosure of such matters is reasonably necessary in order to comply with applicable securities laws.

11.5 Publications.

11.5.1 Zai will not publicly present or publish any Clinical Trial data, non-clinical or preclinical data, clinical case study or review article, or any associated results or conclusions generated by or on behalf of Zai with respect to Licensed Products pursuant to this Agreement (each such proposed abstract, presentation or publication, a "**Zai Publication**"), except [****] with respect to the applicable Licensed Product as provided to Zai [****] during the Term upon Zai's request therefor, and subject to the additional limitations set forth in this Section 11.5 (Publications) and Section 11.6 (Publication and Listing of Clinical Trials). Blueprint will comply with this Section 11.5 (Publications) with respect to any presentation or publication of solely containing Clinical Trial data, non-clinical or preclinical data, clinical case study or review article, or any associated results or conclusions that were generated by or on behalf of Zai with respect to Licensed Products pursuant to this Agreement (each such proposed abstract, presentation or publication, a "**Blueprint Publication**" and together with a Zai Publication, a "**Publication**").

11.5.2 If Zai desires to publicly present or publish a Zai Publication or Blueprint desires to publicly present or publish a Blueprint Publication, then the publishing Party will provide the other Party (including the Alliance Manager and all of the other Party's members of the JSC) with a copy of such proposed Publication at least [****] prior to the earlier of its presentation or intended submission for publication (such applicable period, the "**Review Period**"). The publishing Party agrees that it will not submit or present any Publication until (a) [****]or (b) [****] in which case the publishing Party may proceed and the Publication will be considered approved in its entirety. If the publishing Party receives written comments from the other Party on any Publication during the applicable Review Period, then it will consider the other Party's comments [****] and incorporate such comments [****], but will retain the sole authority to publish the Publication.

11.5.3 Notwithstanding any provision to contrary set forth in this Agreement, each Party will (i) delete any Confidential Information of the other Party that the other Party identifies for deletion in the other Party's written comments, (ii) at the request of Blueprint, delete any Clinical Trial data, results, conclusions, or other related information for a Licensed Product the publication of which Blueprint determines, [****] would conflict with Blueprint's global publication strategy with respect to the applicable Licensed Product, except where required by Applicable Law to publicly disclose such information, (iii) at the request of the other Party, delete the structure or generic or internal name of the Licensed Product if such structure or name has not yet been publicly disclosed, and (iv) delay such Publication for a period of up to an additional [****] after the end of the applicable Review Period to enable the other Party, if applicable, to draft and file one or more patent applications with respect to any subject matter to be made public in such Publication. The publishing Party will provide the other Party a copy of the Publication at the time of the submission or presentation thereof. The publishing Party agrees to acknowledge the contributions of the other Party and the employees of the other Party, in each case, in all Publications as scientifically appropriate. Without limiting the foregoing, Blueprint agrees to acknowledge the contributions of Zai and the employees of Zai, in each case, in all presentations and publications as scientifically appropriate to the extent related to any Global Clinical Trials in which Zai assists in the enrollment of patients from the PRC. Each Party will require its Affiliates and licensees and Sublicensees, as applicable, to comply with the obligations of this Section 11.5 (Publications) as if they were such Party, and such Party will be liable for any non-compliance of such Persons.

11.6 Publication and Listing of Clinical Trials. With respect to the listing of Clinical Trials or the publication of Clinical Trial results for the Licensed Products and to the extent applicable to a Party's activities conducted under this Agreement, each Party will comply with (a) the Pharmaceutical Research and Manufacturers of America (PhRMA) Guidelines on the listing of Clinical Trials and the Publication of Clinical Trial results, and (b) any Applicable Law or applicable court order, stipulations, consent agreements, and settlements entered into by such Party. The Parties agree that any such listings or publications made pursuant to this Section 11.6 (Publication and Listing of Clinical Trials) will be considered a Publication for purposes of this Agreement and will be subject to Section 11.5 (Publications).

11.7 Publicity; Use of Names.

11.7.1 **Press Release**. The Parties have agreed on a joint press release announcing this Agreement, set forth on **Schedule 11.7.1** (Press Release), to be issued by the Parties on such date and time as may be agreed by the Parties. Other than the press release set forth on **Schedule 11.7.1** (Press Release) and the public disclosures permitted by this Section 11.7 (Publicity; Use of Names), and Section 11.3 (Authorized Disclosures), the Parties agree that [****]. However, the Parties agree that after (a) a disclosure pursuant to Section 11.7 (Publicity; Use of Names) or Section 11.3 (Authorized Disclosures) or (b) the issuance of a press release (including the initial press release) or other public announcement pursuant to this Section 11.7.1 (Press Release) that has been reviewed and approved by the other Party, the disclosing Party may make subsequent public disclosures reiterating such information without having to obtain the other Party's prior consent and approval so long as the information in such press release or other public announcement remains true, correct, and the most current information with respect to the subject matters set forth therein. Similarly, after a Publication has been made available to the public, each Party may post such Publication or a link to it on its corporate web site (or any website managed by such Party in connection with a Clinical Trial for a Licensed Product, as appropriate) without the prior

written consent of the other Party, so long as the information in such Publication remains true, correct, and the most current information with respect to the subject matters set forth therein.

11.7.2 **Authorized Disclosures**. Notwithstanding any provision to the contrary set forth in this Agreement, each Party has the right to publicly disclose (in written, oral, or other form): (a) the achievement of Milestone Events under this Agreement (including the amount, payment, and timing of any such Milestone Event); (b) the commencement, completion, material data, or key results of any Territory-Specific Clinical Trials for the Licensed Products; (c) any information relating to any Global Clinical Trial, including the commencement, completion, material data, or key results of any such Global Clinical Trial; and (d) the achievement of Regulatory Approval for any Licensed Product in the Territory; *provided*, that, in each case of (a) – (d), any such public disclosure will (i) to the extent feasible, be provided to the other Party for review and comment [****] and (ii) in any event, be provided to the other Party for review and comment no later than [****] prior to public disclosure (unless a shorter timeframe is required under Applicable Law).

11.7.3 **Use of Names**. Each Party will have the right to use the other Party's name and logo in presentations, its website, collateral materials, and corporate overviews to describe the collaboration relationship, as well as in taglines of press releases issued pursuant to this Section 11.7 (Publicity; Use of Names); *provided* that each Party will use the other Party's corporate name in such manner that the distinctiveness, reputation, and validity of any trademarks and corporate or trade names of such other Party will not be impaired, and consistent with best practices used by such other Party for its other collaborators. Except as permitted under this Section 11.7 (Publicity; Use of Names) or with the prior express written permission of the other Party, neither Party will use the name, trademark, trade name, or logo of the other Party or its Affiliates or their respective employees in any publicity, promotion, news release, or disclosure relating to this Agreement or its subject matter except as may be required by Applicable Law. Each Party will use the other Party's corporate name in all publicity relating to this Agreement, including the initial press release and all subsequent press releases issued pursuant to the terms of this Agreement. Zai will, to the extent consistent with Applicable Law, include explanatory text such as (a) "*Discovered by Blueprint Medicines Corporation*" in all publicity, promotion, news releases, or similar disclosures relating to the Licensed Products that are not Blueprint/Zai Combinations, and (b) "*Discovered in Collaboration by Blueprint Medicines Corporation and Zai Pharmaceuticals*" in all publicity, promotion, news releases, or similar disclosures relating to any Blueprint/Zai Combinations, in each case ((a) and (b)), or such other similar text provided by Blueprint and reasonably acceptable to Zai.

11.8 Attorney-Client Privilege. Neither Party is waiving, nor will be deemed to have waived or diminished, any of its attorney work product protections, attorney-client privileges or similar protections and privileges or the like as a result of disclosing information pursuant to this Agreement, or any of its Confidential Information (including Confidential Information related to pending or threatened litigation) to the Receiving Party, regardless of whether the Disclosing Party has asserted such privileges and protections. The Parties: (a) share a common legal and commercial interest in such disclosure that is subject to such privileges and protections; (b) are or may become joint defendants in proceedings to which the information covered by such protections and privileges relates; (c) intend that such privileges and protections remain intact should either Party become subject to any actual or threatened proceeding to which the Disclosing Party's Confidential Information covered by such protections and privileges relates; and (d) intend that after the Effective Date both the Receiving Party and the Disclosing Party will have the right to assert such

protections and privileges. Notwithstanding the foregoing, nothing in this Section 11.8 (Attorney-Client Privilege) will apply with respect to a Dispute between the Parties (including their respective Affiliates).

Article 12
REPRESENTATIONS, WARRANTIES, AND COVENANTS

12.1 Representations and Warranties of Each Party. Each Party represents and warrants to the other Party as of the Effective Date as follows:

12.1.1 It is a corporation or limited company duly organized, validly existing, and in good standing under the laws of the jurisdiction of its organization, and it has the full right, power and authority to enter into this Agreement and to perform its obligations hereunder.

12.1.2 It has not been Debarred/Excluded and no proceeding that could result it in being Debarred/Excluded is pending, and neither it nor any of its Affiliates has used, in any capacity in the performance of obligations relating to the Licensed Products, any employee, Subcontractor, consultant, agent, representative, or other Person who has been Debarred/Excluded.

12.1.3 All consents, approvals and authorizations from all Governmental Authorities or other Third Parties required to be obtained by such Party in connection with this Agreement have been obtained.

12.1.4 This Agreement has been duly executed by it and is legally binding upon it, enforceable in accordance with its terms, and does not conflict with any agreement, instrument or understanding, oral or written, to which it is a party or by which it may be bound, nor violate any material Applicable Law or regulation of any court, governmental body, or administrative or other agency having jurisdiction over it.

12.1.5 To its Knowledge, neither it nor any of its Affiliates, or its or their directors, officers, employees, distributors, agents, representatives, sales intermediaries, or other Third Parties acting on its behalf or any of its Affiliates:

(a) has taken any action in violation of any local and other anti-corruption laws (including the provisions of the United States Foreign Corrupt Practices Act, collectively "**Anti-Corruption Laws**"); or

(b) has corruptly offered, paid, given, promised to pay or give, or authorized the payment or gift of anything of value, directly or indirectly, to any Public Official, for the purposes of:

(i) influencing any act or decision of any Public Official in his or her official capacity;

(ii) inducing such Public Official to do or omit to do any act in violation of his or her lawful duty;

(iii) securing any improper advantage; or

(iv) inducing such Public Official to use his or her influence with a government, governmental entity, or commercial enterprise owned or controlled by any government (including state-owned or controlled veterinary, laboratory or medical facilities) in obtaining or retaining any business whatsoever.

12.2 Representations and Warranties of Blueprint. Blueprint represents and warrants to Zai as of the Effective Date with respect to itself and its Affiliates as follows:

12.2.1 It has the right under the Blueprint Technology to grant to Zai the licenses set forth in this Agreement, and it has not granted any license or other right under the Blueprint Technology that is inconsistent with the licenses purported to be granted to Zai hereunder.

12.2.2 [****]

12.2.3 There is no pending or, to Blueprint's Knowledge, threatened (in writing) litigation, nor has Blueprint received any written notice from any Third Party, asserting or alleging that the Exploitation of the Blueprint Compounds or the Licensed Products prior to the Effective Date infringed or misappropriated the intellectual property rights of such Third Party.

12.2.4 There are no legal claims, judgments, or settlements against or owed by Blueprint or any of its Affiliates, or pending or, to Blueprint's Knowledge, threatened, legal claims or litigation, in each case, relating to antitrust, anti-competition, or Anti-Corruption Law violations.

12.2.5 To Blueprint's Knowledge, the Exploitation of the Blueprint Compounds as contemplated under this Agreement does not infringe any issued Patent Right of any Third Party.

12.2.6 [****]

12.2.7 Each employee of Blueprint and its Affiliates involved in the programs related to the Blueprint Compounds is bound by an agreement or policy requiring such employee to assign Inventions invented by such employee to Blueprint or such Affiliate.

12.2.8 Blueprint does not have agreements with any Third Parties under which Blueprint Controls any Blueprint Patent Rights or Blueprint Know-How as of the Effective Date.

12.2.9 All information provided by Blueprint to Zai for due diligence purposes in relation to this Agreement, to Blueprint's Knowledge, is complete and accurate in all material respects.

12.3 Representations and Warranties of Zai. Zai represents and warrants to Blueprint as follows (a) [****], and (b) [****]:

12.3.1 It has the right under the Zai Technology to grant to Blueprint the licenses set forth in this Agreement, and it has not granted any license or other right under the Zai Technology that is inconsistent with the licenses purported to be granted to Blueprint hereunder.

12.3.2 There is no Zai Technology in existence as of the Effective Date.

12.3.3 There is no pending or, to Zai's Knowledge, threatened (in writing) litigation, nor has Zai received any written notice from any Third Party, asserting or alleging that the Exploitation of any Zai Product as part of any Blueprint/Zai Combination in the Territory as contemplated under this Agreement will infringe or misappropriate the intellectual property rights of such Third Party.

12.3.4 There are no legal claims, judgments, or settlements against or owed by Zai or any of its Affiliates, or pending or, to Zai's Knowledge, threatened, legal claims or litigation, in each case, relating to antitrust, anti-competition, or Anti-Corruption Law violations.

12.3.5 Zai has sufficient financial wherewithal to perform all of its obligations set forth under this Agreement as they come due.

12.3.6 Each employee of Zai and its Affiliates is bound by an agreement or policy requiring such employee to assign Inventions invented by such employee to Zai or such Affiliate.

12.3.7 Zai has, or can readily obtain, sufficient technical, clinical, and regulatory expertise to perform all of its obligations pursuant to this Agreement, including its obligations relating to Development, Manufacturing, Medical Affairs, Commercialization, and obtaining Regulatory Approvals, in each case, of the Blueprint Compounds and Licensed Products as contemplated under this Agreement.

12.3.8 None of the officers, directors, or employees of Zai or of any of its Affiliates or agents acting on behalf of Zai or any of its Affiliates, in each case, that are employed or reside outside the United States, is a Public Official.

12.3.9 Zai or its Affiliate that will serve as Blueprint's regulatory agent (as applicable) in the PRC as contemplated by this Agreement has met all qualification requirements required under Applicable Law to be Blueprint's regulatory agent in the PRC as contemplated by this Agreement.

12.4 Covenants of Zai. Zai covenants to Blueprint that:

12.4.1 In the course of performing its obligations or exercising its rights under this Agreement, it will comply with all Applicable Law, including, as applicable, cGMP, GCP, and GLP standards, and all ethics policies agreed upon by the Parties in good faith, and will not employ or engage, and if so employed and engaged, will thereafter terminate any Person who has been Debarred/Excluded, or is the subject of any proceedings that could result in such Person being Debarred/Excluded. Zai will make all related disclosures with respect to and record all transfers of value to health care providers in the Territory to the extent required by Applicable Laws. Zai will require any Affiliate, Sublicensee, Subcontractor, or other Person that provides services to or on behalf of Zai in connection with this Agreement to comply with Zai's obligations under this Section 12.4.1.

12.4.2 Zai will perform, and will cause its Affiliates and Sublicensees and their respective Subcontractors to, perform all necessary or required record filings with, and obtain all necessary or required licenses, approvals and permits from, all applicable Governmental Authorities in the Territory [****] for the conduct of activities, including Development activities and data sharing, under this Agreement, and provide Blueprint with copies of such record filings, licenses, approvals, and permits.

12.4.3 Throughout the Term, Zai or its Affiliate who will serve as Blueprint's regulatory agent in the PRC will at all times meet all qualification requirements required under Applicable Law to be Blueprint's regulatory agent in the PRC as contemplated by this Agreement. Zai will promptly notify Blueprint of any significant change to these qualification requirements and upon receiving any notice from any Third Party indicating, or otherwise becoming aware, that Zai or its Affiliate may not meet these requirements.

12.5 Mutual Covenants. Each Party covenants to the other Party that:

12.5.1 Notwithstanding any provision to the contrary in this Agreement, each Party agrees as follows:

(a) It will not, in the performance of this Agreement, perform any actions that are prohibited by Anti-Corruption Laws that may be applicable to one or both Parties.

(b) It will not, in the performance of this Agreement, directly or indirectly, make any payment, or offer or transfer anything of value, or agree or promise to make any payment or offer or transfer anything of value, to a government official or government employee, to any political party or any candidate for political office or to any other Third Party with the purpose of influencing decisions related to either Party or its business in a manner that would violate Anti-Corruption Laws.

(c) At the request of the other Party, not more than [****], it will verify in writing to the requesting Party that to its Knowledge, there have been no violations of Anti-Corruption Laws by it or its Affiliates or Sublicensees, or persons employed by or Subcontractors used by it or its Affiliates or Sublicensees in the performance of this Agreement, or will provide details of any exception to the foregoing.

(d) It will maintain records (financial and otherwise) and supporting documentation related to the subject matter of this Section 12.5 (Mutual Covenants) in order to document or verify compliance with the provisions of this Section 12.5 (Mutual Covenants), and upon request of the other Party upon reasonable advance notice, will provide to such requesting Party or its representative with access to such records for purposes of verifying compliance with the provisions of this Section 12.5 (Mutual Covenants).

12.5.2 It and its Affiliates will, and will cause its and their licensees subcontractors (or Sublicensees and Subcontractors, as applicable) to, comply with all Applicable Laws pertaining to Personal Information (the "**Privacy Laws**") to which it is subject in connection with such Party's and its Affiliate's, licensees (or Sublicensee's, as applicable) or subcontractors (or Subcontractor's, as applicable) activities related to this Agreement. To the extent that such Party or its Affiliates, licensees (or Sublicensees, as applicable), or subcontractors (or Subcontractors, as applicable) access or come into possession of Personal Information in connection with activities related to this Agreement, such Party and its Affiliates agree, and will cause its and their licensees (or Sublicensees, as applicable) and subcontractors (or Subcontractors, as applicable), to comply with applicable Privacy Laws to which it may be subject as a result thereof. Any processing (including the collection, storage, use, transfer, provision, publication, and deletion) by such Party or its Affiliates, licensees (or Sublicensees, as applicable), or subcontractors (or Subcontractors, as applicable) of Personal Information obtained in connection with activities under this Agreement will be done solely for the purpose of performing such Party's obligations or exercising such Party's rights in connection with the Development of Licensed Products consistent with the terms of this Agreement, will be in accordance with notices provided to and consents obtained from the data subjects whose Personal Information is being processed, and will be in accordance with all applicable Privacy Laws. From and after the Effective Date, each Party and its Affiliates will take, and ensure that its licensees (or Sublicensees, as applicable) and subcontractors (or Subcontractors, as applicable) take, commercially reasonable and appropriate technical and organizational

measures to protect Personal Information (including the results and any clinical data obtained in connection with any Clinical Trials conducted by or on behalf of such Party) in its possession against unauthorized access, accidental loss or damage, and unauthorized destruction. Such Party and its Affiliates will further maintain, and ensure that its licensees (or Sublicensees, as applicable) and subcontractors (or Subcontractors, as applicable) maintain, a commercially reasonable program for protecting against unauthorized access to or loss, misuse, alteration, destruction, damage or disclosure of Personal Information (including the results and any clinical data obtained in connection with Clinical Trials conducted by or on behalf of such Party) in its possession pursuant to its activities under this Agreement ("**Data Breach**"). In the event of a Data Breach, such Party will (i) promptly, and in any event so as to allow the other Party to comply with its obligations under Applicable Law, notify the other Party by phone and email after becoming aware of such Data Breach, and (ii) comply with the relevant requirements and procedures of the applicable Privacy Laws in resolving such Data Breach. With respect to all activities performed by such Party and its Affiliates under the Agreement, such Party and its Affiliates will use reasonable efforts to, and to ensure that its subcontractors (or Subcontractors, as applicable), implement multi-factor authentication and encryption promptly following the Effective Date. Prior to transferring any data, files, or results containing any Personal Information to the other Party its Affiliate, subcontractor (or Subcontractor, as applicable) or licensee (or Sublicensee, as applicable) hereunder, the Parties will agree upon the manner and format of such transfer and the transferring Party will provide any required notices to and obtain any necessary consents from Governmental Authorities and data subjects prior to a transfer. With respect to such transferred data, each Party will promptly notify the other Party by phone and email after receiving a data subject request from an individual whose Personal Information was transferred to the other Party or its Affiliate, subcontractor (or Subcontractor, as applicable) or licensee (or Sublicensee, as applicable), and will comply with, and inform its Affiliates, subcontractors (or Subcontractors, as applicable) or licensees (or Sublicensees, as applicable) of the need to comply with, the relevant requirements and procedures of the applicable Privacy Laws in responding to such data subject request. Each Party will have the right, upon reasonable advance notice and at a time agreed by the Parties, to audit the other Party's and its Affiliates' compliance with the requirements of this Section 12.5.2. To the extent permitted under Zai's agreements with its Sublicensees or Subcontractors, Blueprint will have the right to audit the data privacy and information security measures implemented by Zai's Sublicensees and Subcontractors performing activities under this Agreement. If such audit is not permitted under Zai's one or more agreements with its Sublicensees or Subcontractors, Zai will use reasonable efforts to obtain the right to conduct such an audit of the data privacy and information security measures of any such Sublicensees and Subcontractors.

12.6 Covenants of Blueprint. Blueprint covenants to Zai that:

12.6.1 Neither Blueprint nor any of its Affiliates will grant any license, sublicense, or other rights in or to the Blueprint Technology that is inconsistent with the terms and conditions of this Agreement.

12.6.2 During the Term Blueprint will comply with all Applicable Law applicable to its Development and Manufacture of the Blueprint Compounds and the Licensed Products pursuant to this Agreement, including, as applicable, cGMP, GCP, and GLP standards, and all ethics policies agreed upon by the Parties in good faith, and will not employ or engage, and if so employed and engaged, will thereafter terminate any Person who has

been Debarred/Excluded, or is the subject of any proceedings that could result in such Person being Debarred/Excluded.

12.7 **NO OTHER WARRANTIES**. EXCEPT AS EXPRESSLY STATED IN THIS Article 12 (REPRESENTATIONS, WARRANTIES, AND COVENANTS), (A) NO REPRESENTATION, CONDITION, OR WARRANTY WHATSOEVER IS MADE OR GIVEN BY OR ON BEHALF OF BLUEPRINT OR ZAI; AND (B) ALL OTHER CONDITIONS AND WARRANTIES WHETHER ARISING BY OPERATION OF LAW OR OTHERWISE ARE EXPRESSLY EXCLUDED, INCLUDING ANY CONDITIONS AND WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, TITLE, OR NON-INFRINGEMENT. ANY INFORMATION PROVIDED BY BLUEPRINT OR ITS AFFILIATES IS MADE AVAILABLE ON AN "AS IS" BASIS WITHOUT WARRANTY WITH RESPECT TO COMPLETENESS, COMPLIANCE WITH REGULATORY STANDARDS OR REGULATIONS, OR FITNESS FOR A PARTICULAR PURPOSE OR ANY OTHER KIND OF WARRANTY WHETHER EXPRESS OR IMPLIED.

12.8 **Time for Claims**. Except in the case of any fraud or intentional misrepresentation by a Party: (a) the representations and warranties of the Parties contained in Section 12.1 (Representations and Warranties of Each Party), Section 12.2 (Representations and Warranties of Blueprint), and Section 12.3 (Representations and Warranties of Zai) will survive, with respect to direct claims made by one Party against the other Party, until the date that is [****] and (b) no claim may be made or suit instituted seeking indemnification pursuant to Article 13 (Indemnification) for any breach of, or inaccuracy in, any representation or warranty contained in Section 12.1 (Representations and Warranties of Each Party), Section 12.2 (Representations and Warranties of Blueprint), or Section 12.3 (Representations and Warranties of Zai) unless a written notice is provided to the Indemnifying Party at any time prior to the date that is [****].

Article 13

INDEMNIFICATION

13.1 **By Zai**. Zai will indemnify, defend, and hold harmless Blueprint and its Affiliates, and their respective directors, officers, employees, successors, heirs and assigns, and agents (individually and collectively, the "**Blueprint Indemnitee(s)**") from and against all Losses incurred in connection with any Third Party Claims to the extent arising from or relating to (a) the Exploitation of the Blueprint Compounds or the Licensed Products by or on behalf of Zai or any of its Affiliates, Sublicensees, or Subcontractors, including product liability claims arising from such Exploitation, (b) Zai's actions (or omissions) in the performance of its obligations with respect to Regulatory Submissions or interactions with Regulatory Authorities, in each case, as the authorized regulatory agent of record for Blueprint in the PRC, (c) the negligence or willful misconduct of Zai or any of its Affiliates, Sublicensees, or Subcontractors, (d) Zai's or its Affiliate's, Sublicensee's, or Subcontractor's breach of any of its representations, warranties, covenants, or obligations set forth in this Agreement, (e) the failure of Zai or any of its Affiliates, Sublicensees, or Subcontractors to abide by any Applicable Law, or (f) any claim or demand from any employee or contractor of Zai or its Affiliate who is an inventor of any Assigned Collaboration Technology or Joint Collaboration Technology with respect to the ownership thereof, in each case of clauses (a) through (f) above, except to the extent such Third Party Claims arise out of a Blueprint Indemnitee's negligence or willful misconduct, breach of its representations, warranties, covenants, or obligations set forth in this Agreement, or failure to abide by any Applicable Law.

13.2 **By Blueprint**. Blueprint will indemnify, defend, and hold harmless Zai, its Affiliates, and their directors, officers, employees, successors, heirs and assigns, and agents (individually and collectively, the "**Zai Indemnitee(s)**") from and against all Losses incurred in connection with any Third Party Claims to the extent from or relating to (a) the Exploitation of the Blueprint Compounds or the Licensed Products, by or on behalf of Blueprint or any of its Affiliates, licensees (not including Zai or its Affiliates, Sublicensees, or its Subcontractors), Sublicensees, or Subcontractors, including product liability claims arising from such Exploitation, and including such Exploitation prior to the Effective Date or after the effective date of termination of this Agreement (including when acting as an exclusive distributor pursuant to Section 15.3.2 (Appointment as Exclusive Distributor), if applicable), (b) the negligence or willful misconduct of Blueprint or any of its Affiliates, licensees (not including Zai or its Affiliates, Sublicensees, or its Subcontractors), Sublicensees, or Subcontractors, (c) Blueprint's or its Affiliate's, licensee's (not including Zai or its Affiliates, Sublicensees, or its Subcontractors), Sublicensee's, or Subcontractor's breach of any of its representations, warranties, covenants, or obligations set forth in this Agreement, (d) the failure of Blueprint or any of its Affiliates, licensees (not including Zai or its Affiliates, Sublicensees, or Subcontractors), Sublicensees, or Subcontractors to abide by any Applicable Law, or (e) any claim or demand from any employee or contractor of Blueprint or its Affiliate who is an inventor of any Joint Collaboration Technology with respect to the ownership thereof, in each case of clauses (a) through (e) above, except to the extent such Third Party Claims arise out of any of a Zai Indemnitee's negligence or willful misconduct, breach of its representations, warranties, covenants, or obligations set forth in this Agreement or failure to abide by any Applicable Law.

13.3 **Indemnification Procedure**. If either Party is seeking indemnification under Section 13.1 (By Zai) or Section 13.2 (By Blueprint) (the "**Indemnified Party**"), then it will inform the other Party (the "**Indemnifying Party**") of the Third Party Claim giving rise to such indemnification obligations within [****] after receiving written notice of the Third Party Claim (it being understood and agreed, however, that the failure or delay by an Indemnified Party to give such notice of a Third Party Claim will not affect the Indemnifying Party's indemnification obligations hereunder except to the extent the Indemnifying Party will have been actually and materially prejudiced as a result of such failure or delay to give notice). The Indemnifying Party will have the right to assume the defense of any such Third Party Claim for which it is obligated to indemnify the Indemnified Party. The Indemnified Party will cooperate with the Indemnifying Party and the Indemnifying Party's insurer as the Indemnifying Party may reasonably request, and at the Indemnifying Party's cost and expense. The Indemnified Party will have the right to participate, at its own expense and with counsel of its choice, in the defense of any Third Party that has been assumed by the Indemnifying Party. Neither Party will have the obligation to indemnify the other Party in connection with any settlement made without the Indemnifying Party's written consent, which consent will not be unreasonably withheld, conditioned, or delayed. The Indemnifying Party will not admit liability of the Indemnified Party without the Indemnified Party's prior written consent, which consent will not be unreasonably withheld, conditioned, or delayed. If the Parties cannot agree as to the application of Section 13.1 (By Zai) or Section 13.2 (By Blueprint) as to any Third Party Claim, pending resolution of the Dispute pursuant to Article 16 (Dispute Resolution), the Parties may conduct separate defenses of such Third Party Claims, with each Party retaining the right to claim indemnification from the other Party in accordance with Section 13.1 (By Zai) or Section 13.2 (By Blueprint), as applicable, upon resolution of the underlying Third Party Claim.

13.4 **Insurance**. Each Party will procure and maintain during the Term of this Agreement [****], commercial general liability insurance from a minimum of "A-" AM Bests rated insurance company or insurer reasonably acceptable to Blueprint, including contractual liability and product liability or clinical trials, with coverage in an amount consistent with sound business practice and industry standards, and reasonable in light of the risks involved in its activities hereunder and its

obligations under this Agreement. Such policies will name the other Party and its Affiliates as additional insureds and provide a waiver of subrogation in favor of the other Party and its Affiliates. Such insurance policies will be primary and non-contributing with respect to any other similar insurance policies available to the other Party or its Affiliates. Any deductibles for such insurance will be assumed by insured Party. Each Party will provide the other Party with evidence of such insurance upon the other Party's request and prior to expiration of any one coverage. Each Party will provide the other Party with written notice at least [****] prior to the cancellation or non-renewal of, or material adverse changes in, such insurance except for cancellation due to non-payment of premiums, in which case notice will be provided at least [****] prior to such cancellation. Such insurance will not be construed to create a limit of the insured Party's liability with respect to its indemnification obligations under this Article 13 (Indemnification).

Article 14
INTELLECTUAL PROPERTY

14.1 Inventions.

14.1.1 **Ownership**. As between the Parties, (a) Blueprint will solely own all Blueprint Technology, including Assigned Collaboration Technology, and Blueprint Manufacturing Technology, (b) Zai will solely own all Zai Technology, and (c) the Parties will jointly own all Blueprint/Zai Combination Technology and other Joint Collaboration Technology.

14.1.2 **Disclosure**. Each Party will promptly disclose to the other Party all Inventions within the Collaboration Know-How that it develops or invents, whether solely or jointly with others (in any event, prior to the filing of any patent application with respect to such Inventions), including all invention disclosures or other similar documents submitted to such Party by its or its Affiliates' employees, agents, or independent contractors relating thereto. Each Party will also promptly respond to reasonable requests from the other Party for additional information relating thereto.

14.1.3 **Inventorship**. For purposes of this Agreement, all determinations of inventorship will be in accordance with U.S. patent law.

14.1.4 **Assignment; Ownership of Joint Collaboration Technology**.

(a) **Assigned Collaboration Technology**. Zai will and hereby does assign to Blueprint all of its rights, title, and interests in and to all Assigned Collaboration Technology, and Blueprint hereby accepts such assignment. Zai will take (and cause its Affiliates, Sublicensees, Subcontractors, and their respective employees, agents, and contractors to take) such further actions reasonably requested by Blueprint to evidence such assignment and to assist Blueprint in obtaining patent and other intellectual property rights protection for Inventions within the Assigned Collaboration Know-How including executing further assignments, consents, releases, and other commercially reasonable documentation and providing good faith testimony by affidavit, declaration, in-person, or other proper means in support of any effort by Blueprint to establish, perfect, defend, or enforce its rights in any Assigned Collaboration Technology through prosecution of governmental filings, regulatory proceedings, litigation, and other means, including through the filing, prosecution, maintenance, and enforcement of the Assigned Collaboration Technology. Zai will obligate its Affiliates, Sublicensees, and Subcontractors to assign all Assigned Collaboration Technology to Zai (or directly to Blueprint) so

that Zai can comply with its obligations under this Section 14.1 (Inventions), and Zai will promptly obtain such assignment. Without limitation, Zai will cooperate with Blueprint if Blueprint applies for U.S. or foreign patent protection for such Assigned Collaboration Technology and will obtain the cooperation of the individual inventors of any such Assigned Collaboration Technology. If Zai is unable to assign any Assigned Collaboration Technology, then Zai hereby grants and agrees to grant to Blueprint a royalty-free, fully paid-up, exclusive (even as to Zai, subject to the terms of this Agreement, including the licenses granted to Zai pursuant to Section 2.1 (License Grants to Zai)), perpetual, irrevocable license (with the right to grant sublicenses through multiple tiers) under such Assigned Collaboration Technology for any and all purposes.

(b) **Ownership of Joint Collaboration Technology**. The Parties will jointly own all Blueprint/Zai Combination Technology and all other Joint Collaboration Technology, [****] (subject to the terms of this Agreement, including the licenses granted under Article 2 (Licenses) and the rights retained under such licenses pursuant to Section 2.4 (Retained Rights)). For Blueprint/Zai Combination Technology solely invented by one Party, the inventing Party will and hereby does assign to the other Party a joint interest in and to all Blueprint/Zai Combination Technology, and the other Party hereby accepts such assignment. Each Party will take (and cause its Affiliates and Sublicensees, and their respective employees, agents, and contractors to take) such further actions reasonably requested by the other Party to evidence such assignment and to assist the Parties in obtaining jointly-owned Patent Rights and other intellectual property rights protection for Inventions within the Blueprint/Zai Combination Know-How including executing further assignments, consents, releases, and other commercially reasonable documentation and providing good faith testimony by affidavit, declaration, in-person, or other proper means in support of any effort by the Parties to establish, perfect, defend, or enforce their rights in any Blueprint/Zai Combination Technology through prosecution of governmental filings, regulatory proceedings, litigation, and other means, including through the filing, prosecution, maintenance, and enforcement of the Blueprint/Zai Combination Technology. Each Party will obligate its Affiliates, Sublicensees, and Third Party contractors (including all Subcontractors) to assign all Blueprint/Zai Combination Technology to such Party so that each Party can comply with its obligations under this Section 14.1 (Inventions), and each Party will promptly obtain such assignment. Without limitation, each Party will cooperate with the other Party if the Parties determine to apply for U.S. or foreign patent protection for such Blueprint/Zai Combination Technology in accordance with this Agreement and will obtain the cooperation of the individual inventors of any such Blueprint/Zai Combination Technology. If a solely inventing Party is unable to assign a joint interest in any Blueprint/Zai Combination Technology, then such Party hereby grants and agrees to grant to the other Party a royalty-free, fully paid-up, non-exclusive (subject to the terms of this Agreement, including the licenses granted to Zai pursuant to Section 2.1 (License Grants to Zai)), perpetual, irrevocable license (with the right to grant sublicenses through multiple tiers) under such Blueprint/Zai Combination Technology for any and all purposes.

(c) **Practice Under and other Use of Blueprint/Zai Combination Technology and other Joint Collaboration Technology**. Subject to the rights granted under and the restrictions set forth in this Agreement (including Section 2.8.1 (Exclusivity Covenant)), neither Party will have any obligation to account to the other Party for

profits, or to obtain any approval of the other Party to license, assign, or otherwise exploit any Blueprint/Zai Combination Technology or other Joint Collaboration Technology by reason of joint ownership thereof, and each Party hereby waives any right it may have under the Applicable Law of any jurisdiction to require any such approval or accounting. To the extent any further consent is required to enable a Party to so license or exploit its interest in the Blueprint/Zai Combination Technology or other Joint Collaboration Technology, the other Party hereby grants such consent.

(d) **Employee Assignment**. Each Party and its respective Affiliates performing activities under this Agreement will enter into with each of their respective employees legally binding and sufficient agreements or employment policies providing for the payment by such Party or its Affiliate of any reward or remuneration required under Applicable Law in the applicable country or region in consideration for the development of Inventions by such employees. Without limiting the generality of the foregoing, each Party and its respective Affiliates will, and will cause its applicable licensees and Sublicensees, as applicable, to, enter into an agreement or employment policy with each of its employees performing activities under this Agreement that (a) compels prompt disclosure to such Party (or its licensee or Sublicensee, as applicable) of all Collaboration Technology developed, invented, or filed by such employee during any performance under this Agreement; (b) automatically assigns to such Party (or its licensee or Sublicensee, as applicable) all rights, title, and interests in and to all Collaboration Technology, and requires each employee to execute all documents and take such other actions as may be necessary to effectuate such assignment; (c) includes an invention and patent reward and remuneration policy providing for the payment by such Party of any reward or remuneration required under Applicable Law in such region in consideration for the development of Inventions by such employees that is legally sufficient under Applicable Law; and (d) solely to the extent applicable, includes a waiver of pre-emption rights under any Applicable Law in such region, including in the case of an employee in the PRC, Article 326 of the Contract Law of the PRC to the effect that the employee will confirm that he/she will not have any right or claim with respect to any Collaboration Technology derived from his/her work, except for the reward and remuneration he/she is entitled to under the invention and patent reward and remuneration policy. [****]

(e) **Payments in Consideration of Assignments of Intellectual Property**.

(i) **Payment by Blueprint**. In consideration of the assignment by Zai to Blueprint of all Assigned Collaboration Technology and a joint ownership interest in all Blueprint/Zai Combination Technology, Blueprint will pay to Zai a one-time payment of [****], which payment will be payment in-full for the assignment of all Assigned Collaboration Technology and Blueprint/Zai Combination Technology hereunder regardless of how many patent applications are filed or patents are issued Covering the Assigned Collaboration Know-How or Blueprint/Zai Combination Know-How. Blueprint will notify Zai of Blueprint's filing of the first patent application claiming any Assigned Collaboration Know-How or Blueprint/Zai Combination Know-How with respect to which an employee of Zai is an inventor. Promptly thereafter, Zai will invoice Blueprint for the foregoing amount, and Blueprint will pay the undisputed

invoiced amounts within [****] after the date of such invoice. The Parties expressly acknowledge that the foregoing amount is [****] and is [****].

(ii) **Reward and Remuneration Payments to Employees**. As between the Parties, Zai will be solely responsible for the payment of, and Zai will pay, any rewards and remuneration for inventions and technical achievements required by Applicable Law to be paid to its employees for the development or invention of any Collaboration Technology. As between the Parties, Blueprint will be solely responsible for the payment of, and Blueprint will pay, any rewards and remuneration for inventions and technical achievements required by Applicable Law to be paid to its employees for the development or invention of any Collaboration Technology.

14.2 Patent Prosecution.

14.2.1 **Blueprint Patent Rights**.

(a) **Right to Prosecute**. Subject to Section 14.2.3 (Joint Collaboration Technology), as between the Parties, Blueprint will have the right to control the Patent Prosecution of all Blueprint Patent Rights (including any Assigned Collaboration Patent Rights) and Blueprint Manufacturing Patent Rights throughout the world. Zai will obtain any necessary assignment documents for Blueprint with respect to the Patent Prosecution of such Patent Rights, to render all signatures that will be necessary for such patent filings, and to assist Blueprint in all other reasonably ways that are necessary for the issuance of such Patent Rights as well as for the Patent Prosecution of such Patent Rights. Zai will be responsible for [****] of the reasonable out-of-pocket costs incurred by or on behalf of Blueprint after the Effective Date with respect to the Patent Prosecution of such Patent Rights in the Territory, and will reimburse Blueprint for such costs [****] [****] after receiving an invoice with reasonable supporting documentation for such costs. Blueprint will be responsible for [****] of the out-of-pocket costs incurred by or on behalf of Blueprint with respect to the Patent Prosecution of such Patent Rights outside of the Territory.

(b) **Review and Consult**. Blueprint will consult with Zai and keep Zai reasonably informed of the Patent Prosecution of the Blueprint Patent Rights and Blueprint Manufacturing Patent Rights (following the applicable Manufacturing Technology Transfer) in the Territory and will provide Zai with all substantive correspondence received from any patent authority in the Territory in connection therewith. In addition, Blueprint will provide Zai with drafts of all proposed substantive filings in the Territory and correspondence to any patent authority in the Territory in connection with the Patent Prosecution of the Blueprint Patent Rights and Blueprint Manufacturing Patent Rights (following the applicable Manufacturing Technology Transfer) in the Territory for Zai's review and comment prior to the submission of such proposed filings and correspondence. Further, Blueprint will notify Zai of any decision to cease Patent Prosecution of any Blueprint Patent Rights or Blueprint Manufacturing Patent Rights (following the applicable Manufacturing Technology Transfer) in the Territory. Blueprint will consider Zai's comments on Patent Prosecution [****] and will incorporate such comments [****].

(c) **Abandonment**. If Blueprint decides not to continue the Patent Prosecution of a particular Blueprint Patent Right or Blueprint Manufacturing Patent Right (following the applicable Manufacturing Technology Transfer) in any region in the Territory during the Term, then it will promptly [****] provide written notice to Zai of such decision. Zai may, upon written notice to Blueprint, assume the Patent Prosecution of such Patent Right in Blueprint's name [****]. In such event, (i) Blueprint will promptly deliver to Zai copies of all necessary files related to such Blueprint Patent Right or Blueprint Manufacturing Patent Right in such region(s) in the Territory and will take all actions and execute all documents reasonably necessary for Zai to assume such responsibility, (ii) Zai will continue to be responsible for [****] of the costs and expenses of the Patent Prosecution of such Patent Right, and (iii) Blueprint will have the rights to review and consult set forth in Section 14.2.1(b) (Review and Consult) *mutatis mutandis* (including that Zai will have final decision-making authority with respect to such Patent Prosecution activities).

14.2.2 **Zai Collaboration Patent Rights**.

(a) **Right to Prosecute**. As between the Parties, Zai will have the right to control the Patent Prosecution of all Zai Collaboration Patent Rights throughout the world. Zai will be responsible for [****] of the costs and expenses incurred with respect to the Patent Prosecution of such Patent Rights throughout the world.

(b) **Review and Consult**. Zai will consult with Blueprint and keep Blueprint reasonably informed of the Patent Prosecution of the Zai Collaboration Patent Rights inside and outside the Territory and will provide Blueprint with all substantive correspondence received from any patent authority in connection therewith. In addition, Zai will provide Blueprint with drafts of all proposed substantive filings and correspondence to any patent authority in connection with the Patent Prosecution of the Zai Collaboration Patent Rights for Blueprint's review and comment prior to the submission of such proposed filings and correspondence, [****]. Further, Zai will notify Blueprint of any decision to cease Patent Prosecution of any Zai Collaboration Patent Rights inside or outside the Territory. Zai will consider Blueprint's comments on Patent Prosecution [****] and will incorporate such comments [****].

(c) **Abandonment**. If Zai decides not to continue the Patent Prosecution of a particular Zai Collaboration Patent Right in any country or region inside or outside the Territory during the Term, then it will promptly [****] provide written notice to Blueprint of such decision. Blueprint may, upon written notice to Zai, assume such Patent Prosecution of such Zai Collaboration Patent Right in Zai's name [****]. In such event, (i) Zai will promptly deliver to Blueprint copies of all necessary files related to such Zai Collaboration Patent Right in such country(ies) or region(s) and will take all actions and execute all documents reasonably necessary for Blueprint to assume such responsibility, (ii) Blueprint will then be responsible for [****] of the future costs and expenses of the Patent Prosecution of such Patent Right, and (iii) Zai will have the rights to review and consult set forth in Section 14.2.2(b) (Review and Consult) *mutatis mutandis* (including that Blueprint will have final decision-making authority with respect to such Patent Prosecution activities).

14.2.3 **Joint Collaboration Technology**.

(a) **Joint Collaboration Technology and Blueprint/Zai Combination Technology**. Unless otherwise agreed upon by the Parties in connection with the JSC's approval of any Blueprint/Zai Combination, the provisions of this Section 14.2.3(a) (Joint Collaboration Technology and Blueprint/Zai Combination Technology) will apply with respect to the Patent Prosecution of the Blueprint/Zai Combination Patent Rights in addition to the other Joint Collaboration Patent Rights. Blueprint will control the Patent Prosecution of any Blueprint/Zai Combination Patent Rights and any other Joint Collaboration Patent Rights outside of the Territory, and Zai will control the Patent Prosecution of any Blueprint/Zai Combination Patent Rights and any other Joint Collaboration Patent Right inside of the Territory, *provided* that Blueprint will control [****]. The Parties will use [****] to agree on a mutually acceptable strategy for the Patent Prosecution of the Blueprint/Zai Combination Patent Rights and any other Joint Collaboration Patent Rights and will ensure that the external counsels engaged by each Party for the Patent Prosecution of such Blueprint/Zai Combination Patent Rights and any other Joint Collaboration Patent Rights coordinate with each other with respect to such Patent Prosecution of the Blueprint/Zai Combination Patent Rights and any other Joint Collaboration Patent Rights inside and outside of the Territory (including with respect to the timing of the filing of patent applications inside and outside of the Territory). The Party with the right to control the Patent Prosecution of any Blueprint/Zai Combination Patent Rights and any other Joint Collaboration Patent Right pursuant to this Section 14.2.3(a) (Joint Collaboration Technology and Blueprint/Zai Combination Technology) (the "**Prosecuting Party**") will be responsible for the costs and expenses incurred with respect to the Patent Prosecution of such Patent Rights in their respective territory[****].

(b) **Review and Consult**. The Prosecuting Party will consult with the other Party and keep the other Party reasonably informed of the Patent Prosecution of the Joint Collaboration Patent Rights in its respective territory and will provide the other Party with all substantive correspondence received from any patent authority in such territory in connection therewith. In addition, the Prosecuting Party will provide the other Party with drafts of all proposed substantive filings and correspondence to any patent authority in its respective territory in connection with the Patent Prosecution of the Joint Collaboration Patent Rights for the other Party's review and comment prior to the submission of such proposed filings and correspondence. Further, the Prosecuting Party will notify the other Party of any decision to cease Patent Prosecution of any of the Joint Collaboration Patent Rights in its respective territory. The Prosecuting Party will consider the other Party's comments on Patent Prosecution but will have final decision-making authority under this Section 14.2.3(b) (Review and Consult).

(c) **Abandonment**. If the Prosecuting Party decides not to continue the Patent Prosecution of a particular Joint Collaboration Patent Right in its respective territory during the Term, then it will promptly [****] provide written notice to the other Party of such decision. The other Party may, upon written notice to the Prosecuting Party, assume the Patent Prosecution of such Patent Right in the applicable territory. In such event, (i) such Party will [****] deliver to the other Party copies of all necessary files related to such Joint Collaboration Patent Right in such country(ies) or region(s) and will take all actions and execute all documents reasonably

necessary for the other Party to assume such responsibility, (ii) the other Party will become the Prosecuting Party with respect to such Joint Collaboration Patent Rights in the applicable territory, (iii) the other Party will be responsible for [****] of the out-of-pocket costs incurred by the Prosecuting Party as set forth under Section 14.2.3(a) (Joint Collaboration Technology and Blueprint/Zai Combination Technology), and (iv) the other Party (that is no longer the Prosecuting Party) will retain the rights to review and consult set forth in Section 14.2.3(b) (Review and Consult).

14.2.4 **Cooperation**. Each Party will provide the other Party all reasonable assistance and cooperation in the Patent Prosecution efforts under this Section 14.2 (Patent Prosecution), including providing any necessary powers of attorney and executing any other required documents or instruments for such prosecution.

14.3 Patent Enforcement.

14.3.1 **Notice**. Each Party will notify the other within [****] of becoming aware of any alleged or threatened infringement by a Third Party of any of the (a) Blueprint Patent Rights or Blueprint Manufacturing Patent Rights in the Territory, (b) Zai Collaboration Patent Rights in the Territory, or (c) Blueprint/Zai Combination Patent Rights or other Joint Collaboration Patent Rights in the Territory, and, in each case, any related declaratory judgment or equivalent action alleging the invalidity, unenforceability, or non-infringement of such Patent Rights (collectively "**Product Infringement**"). For clarity, Product Infringement excludes any adversarial Patent Prosecution proceedings.

14.3.2 **Enforcement Rights**.

(a) **First Right; Step-In**.

(i) **Blueprint First Right**. Unless otherwise agreed by the Parties in writing, Blueprint will have the first right to bring and control any legal action to enforce any Blueprint Patent Rights, Blueprint Manufacturing Patent Rights, or Joint Collaboration Patent Rights other than the Blueprint/Zai Combination Patent Rights against any Product Infringement in the Territory as it reasonably determines appropriate, [****] and Blueprint will consider [****] the interests of Zai in such enforcement. [****]

(ii) **Zai First Right**. Zai will have the first right to bring and control any legal action to enforce the Blueprint/Zai Combination Patent Rights and Zai Collaboration Patent Rights against any Product Infringement in the Territory as it reasonably determines appropriate, [****] and Zai will consider [****] the interests of Blueprint in such enforcement. The Party with the first right to bring and control any legal action to enforce the Blueprint Patent Rights, Blueprint Manufacturing Patent Rights, Zai Collaboration Patent Rights, Blueprint/Zai Combination Patent Rights, or other Joint Collaboration Patent Rights, as applicable, will be referred to herein as the "**Controlling Party**."

(iii) **Step-In Rights**. If the Controlling Party or its designee fails to abate such Product Infringement in the Territory or to file an action to abate such

Product Infringement in the Territory related to Blueprint Patent Rights, Blueprint Manufacturing Patent Rights, Zai Collaboration Patent Rights, or Joint Collaboration Patent Rights (including Blueprint/Zai Combination Patent Rights) within [****] after a written request from the other Party to do so, or if the Controlling Party discontinues the prosecution of any such action after filing without abating such infringement, then, in either case, the other Party will have the right, at such other Party's cost and expense, to enforce the applicable Patent Rights against such Product Infringement in the Territory as it reasonably determines appropriate *provided* that (A) the Controlling Party does not provide reasonable rationale for not doing so or continuing to do so (including a substantive concern regarding counter-claims by the infringing Third Party), and (B) the other Party will not enter into any settlement admitting the invalidity of, or otherwise impairing, any such Patent Rights without the prior written consent of the Controlling Party.

(iv) **Zai's Rights**. Zai will have the sole right to bring and control any legal action to enforce Zai Patent Rights (other than Zai Collaboration Patent Rights) against any Product Infringement in the Territory at its own expense as it reasonably determines appropriate. Zai will not have the right to enforce any Blueprint Patent Rights, Blueprint Manufacturing Patent Rights, Zai Collaboration Patent Rights, Blueprint/Zai Combination Patent Rights, or other Joint Collaboration Patent Rights outside of the Territory.

14.3.3 **Cooperation**. At the request of the Party bringing an action related to a Product Infringement, the other Party will provide reasonable assistance in connection therewith, including by executing reasonably appropriate documents, cooperating in discovery, and joining as a party to the action if required by Applicable Law to pursue such action.

14.3.4 **Recoveries**. Any recoveries resulting from an enforcement action relating to a claim of Product Infringement in the Territory will be first applied against payment of each Party's costs and expenses in connection therewith. Any such recoveries relating to a claim of Product Infringement in the Territory in excess of such costs and expenses will be split as follows: [****].

14.4 Infringement of Third Party Rights.

14.4.1 **Notice**. If any Licensed Product used, sold, or manufactured (if applicable) by Zai or its Affiliates or Sublicensees becomes the subject of a Third Party's claim or assertion of infringement of a Patent Right or other rights in the Territory that are owned or controlled by such Third Party, then Zai will promptly notify Blueprint within [****] after receipt of such claim or assertion and will include in such notice a copy of any summons or complaint (or the equivalent thereof) received regarding the foregoing. Thereafter, the Parties will promptly meet to consider the claim or assertion and the appropriate course of action and may, if appropriate, agree on and enter into a "common interest agreement" wherein the Parties agree to their shared, mutual interest in the outcome of such potential dispute. The Parties will assert and not waive the joint defense privilege with respect to any communications between the Parties in connection with the defense of such claim or assertion.

14.4.2 **Defense**. Subject to any indemnification obligations under Section 13.2 (By Blueprint), Zai will be solely responsible for the defense of any such infringement claims brought against Zai[****]; *provided* that Zai will not agree to any settlement, consent to judgment, or other voluntary final disposition in connection with such defense action, in each case, without Blueprint's prior written consent (which consent will not be unreasonably delayed, withheld, or conditioned) if such settlement, consent to judgment, or other voluntary final disposition would (a) result in the admission of any liability or fault on behalf of Blueprint, (b) result in or impose any payment obligations upon Blueprint, or (c) subject Blueprint to an injunction or otherwise limit Blueprint's ability to take any actions or refrain from taking any actions under this Agreement or with respect to any Blueprint Compound or Licensed Product. Zai will keep Blueprint informed on the status of such defense action, and Blueprint will have the right, but not the obligation, to participate and be separately represented in such defense action at its sole option and at its own expense.

14.5 Patents Licensed from Third Parties. Each Party's rights under this Article 14 (Intellectual Property) with respect to the Patent Prosecution and enforcement of any Patent Right that is in-licensed by Blueprint or Zai from a Third Party will be subject to the rights of such Third Party to prosecute, enforce, and defend such Patent Right.

14.6 Patent Listings. With respect to patent listings in any patent listing system established by any applicable Regulatory Authority in a region in the Territory or under Applicable Law, including, (a) in the PRC, under Article 76 of the Patent Law of the PRC and its implementing measures and interpretations promulgated by relevant PRC Governmental Authorities, including the National Medical Products Administration (NMPA), the China National Intellectual Property Administration (CNIPA), and the Supreme People's Court, and (b) other equivalents thereof in the Territory, for Blueprint Patent Rights, Blueprint Manufacturing Patent Rights, or Collaboration Patent Rights Covering any Licensed Product, the Parties will discuss and agree which Patent Rights to list in such patent listing in such region (the "**Listing Patents**") (i) prior to the submission of the first and any subsequent MAA for such Licensed Product in such region to such applicable Regulatory Authority, (ii) within [****], but in any event reasonably in advance of the deadline for listing under Applicable Laws, after the receipt of the first and any subsequent Regulatory Approval in such region for such Licensed Product from such Regulatory Authority, including any additional Indication for such Licensed Product, (iii) within [****], but in any event reasonably in advance of the deadline for listing under Applicable Laws, after the issuance in such region of a patent included in the Listing Patents, and (iv) within [****] following the submission of a new patent application in such region Covering any Licensed Product included in the Blueprint Patent Rights, Blueprint Manufacturing Patent Rights, or Collaboration Patent Rights that has not been previously considered in any prior discussion and agreement of the Parties regarding Listing Patents; *provided* that, except as otherwise permitted under Applicable Laws, the Party holding the MAA for such Licensed Product in the Territory will not list, and will not be obligated to list, as of the date of listing, (A) any unissued patent, (B) any Patent Right that does not Cover the Licensed Product, (C) any patent that is of a type or that contains patent claims that are of a type not permitted to be listed under Applicable Law, or (D) any patent that such Party knows or has a reasonable basis to know is reasonably likely to be declared invalid by a competent Governmental Authority in such region. In furtherance of the foregoing clause (D), if either Party has such knowledge or reasonable basis, such Party will promptly notify and inform the Party of all facts and circumstances it is aware of underlying such knowledge or reasonable basis. In the event the Parties are unable to agree on which Patent Rights to list by the time required as provided under clause (i) to (iv) above, subject to the above proviso, Blueprint will have the final decision-making right over whether the Party holding the MAA for the applicable Licensed Product in the Territory will list any Blueprint Patent Rights, Blueprint Manufacturing Patent Rights, or Joint Collaboration Patent Rights, and Zai will

have the final decision-making right over whether the Party holding the MAA for the applicable Licensed Product in the Territory will list any issued patents included in the Zai Collaboration Patent Rights. The Party holding the MAA for the applicable Licensed Product in the Territory will promptly, and in any event at least [****] prior to the applicable deadline for listing under Applicable Laws, list the Listing Patents in the applicable patent listing system in the applicable regions in the Territory *provided*, that, without limiting the foregoing, if the Party holding the MAA for the applicable Licensed Product in the Territory has not listed the Listing Patents in the patent listing system of an applicable region before [****] prior to the deadline for listing in the applicable region, then the other Party may list the Listing Patents at anytime when permitted by Applicable Laws by providing prior written notice to the Party holding the MAA for the applicable Licensed Product in the Territory. The Party holding the MAA for the applicable Licensed Product in the Territory will provide copies of all documentation to be filed in connection with any such listing of Blueprint Patent Rights, Blueprint Manufacturing Patent Rights, or Joint Collaboration Patent Rights to the other Party prior to filing thereof and will consider the other Party's comments with respect to such documentation in good faith. The Party holding the MAA for the applicable Licensed Product in the Territory will cooperate with the other Party to the extent reasonably requested by the other Party to effectuate the intent of this Section 14.6 (Patent Listings), including providing all documentation, certifications, and consents necessary to effectuate the foregoing and setting up an account to list patents on the applicable patent listing system, and granting the other Party access to and a right to use such account as reasonably necessary to effectuate the intent of this Section 14.6 (Patent Listings). Neither Party will list any patent in any patent listing system in a region in the Territory for the Licensed Product, except in accordance with this Section 14.6 (Patent Listings).

14.7 **Patent Term Extensions**. With respect to any system for extending the term of Patent Rights in the Territory due to the time needed to obtain Regulatory Approval of a pharmaceutical product established by any applicable Regulatory Authority in any region in the Territory (a "**Patent Term Extension**"), adjusting the term of Patent Rights in the Territory due to the time needed to prosecute and obtain a grant of a Patent Right under Applicable Laws in any region in the Territory (a "**Patent Term Adjustment**"), or supplementary protection certificates and any other extensions that are now or become available in the future under Applicable Laws in any region in the Territory ("**Other Extensions**"), (a) Blueprint will have the right, but not the obligation, and will be solely responsible for making all decisions regarding Patent Term Extensions, Patent Term Adjustments, or Other Extensions in the Territory that are applicable to Blueprint Patent Rights, Blueprint Manufacturing Patent Rights, or Joint Collaboration Patent Rights and that become available directly as a result of the Regulatory Approval of a Licensed Product in the Territory or following issuance of a patent included in the Blueprint Patent Rights, Blueprint Manufacturing Patent Rights, or Joint Collaboration Patent Rights *provided* that Blueprint will consult with Zai with respect to such decisions and consider [****] the reasonable comments and concerns raised by Zai; and (b) Zai will have the right, but not the obligation, and will be solely responsible for making all decisions regarding Patent Term Extensions, Patent Term Adjustments, and Other Extensions in the Territory that are applicable to Zai Collaboration Patent Rights and that become available directly as a result of the Regulatory Approval of a Licensed Product in the Territory or following issuance of a patent included in the Zai Collaboration Patent Rights; *provided* that Zai will consult with Blueprint with respect to such decisions and consider [****] the reasonable comments and concerns raised by Blueprint. The Party holding the MAA for the applicable Licensed Product in the Territory will make the appropriate filings and applications in the Territory in order to effectuate each Party's decisions regarding Patent Term Extensions, Patent Term Adjustments, or Other Extensions in the Territory in accordance with the foregoing sentence. The Party holding the MAA for the applicable Licensed Product in the Territory will cooperate with the other Party to the extent reasonably requested by the other Party to effectuate the intent of this Section 14.7 (Patent Term Extensions),

including providing to the other Party all documentation, certifications, and consents necessary to make and prosecute such application and obtain such Patent Term Extension, Patent Term Adjustment, or Other Extension.

14.8 Filing of Agreement with CNIPA. The Parties will file a redacted copy of this Agreement with the CNIPA as required by Applicable Law in the Territory no later than the date required under such Applicable Law.

14.9 Product Trademarks.

14.9.1 **Global Brand Elements**. Zai acknowledges that Blueprint may decide to develop and adopt certain distinctive colors, logos, images, symbols, and trademarks to be used in connection with the Commercialization of each Licensed Product on a global basis (such trademarks, the "**Product Marks**" and such other branding elements together with the Product Marks, collectively, the "**Global Brand Elements**"). Blueprint will and hereby does grant Zai the exclusive right to use such Global Brand Elements in connection with the Commercialization of each Licensed Product in the Field in the Territory in accordance with the applicable Commercialization Plan.

14.9.2 **Product Marks in the Territory**. Zai will brand the Licensed Products in the Territory using Blueprint's Global Brand Elements; *provided*, *however*, a Product Mark may deviate from Blueprint's Global Brand Elements if (a) the JSC determines such Product Mark is not appropriate for the Territory due to linguistic reasons or market research showing that such Product Mark is not appropriate, (b) a Governmental Authority rejects or refuses such Product Mark for use in the Territory or such Product Mark is not registrable in the Territory, or (c) Zai reasonably desires alternative or additional trademarks in the applicable local language in the Territory. In the event of the foregoing (a), (b), or (c), Zai may select an alternative Licensed Product-specific trademark to use in connection with the Commercialization of Licensed Products in the Territory and will provide any such proposed Licensed Product-specific trademark to the JSC for review and comment prior to finally selecting and using any such proposed Licensed Product-specific trademark. Zai will not use any trademarks of Blueprint (including Blueprint's corporate name) or any trademark confusingly similar thereto without Blueprint's prior written consent. Following review thereof by the JSC, such Licensed Product-specific trademark will become a Product Mark for all purposes under this Agreement.

14.9.3 **Ownership**. Blueprint will be the sole and exclusive owner of all Product Marks and Global Brand Elements, including all trademark registrations and applications therefor and all goodwill associated therewith. To the extent Zai acquires any rights, title, or interests in or to any Product Mark or Global Brand Element (including any trademark registration or application therefore or goodwill associated with any Product Mark), Zai will, and hereby does, assign the same to Blueprint. Blueprint will and hereby does grant Zai the exclusive right to use such Product Marks in connection with the Commercialization of the applicable Licensed Product in the Territory. Upon Zai's request, Blueprint will register and maintain the Product Marks in the Territory using counsel of Blueprint's choice and [****].

14.9.4 **Use**. Zai agrees that it and its Affiliates and Sublicensees will Commercialize each of the Licensed Products in the Territory in a manner consistent with the Global Brand Elements and will: (a) ensure that all Licensed Products that are sold bearing the Product Marks and Global Brand Elements are of a high quality consistent with industry standards for global pharmaceutical and biologic therapeutic products; (b) ensure that each use of the Global

Brand Elements and Product Marks by Zai and its Affiliates and Sublicensees is accompanied by an acknowledgement that such Global Brand Elements and Product Marks are owned by Blueprint; (c) not use such Global Brand Elements or Product Marks in a way that might materially prejudice their distinctiveness or validity or the goodwill of Blueprint therein and includes the trademark registration symbol ® or ™ as appropriate; (d) not use any trademarks or trade names so resembling any of such Global Brand Elements or Product Marks as to be likely to cause confusion or deception; and (e) place and display the Global Brand Elements and the Product Marks on and in connection with the Licensed Products in a way that acknowledges Blueprint's role in discovering the Licensed Products and that such Licensed Product is under license from Blueprint. To the extent permitted by and consistent with Applicable Law, Zai will include the words (a) "*Discovered by Blueprint Medicines Corporation*" (or such other similar text provided by Blueprint and reasonably acceptable to Zai) on all packaging and labeling for any Licensed Product that is not a Blueprint/Zai Combination and in relevant scientific, medical, and other Licensed Product-related communications to the extent such communications address the Development or Commercialization of such a Licensed Product (that is not a Blueprint/Zai Combination), and (b) "*Discovered in Collaboration by Blueprint Medicines Corporation and Zai Pharmaceuticals*" (or such other similar text provided by Blueprint and reasonably acceptable to Zai) on all packaging and labeling for any Blueprint/Zai Combination (to the extent feasible, for example, if the Zai Product and the Blueprint Compound are co-packaged) and in relevant scientific, medical, and other Blueprint/Zai Combination-related communications to the extent such communications address the Development or Commercialization of a Blueprint/Zai Combination, in each case ((a) and (b)), in English unless required under Applicable Law to be in another language.

14.10 **Patent Marking**. Zai will mark all Licensed Products in accordance with the applicable patent marking laws, and will require all of its Affiliates and Sublicensees to do the same. To the extent permitted by Applicable Law, Zai will indicate on the product packaging, advertisement and promotional materials that such Licensed Product is in-licensed from Blueprint.

Article 15
TERM AND TERMINATION

15.1 **Term**. This Agreement will be effective as of the Effective Date, and will continue, on a Licensed Product-by-Licensed Product and region-by-region basis, in effect until the expiration of all payment obligations set forth under this Agreement with respect to such Licensed Product in such region (the "**Term**"). On a Licensed Product-by-Licensed Product and region-by-region basis, upon the natural expiration of this Agreement as contemplated in this Section 15.1 (Term), so long as at such time Zai has paid to Blueprint all undisputed amounts due under this Agreement and accrued prior to such natural expiration of the Term in accordance with the terms hereof and is not at such time in material breach of any term of this Agreement, the licenses granted to Zai under Section 2.1 (License Grants to Zai) will become non-exclusive, perpetual, and irrevocable.

15.2 **Termination**.

15.2.1 **Termination by Zai for Convenience**. Zai may terminate this Agreement in its entirety by providing a written notice of termination to Blueprint after the [****] anniversary of the Effective Date that includes an effective date of termination [****].

15.2.2 **Termination for Material Breach**.

(a) **Notice and Cure Period**. If either Party believes in good faith that the other is in material breach of any term of this Agreement, then the non-breaching Party may deliver notice of such breach to the other Party stating the cause and proposed remedy ("**Breach Notification**"). For any breach arising from a failure to make a payment set forth in this Agreement, the allegedly breaching Party will have [****] from the receipt of the applicable Breach Notice to dispute or cure such breach. If the Party receiving notice of breach fails to cure, or fails to dispute, that breach within the applicable period set forth above, then the Party originally delivering the Breach Notification may terminate this Agreement effective on written notice of termination to the other Party. For all breaches other than a failure to make a payment as set forth in this Agreement, the allegedly breaching Party will have [****] from the date of the Breach Notification to dispute or cure such breach, *provided* that if such breach (other than a payment breach) is not reasonably capable of cure within such [****] period, but is capable of cure within [****] from the date of such Breach Notification, then the breaching Party may submit, within [****] of such Breach Notification, a reasonable cure plan to remedy such breach as soon as possible and in any event prior to the end of such [****] period that is reasonably acceptable to the non-breaching Party, and, upon such submission, the [****] cure period will be automatically extended for so long as the breaching Party continues to use reasonable efforts to cure such breach in accordance with the cure plan, but for no more than [****]. Notwithstanding the foregoing, if the allegedly breaching Party disputes in good faith the existence or materiality of the alleged breach, then the other Party will not have the right to terminate this Agreement unless and until an arbitrator issues a final award pursuant to Section 16.3 (Arbitration) that the allegedly breaching Party has materially breached a term of this Agreement. During the pendency of such a dispute, all of the terms of this Agreement will remain in effect and the Parties will continue to perform all of their respective obligations hereunder. The cure period will be tolled starting as of the date of such notice of a dispute from the allegedly breaching Party and for the remainder of the pendency of any such dispute and such breaching Party will have the time remaining of the applicable cure period to cure the applicable breach after such award finding such breach is issued.

15.2.3 **Termination for Patent Challenge**. Except to the extent unenforceable under the Applicable Law, Blueprint may terminate this Agreement by providing written notice of termination to Zai if Zai or its Affiliates or Sublicensees (individually or in association with any Person) contests or assists a Third Party in contesting the scope, validity, or enforceability of any Blueprint Patent Right, Blueprint Manufacturing Patent Right, or Joint Collaboration Patent Right anywhere in the world in any court, tribunal, arbitration proceeding, or other proceeding, including the U.S. Patent and Trademark Office and the U.S. International Trade Commission (a "**Patent Challenge**") unless Zai or its applicable Affiliate withdraws, cancels, or otherwise terminates such Patent Challenge within [****] following the earlier of (a) Blueprint's notice or (b) the date on which Zai or its applicable Affiliate had written notice, or otherwise first became aware (as evidenced by written records), of such Patent Challenge[****] if: (i) [****] or (ii) [****] this Section 15.2.3 [****] As used herein, a Patent Challenge includes: (A) filing an action under 28 U.S.C. §§ 2201-2202 seeking a declaration of invalidity or unenforceability of any such Patent Right; (B) filing, or joining in, a petition under 35 U.S.C. § 311 to institute inter partes review of any such Patent Right; (C) filing, or joining in, a petition under 35 U.S.C. § 321 to institute post-grant review of any such Patent Right or any portion thereof; (D) filing

or commencing any opposition, nullity, or similar proceedings challenging the validity of any such Patent Right in any country or region; or (E) any foreign equivalent of clauses (A), (B), (C), or (D) [****].

15.2.4 **Cessation of Development and Commercialization**. If Zai and its Affiliates do not conduct any material Development or Commercialization activities with respect to one or more Licensed Products [****], and such suspension of activity is not: [****] then Blueprint may, at its election, terminate this Agreement upon [****] prior written notice to Zai if Zai does not commence material Development or Commercialization activities with respect to one or more Licensed Products before the expiration of such [****] notice period. Notwithstanding the foregoing, if Blueprint gives a notice of termination to Zai pursuant to this Section 15.2.4 (Cessation of Development or Commercialization), and Zai provides notice during such [****] period that it disputes the basis for termination pursuant to this Section 15.2.4 (Cessation of Development or Commercialization), then this Agreement will not terminate unless and until an arbitrator issues a final award pursuant to Section 16.3 (Arbitration) upholding such basis for termination. During the pendency of such a dispute, all of the terms of this Agreement will remain in effect and the Parties will continue to perform all of their respective obligations hereunder. The [****] notice period will be tolled starting as of the date of such notice of a dispute from Zai and for the remainder of the pendency of any such dispute and Zai will have the time remaining of the notice period to commence material Development or Commercialization activities with respect to one or more Licensed Products after the arbitrator has upheld the basis for termination.

15.2.5 **Termination for Insolvency**. Each Party will have the right to terminate this Agreement upon delivery of written notice to the other Party if (a) such other Party files in any court or agency pursuant to any statute or regulation of any jurisdiction a petition in bankruptcy or insolvency or for reorganization or similar arrangement for the benefit of creditors or for the appointment of a receiver or trustee of such other Party or its assets, (b) such other Party is served with an involuntary petition against it in any insolvency proceeding and such involuntary petition has not been stayed or dismissed within [****] of its filing, or (c) such other Party makes an assignment of substantially all of its assets for the benefit of its creditors.

15.2.6 **Full Force and Effect During Notice Period**. This Agreement will remain in full force and effect until the expiration of the applicable termination notice period. For clarity, if Zai or any of its Affiliates or Sublicensees achieve any Milestone Event during the termination notice period, then the corresponding Milestone Payment is accrued and Zai will remain responsible for the payment of such Milestone Payment even if the due date of such Milestone Payment occurs after the effective date of the termination.

15.3 Effect of Termination. Upon the termination of this Agreement (but not expiration of this Agreement):

15.3.1 **Licenses**. As of the effective date of termination of this Agreement (but not expiration of this Agreement), all licenses and all other rights granted by Blueprint to Zai under the Blueprint Technology and Blueprint Manufacturing Technology will terminate and all sublicenses granted by Zai pursuant to Section 2.2 (Sublicensing and Subcontractors) will also terminate. Each Party will retain its joint ownership interests in the Joint Collaboration Technology. In addition, upon the termination of this Agreement (but not expiration of this Agreement) Blueprint will have, and Zai hereby grants to Blueprint,

effective upon such termination, a worldwide, exclusive, perpetual, royalty-bearing [****] and sublicenseable (through multiple tiers) license under the Zai Technology, Zai's interests in the Joint Collaboration Technology and any Zai Identified Rights, in each case, Controlled by Zai as of the effective date of such termination and solely to Exploit the Licensed Products (in the form that such Licensed Products exist as of the effective date of termination). In addition to [****], subject to Blueprint's right to decline a license or sublicense of Zai In-Licensed Rights in accordance with the terms of Section 2.6.6(b) (Right to Decline Zai In-Licensed Rights) or by providing written notice to Zai within [****] of the effective date of termination of this Agreement declining such rights, Blueprint will reimburse Zai for amounts owed under such Zai Third Party IP Agreement in accordance with Section 2.6.6(c) (Responsibility for Costs of Zai In-Licensed Rights). In addition, Zai will assign to Blueprint any Third Party IP Agreement pursuant to which Zai then Controls any Zai Identified Rights, if such Third Party IP Agreement is specific to the terminated Licensed Product and if permitted under such Third Party IP Agreement (and will use reasonable efforts to seek any consent required from the applicable Third Party in connection with such an assignment). If such Third Party IP Agreement cannot be assigned to Blueprint, then upon Blueprint's reasonable request, Zai will maintain such Third Party IP Agreement and Blueprint will pay to Zai [****] of all payments due to the applicable Third Party under any such Third Party IP Agreement in consideration of the sublicense to Blueprint and Blueprint's Exploitation of such Zai Identified Rights. If Zai is unable to sublicense any Zai Identified Rights to Blueprint pursuant to this Section 15.3.1 (Effect of Termination; Licenses) without the consent of the Third Party, then Zai undertakes, on request from Blueprint, to use reasonable efforts to procure such licenses with respect to the applicable Licensed Products on behalf of Blueprint to the extent that it is able to do so, and Blueprint will pay such fees and agree to be bound by the terms agreed between Zai and the Third Party licensor.

15.3.2 **Appointment as Exclusive Distributor**. If Zai is Commercializing any Licensed Product in any region in the Territory as of the effective date of termination of this Agreement (but not expiration of this Agreement), then, at Blueprint's election (in its sole discretion) in the event of termination of this Agreement by Blueprint pursuant to Section 15.2.2 (Termination for Material Breach), Section 15.2.5 (Termination for Insolvency), or Section 15.2.4 (Cessation of Development and Commercialization), by Zai pursuant to Section 15.2.1 (Termination by Zai for Convenience), or in all other cases, at Zai's election (in its sole discretion), on a region-by-region basis in the Territory, until such time as all Regulatory Approvals with respect to such Licensed Product in such region have been assigned and transferred to Blueprint, either (a) Zai will (with Blueprint's consent in the event such election is made by Zai) appoint Blueprint or its designee as its exclusive distributor of such Licensed Product in such region and grant Blueprint or its designee the right to appoint sub-distributors, to the extent not prohibited by any written agreement between Zai or any of its Affiliates and a Third Party; *provided that* Blueprint will purchase any and all salable inventory of the Licensed Product held by Zai or its Affiliates as of the effective date of termination [****] or (b) Zai will have the continued right to sell the Licensed Product in such region from its inventory; *provided*, *however*, that Zai's obligations under this Agreement with respect to all such Licensed Product that Zai sells following termination, including the obligation to remit Royalty Payments to Blueprint hereunder, will continue in full force and effect during such period.

15.3.3 **Regulatory Submissions and Regulatory Approvals**. To the extent requested by Blueprint following the date that a Party provides notice of termination of this Agreement (but not expiration of this Agreement), Zai will and hereby does, and will cause its

Affiliates and Sublicensees to, (a) [****] assign and transfer to Blueprint or its designee all of Zai's rights, title, and interests in and to all Regulatory Submissions and Regulatory Approvals for Licensed Products then owned or Controlled by Zai or any of its Affiliates or Sublicensees, and (b) to the extent assignment pursuant to clause (a) is delayed or is not permitted by the applicable Regulatory Authority, permit Blueprint to cross-reference and rely upon any Regulatory Submissions and Regulatory Approvals filed by Zai with respect to a Licensed Product. Zai will take all steps necessary to transfer ownership of all such assigned Regulatory Submissions and Regulatory Approvals to Blueprint, including submitting to each applicable Regulatory Authority a letter or other necessary documentation (with a copy to Blueprint) notifying such Regulatory Authority of the transfer of such ownership of each Regulatory Submission and Regulatory Approval. In addition, upon Blueprint's written request, Zai will [****] provide to Blueprint copies of all material related documentation, including material non-clinical, preclinical, and clinical data that are held by or reasonably available to Zai or its Affiliates or Sublicensees. The Parties will discuss and establish appropriate arrangements with respect to safety data exchange, *provided* that Blueprint will assume all safety and safety database activities with respect to all Licensed Products no later than [****] after the effective date of termination of this Agreement.

15.3.4 **Assignment and Disclosure**. To the extent requested by Blueprint following the date that a Party provides notice of termination of this Agreement, Zai will promptly upon request (and in any event within [****]):

(a) assign and transfer to Blueprint or its designee all of Zai's rights, title, and interests in and to all clinical trial agreements, manufacturing and supply agreements, and distribution agreements (to the extent assignable and not cancelled), confidentiality and other agreements, data and other Know-How (including commercial information) in Zai's Control, in each case, relating solely to any Licensed Product and that are necessary or useful for the Exploitation of any Licensed Product;

(b) disclose to Blueprint or its designee all documents, records, and materials related to Licensed Products that are controlled by Zai or that Zai is able to obtain using reasonable efforts, and that embody the foregoing; and

(c) assign and transfer to Blueprint or its designee all of Zai's rights, title, and interests in and to any promotional materials, training materials, medical education materials, packaging and labeling, and all other literature or other information solely related to Licensed Products and copyrights and any registrations for the foregoing.

Unless this Agreement is terminated by Zai pursuant to Section 15.2.2 (Termination for Material Breach) or Section 15.2.5 (Termination for Insolvency), the costs and expenses associated with the assignments set forth in this Section 15.3.4 (Assignment and Disclosure) will be borne by Zai. To the extent that any agreement or other asset described in this Section 15.3.4 (Assignment and Disclosure) is not assignable by Zai, then such agreement or other asset will not be assigned, and upon the request of Blueprint, Zai will take such steps as may be necessary to allow Blueprint to obtain and to enjoy the benefits of such agreement or other asset, without additional payment therefor, in the form of a license or other right to the extent Zai has the right and ability to do so. For clarity, Blueprint will have the right to request that Zai take any or all of the foregoing actions in whole or in part, or with respect to all or any portion of the assets set forth in this Section 15.3.4 (Assignment and Disclosure).

15.3.5 **Regulatory Transfer Support**. In furtherance of the assignment of Regulatory Submissions and Regulatory Approvals and other data pursuant to Section 15.3.3 (Regulatory Submissions and Regulatory Approvals) and Section 15.3.4 (Assignment and Disclosure), Zai will appoint Blueprint as Zai's or its Affiliate's agent for all Licensed Product-related matters involving Regulatory Authorities until all Regulatory Approvals, Regulatory Submissions, and other governmental or regulatory filings that are not then in Blueprint's or its Affiliate's name have been assigned to Blueprint or its designee. In the event of failure to obtain such assignment, Zai hereby consents and grants to Blueprint the right to access and reference (without any further action required on the part of Zai, whose authorization to file this consent with any Regulatory Authority is hereby granted) any such item with respect to the Licensed Products.

15.3.6 **Know-How Transfer Support**. In furtherance of the assignment of Know-How pursuant to Section 15.3.4 (Assignment and Disclosure) and in addition to the requirements in Section 15.3.9 (Supply Following Termination), Zai will for a period of [****] from the effective date of termination of this Agreement, provide such consultation or other assistance as Blueprint may reasonably request to assist Blueprint in becoming familiar with such Know-How in order for Blueprint to undertake further Exploitation of the Licensed Products following termination of this Agreement [****].

15.3.7 **Inventory**. At Blueprint's election and request, Zai will transfer to Blueprint or its designee some or all inventory of each Licensed Product (including all final product, bulk drug substance, intermediates, works-in-process, formulation materials, reference standards, drug product clinical reserve samples, packaged retention samples, and the like) then in the possession or Control of Zai, its Affiliates or Sublicensees; *provided* that Blueprint will [****] and *provided further* that Zai may retain inventory to the extent retained to exercise its rights under Section 15.3.2 (Appointment of Exclusive Distributor).

15.3.8 **Wind Down and Transition**. Zai will be responsible, [****] for the wind-down of Zai's and its Affiliates' and its Sublicensees' Exploitation of all Licensed Products. Zai will, and will cause its Affiliates and Sublicensees to, reasonably cooperate with Blueprint to facilitate orderly transition of the Exploitation of each Licensed Product to Blueprint or its designee, including (a) assigning or amending as appropriate, upon request of Blueprint, any agreements or arrangements with Third Party vendors (including distributors) solely related to the Exploitation of each Licensed Product or, to the extent any such Third Party agreement or arrangement is not assignable to Blueprint, reasonably cooperating with Blueprint to arrange to continue to provide such services for a reasonable time after termination of this Agreement; and (b) to the extent that Zai or its Affiliate is performing any activities described in the foregoing clause (a), reasonably cooperating with Blueprint to transfer such activities to Blueprint or its designee and continuing to perform such activities on Blueprint's behalf for a reasonable time after termination of this Agreement until such transfer is completed.

15.3.9 **Supply Following Termination**. If, as of the effective date of termination of this Agreement, Blueprint has completed the Manufacturing Technology Transfer for a one or more Licensed Products and Zai is Manufacturing one or more such Licensed Products, then at Blueprint's written request, Zai will supply to Blueprint such quantities of such Licensed Product (in bulk drug substance, bulk drug product, or finished drug product form, as requested by Blueprint, to the extent within Zai's then current capacity restrictions as of the effective date of termination) as Blueprint indicates in written forecasts and orders therefor from time to time [****] until [****] (a) [****] and (b)

[****]. In addition, upon Blueprint's request, Zai will (i) provide a [****] technology transfer to Blueprint or its designee of information and materials [****] for Blueprint or its designee to Manufacture such Licensed Product in each formulation of such Licensed Product (as it exists at the time of termination of this Agreement and to the extent such information was not previously transferred by or on behalf of Blueprint to Zai or its Affiliate or designee), including providing reasonable assistance to Blueprint or its designee in connection therewith upon request, and (ii) assign to Blueprint any agreement that [****] relates to the Manufacture or supply of Licensed Products in the Territory, to the extent that such contract is assignable. If any such agreement is not assignable, then Zai will cooperate with Blueprint in all reasonable respects to secure the consent of the applicable Third Party to such assignment or to cause such Third Party to enter into a separate agreement with Blueprint on terms substantially similar to those granted to Zai. [****]

15.3.10 **Ongoing Clinical Trials**.

(a) **Transfer to Blueprint**. If, as of the effective date of termination of this Agreement, Zai or its Affiliates are conducting any Clinical Trials for Licensed Products, then, at Blueprint's election on a Clinical Trial-by-Clinical Trial basis, Zai will fully cooperate, and will ensure that its Affiliates fully cooperate, with Blueprint to transfer the conduct of such Clinical Trial to Blueprint or its designees. If Blueprint so elects, then Zai will continue to conduct such Clinical Trial [****] to enable such transfer to be completed without interruption of any such Clinical Trial (including the assignment of all related Regulatory Submissions and investigator and other agreements related to such Clinical Trials). [****] Zai will provide such knowledge transfer and other training to Blueprint or its designated Affiliate or Third Party as reasonably necessary for Blueprint or such designated Affiliate or Third Party to continue such Clinical Trial for the applicable Licensed Product.

(b) **Wind-Down**. If Blueprint does not elect to assume control over or have Zai continue to conduct any such Clinical Trials for a Licensed Product, then Zai will, in accordance with accepted pharmaceutical industry norms and ethical practices, wind-down the conduct of any such Clinical Trial in an orderly manner. Zai will be responsible for [****].

15.3.11 **Sublicense Survival**. Upon termination of this Agreement, upon the request of any Sublicensee of Zai that was granted a sublicense in accordance with the terms of Section 2.2.1 (Right to Sublicense) and that is not then in breach of its sublicense agreement or the terms of this Agreement applicable to such Sublicensee, Blueprint will negotiate [****] with such Sublicensee with respect to the grant of a direct license to such Sublicensee, which license will not be broader in license scope, territory, or duration than such sublicense agreement granted by Zai to such Sublicensee and not more burdensome on Blueprint [****] and no less favorable to Blueprint than the financial terms of Article 10 (Payments) for the scope, territory, and duration of such sublicense and *provided* that such Sublicensee agrees to comply with all applicable terms of this Agreement.

15.3.12 **Return of Confidential Information**. At the Disclosing Party's election, the Receiving Party will return (at Disclosing Party's expense) or destroy all tangible materials comprising, bearing, or containing any Confidential Information of the Disclosing Party relating to any Licensed Product that are in the Receiving Party's or its Affiliates' or Sublicensees' possession or control and provide written certification of such destruction

(except to the extent any information is the Confidential Information of both Parties or to the extent that the Receiving Party has the continuing right to use the Confidential Information under this Agreement); *provided that* the Receiving Party may retain one copy of such Confidential Information for its legal archives. Notwithstanding anything to the contrary set forth in this Agreement, the Receiving Party will not be required to destroy electronic files containing such Confidential Information that are made in the ordinary course of its business information back-up procedures pursuant to its electronic record retention and destruction practices that apply to its own general electronic files and information.

15.3.13 **Further Assistance**. Zai will provide any other assistance or take any other actions, in each case, reasonably requested by Blueprint as necessary to give effect to this Section 15.3 (Effect of Termination), and will execute all documents as may be reasonably requested by Blueprint in order to give effect to this Section 15.3 (Effect of Termination).

15.3.14 [****]

15.3.15 **Blueprint/Zai Combinations**. Notwithstanding any provision to the contrary set forth in this Agreement, the effects of termination as it relates to any Blueprint/Zai Combination will be subject to the applicable terms agreed upon by the Parties for such Blueprint/Zai Combination under Section 5.8 (Proposed Blueprint/Zai Combinations).

15.4 **Termination Press Releases**. In the event of termination of this Agreement for any reason and subject to the terms of Section 11.7.1 (Press Release), the Parties will cooperate in good faith to coordinate public disclosure of such termination and the reasons therefor, and will not, except to the extent required by Applicable Law, disclose such information without the prior approval of the other Party. In any such disclosures, the Parties will observe the principles of accuracy, compliance with Applicable Law, and regulatory guidance documents, and reasonable sensitivity to potential negative investor reaction to such news.

15.5 **Survival**. Expiration or termination of this Agreement will not relieve the Parties of any obligation accruing prior to such expiration or termination. Without limiting the foregoing, the following provisions of this Agreement will survive the expiration or termination of this Agreement: Article 1 (Definitions), Section 2.3.2 (Outside of Territory), Section 5.15 (Development Records), Section 5.17 (Data Exchange and Use) (to the extent set forth therein), Section 10.3.4 (Royalty Reports and Payments) (with respect to payments becoming due during the Term), Section 10.5 (Other Amounts Payable) (with respect to amounts becoming due during the Term), Section 10.11 (Financial Records and Audits) (with respect to payments becoming due during the Term), Section 11.1 (Duty of Confidence), Section 11.2 (Confidential Information), Section 11.3 (Authorized Disclosures), Section 11.4 (Tax Treatment), Section 11.5 (Publications), Section 11.8 (Attorney-Client Privilege), Section 12.8 (Time for Claims), Article 13 (Indemnification), Section 14.1 (Inventions), Section 14.2.3 (Joint Collaboration Technology), Section 14.2.4 (Cooperation), Section 14.9.3 (Ownership), Section 15.1 (Term), Section 15.3 (Effect of Termination), Section 15.4 (Termination Press Releases), Section 15.5 (Survival), Section 15.6 (Termination Not Sole Remedy), Article 16 (Dispute Resolution), and Article 17 (Miscellaneous).

15.6 **Termination Not Sole Remedy**. Termination is not the sole remedy under this Agreement and, whether or not termination is effected and notwithstanding anything to the contrary set forth in this Agreement, all other remedies will remain available except as expressly set forth herein.

Article 16
DISPUTE RESOLUTION

16.1 **General**. The Parties recognize that a dispute may arise relating to this Agreement or to the breach, enforcement, interpretation, or validity of this Agreement (a "**Dispute**"). Except as otherwise expressly set forth in this Agreement, any Dispute, including Disputes that may involve the Affiliates of any Party, will be resolved in accordance with this Article 16 (Dispute Resolution).

16.2 **Negotiation; Escalation**. The Parties will negotiate [****] to settle any Dispute under this Agreement, other than matters subject to resolution under Article 3 (Governance). Any Dispute relating to this Agreement or the breach, enforcement, interpretation, or validity of this Agreement will be referred to the Executive Officers for attempted resolution. If the Executive Officers are unable to resolve such Dispute within [****] after such Dispute is referred to them, then, upon the written request of either Party to the other Party, other than a Dispute relating to the scope, validity, enforceability, or infringement of any Patent Rights or trademark rights (which will be submitted for resolution to a court of competent jurisdiction in the country or region in which such Patent Rights or trademark rights were granted or arose), the Dispute will be subject to arbitration in accordance with Section 16.3 (Arbitration).

16.3 **Arbitration**.

16.3.1 **Rules**. In the event of a Dispute that cannot be resolved between the Parties or the Executive Officers as set forth in Section 16.2 (Negotiation; Escalation), either Party will be free to institute binding arbitration with respect to such dispute in accordance with this Section 16.3 (Arbitration) upon written notice to the other Party (an "**Arbitration Notice**") and seek remedies as may be available. Any dispute unresolved under this Section 16.3 (Arbitration) will be settled by binding arbitration administered by the International Chamber of Commerce ("**ICC**") (or any successor entity thereto) and in accordance with the ICC Rules of Arbitration then in effect, as modified in this Section 16.3 (Arbitration) (the "**Rules**"), except to the extent such rules are inconsistent with this Section 16.3 (Arbitration), in which case this Section 16.3 (Arbitration) will control.

16.3.2 **Selection of Arbitrators**. Upon receipt of an Arbitration Notice by a Party, the applicable dispute will be resolved by final and binding arbitration before a panel of three arbitrators (the "**Arbitrators**"), with each arbitrator having [****] of experience in the biotechnology or pharmaceutical industry and subject matter expertise with respect to the matter subject to arbitration [****]. Any Arbitrator chosen hereunder will have educational training and industry experience sufficient to demonstrate a reasonable level of scientific, financial, medical, and industry knowledge relevant to the particular dispute. Each Party will promptly select one Arbitrator, which selections will in no event be made later than [****] after receipt of the Arbitration Notice. The third Arbitrator will be chosen promptly by agreement of the Arbitrators chosen by each Party, but in no event later than [****] after the date on which the last of such Arbitrators was appointed. If the two Party-nominated Arbitrators cannot agree on the third Arbitrator, then the third Arbitrator will be appointed by ICC.

16.3.3 **Decisions**. The Arbitrators' decision and award will be made within [****]of the filing of the arbitration demand and the Arbitrators will agree to comply with this schedule before accepting appointment. However, this time limit may be extended by agreement of the Parties or by the Arbitrators. The Arbitrators will be authorized to award compensatory damages, but will not be authorized to reform, modify, or materially change

this Agreement. The Arbitrators will, within [****] after the conclusion of the hearing, issue a written award and statement of decision describing the material facts and the grounds for the conclusions on which the award is based, including the calculation of any damages awarded. The proceedings and decisions of the arbitrator will be confidential, final, and binding on the Parties, and judgment upon the award of such arbitrator may be entered in any court having jurisdiction thereof.

16.3.4 **Responsibility for Costs**. Each Party will bear its own costs and expenses (including legal fees and expenses) relating to the arbitration proceeding, except that the fees of the Arbitrators and other related costs of the arbitration will be shared equally by the Parties, unless the Arbitrators determine that a Party has incurred unreasonable expenses due to vexatious or bad faith positions taken by the other Party, in which event the Arbitrators may make an award of all or any portion of such expenses (including legal fees and expenses) so incurred.

16.3.5 **Limitations**. The Arbitrators will be required to apply the internal laws of the State of New York as the governing law for this Agreement and to render the decision in writing and to comply with, and the award will be limited by, any express provisions of this Agreement relating to damages or the limitation thereof. To the extent punitive or other indirect damages are expressly limited under this Agreement, no Arbitrator will have the power to award punitive damages under this Agreement, regardless of whether any such damages are contained in a proposal.

16.3.6 **Effectiveness of Agreement**. Unless the Parties otherwise agree in writing, during the period of time during which any arbitration proceeding is pending under this Agreement, (a) the Parties will continue to comply with all those terms and provisions of this Agreement that are not the subject of the pending arbitration proceeding; and (b) in the event that the subject of the Dispute relates to the exercise by a Party of a termination right hereunder, including in the case of a material breach of this Agreement, the effectiveness of such termination will be stayed until the conclusion of the proceedings under this Section 16.3 (Arbitration).

16.3.7 **Confidential Proceedings**. All arbitration proceedings and decisions of the Arbitrators under this Section 16.3 (Arbitration) will be Confidential Information of both Parties and subject to the terms of Article 11 (Confidentiality; Publication). The arbitration proceedings will take place in New York, New York, in the English language.

16.3.8 **Equitable Relief**. Nothing in this Section 16.3 (Arbitration) will preclude either Party from seeking equitable relief or interim or provisional relief from a court of competent jurisdiction, including a temporary restraining order, preliminary injunction, or other interim equitable relief, concerning a dispute either prior to or during any arbitration if necessary to protect the interests of such Party or to preserve the *status quo* pending the arbitration proceeding.

Article 17
MISCELLANEOUS

17.1 **Assignment**. This Agreement may not be assigned or otherwise transferred, nor may any right or obligation hereunder be assigned or transferred, by either Party without the prior written consent of the other Party. Notwithstanding the foregoing, Blueprint may assign its rights to receive payments under this Agreement to one or more Persons without consent of Zai [****], and either

Party may, without consent of the other Party, assign this Agreement and its rights and obligations hereunder (a) in whole or in part to an Affiliate of such Party, or (b) in whole to its successor-in-interest in connection with the sale of all or substantially all of its assets to which this Agreement relates, whether in a merger, acquisition, or similar transaction or series of related transactions; *provided* that in the case of the foregoing clause (a) or (b), the assigning Party provides written notice of such assignment to the non-assigning Party within [****] after the effective date of such assignment. Any attempted assignment of this Agreement not in accordance with this Section 17.1 (Assignment) will be null, void, and of no legal effect. Any permitted assignee will assume all assigned obligations of its assignor under this Agreement. The terms of this Agreement will be binding upon, and will inure to the benefit of, the Parties and their respected successors and permitted assigns.

17.2 **Limitation of Liability**. NEITHER PARTY WILL BE LIABLE TO THE OTHER FOR ANY SPECIAL, CONSEQUENTIAL, INCIDENTAL, PUNITIVE, OR INDIRECT DAMAGES ARISING FROM OR RELATING TO ANY BREACH OF THIS AGREEMENT, OR DAMAGES FOR LOSS OF PROFIT IN CONNECTION WITH THIS AGREEMENT, IN EACH CASE, REGARDLESS OF ANY NOTICE OF THE POSSIBILITY OF SUCH DAMAGES. NOTWITHSTANDING THE FOREGOING, NOTHING IN THIS SECTION 17.2 (LIMITATION OF LIABILITY) IS INTENDED TO OR WILL LIMIT OR RESTRICT THE INDEMNIFICATION RIGHTS OR OBLIGATIONS OF ANY PARTY UNDER SECTION 13.1 (BY ZAI) OR SECTION 13.2 (BY BLUEPRINT), OR DAMAGES AVAILABLE TO A PARTY FOR THE OTHER PARTY'S BREACH OF ITS OBLIGATIONS HEREUNDER RELATING TO Article 10 (CONFIDENTIALITY; PUBLICATION), MISAPPROPRIATION OR INFRINGEMENT OF INTELLECTUAL PROPERTY OWNED OR CONTROLLED BY SUCH PARTY, OR A PARTY'S BREACH OF ITS OBLIGATIONS UNDER SECTION 2.8 (EXCLUSIVITY).

17.3 **Severability**. If any one or more of the provisions contained in this Agreement is held invalid, illegal or unenforceable in any respect, the validity, legality, and enforceability of the remaining provisions contained herein will not in any way be affected or impaired thereby, unless the absence of the invalidated provisions adversely affects the substantive rights of the Parties. The Parties will in such an instance use their best efforts to replace the invalid, illegal or unenforceable provisions with valid, legal, and enforceable provisions that, insofar as practical, implement the purposes of this Agreement.

17.4 **Notices**. All notices that are required or permitted hereunder will be in writing and sufficient if delivered by internationally-recognized overnight courier or sent by registered or certified mail, postage prepaid, return receipt requested, and in each case, addressed as follows (with a courtesy copy sent by email, which will not constitute notice):

If to Blueprint:

Blueprint Medicines Corporation
45 Sidney Street
Cambridge MA 02139 USA
Attention: Chief Executive Officer

with a copy to:

Blueprint Medicines Corporation
45 Sidney Street

Cambridge MA 02139 USA
Attention: Chief Legal Officer
Email: [****]

If to Zai:

Zai Lab Limited
4F, Bldg 1, Jinchuang Plaza
4560 Jinke Rd
Shanghai, China, 201210
Attention: [****]
With an electronic copy to [****]

with a copy to:

Cooley LLP
3175 Hanover Street
Palo Alto, CA 94303
USA
Attention: [****]
with an electronic copy to [****]

or to such other address as the Party to whom notice is to be given may have furnished to the other Party in writing in accordance herewith. Any such notice will be deemed to have been given: (a) [****] after dispatch if sent by internationally-recognized overnight courier; or (b) [****] after dispatch if sent by registered or certified mail, postage prepaid, return receipt requested.

17.5 **Governing Law**. This Agreement, and all claims or causes of action (whether in contract, tort or statute) that may be based upon, arise out of or relate to this Agreement, or the negotiation, execution or performance of this Agreement or the breach thereof (including any claim or cause of action based upon, arising out of or related to any representation or warranty made in or in connection with this Agreement or as an inducement to enter into this Agreement), will be governed by, and enforced in accordance with, the internal laws of the State of New York, including its statutes of limitations without giving effect to the conflicts of law provisions thereunder.

17.6 **Force Majeure**. Both Parties will be excused from the performance of their obligations under this Agreement to the extent that such performance is prevented by force majeure and the nonperforming Party promptly provides notice of the prevention to the other Party. Such excuse will continue only so long as the condition constituting force majeure continues and the nonperforming Party takes reasonable efforts to remove the condition. When the force majeure no longer exists, the affected Party must promptly resume performance. For purposes of this Agreement, "force majeure" will include conditions beyond the reasonable control of the non-performing Party, including an act of God, war, civil commotion, terrorist act, labor strike or lock-out, epidemic, pandemic, failure or default of public utilities or common carriers, destruction of production facilities or materials by fire, earthquake, storm or like catastrophe, failure of plant or machinery and act (or failure to act) of a government of any country or of any Governmental Authority (other than as a result of the non-performing Party's failure to comply with Applicable Law). The Parties agree the effects of the COVID-19 pandemic that is ongoing as of the Effective Date may be invoked as a force majeure for the purposes of this Agreement even though the pandemic is ongoing to the extent those effects are not reasonably foreseeable by the Parties as of

the Effective Date. Notwithstanding the foregoing, a Party will not be excused from making undisputed payments that have accrued and are owed hereunder because of a force majeure affecting such Party. The affected Party will notify the other Party in writing of any force majeure circumstances that may affect its performance under this Agreement as soon as reasonably practical, will provide a good faith estimate of the period for which its failure or delay in performance under the Agreement is expected to continue based on currently available information, and will undertake reasonable efforts necessary to mitigate and overcome such force majeure circumstances and resume normal performance of its obligations hereunder as soon as reasonably practicable under the circumstances. If the force majeure circumstance continues, then the affected Party will update such notice to the other Party on a bi-weekly basis, or more frequently if requested by the other Party, to provide updated summaries of its mitigation efforts and its estimates of when normal performance under the Agreement will be able to resume.

17.7 **Entire Agreement; Amendments**. This Agreement, together with the Schedules hereto, contains the entire understanding of the Parties with respect to the collaboration and the licenses granted hereunder. Any other express or implied agreements and understandings, negotiations, writings and commitments, either oral or written, in respect to the collaboration and the licenses granted hereunder, including the Confidentiality Agreement, are superseded by the terms of this Agreement. The Schedules to this Agreement are incorporated herein by reference and will be deemed a part of this Agreement. This Agreement may be amended, or any term hereof modified, only by a written instrument duly executed by authorized representatives of each Party. The foregoing will not be interpreted as a waiver of any remedies available to either Party or its Affiliates as a result of any breach, prior to the Effective Date, by the other Party or its Affiliates of such Party's or its Affiliate's obligations pursuant to the Confidentiality Agreement.

17.8 **Headings**. The captions to the several Article**s**, Sections and subsections hereof are not a part of this Agreement, but are merely for convenience to assist in locating and reading the several Articles and Sections of this Agreement.

17.9 **Independent Contractors**. It is expressly agreed that Blueprint and Zai will be independent contractors and that the relationship between the two Parties will not constitute a partnership, joint venture or agency. Neither Blueprint nor Zai will have the authority to make any statements, representations, or commitments of any kind, or to take any action that is binding on the other Party without the prior written consent of the other Party.

17.10 **Performance by Affiliates**. Notwithstanding anything to the contrary set forth in this Agreement, ether Party will have the right to perform any or all of its obligations and exercise any or all of its rights under this Agreement through any Affiliate. Each Party hereby guarantees the performance by its Affiliates of such Party's obligations under this Agreement and will cause its Affiliates to comply with the provisions of this Agreement in connection with such performance.

17.11 **Waiver**. Any waiver of any provision of this Agreement will be effective only if in writing and signed by Blueprint and Zai. No express or implied waiver by a Party of any default under this Agreement will be a waiver of a future or subsequent default. The failure or delay of any Party in exercising any rights under this Agreement will not constitute a waiver of any such right, and any single or partial exercise of any particular right by any Party will not exhaust the same or constitute a waiver of any other right provided in this Agreement.

17.12 **Waiver of Rule of Construction**. Each Party has had the opportunity to consult with counsel in connection with the review, drafting and negotiation of this Agreement. Accordingly, the rule of

construction that any ambiguity in this Agreement will be construed against the drafting Party will not apply.

17.13 Cumulative Remedies. No remedy referred to in this Agreement is intended to be exclusive, but each will be cumulative and in addition to any other remedy referred to in this Agreement or otherwise available under Applicable Law.

17.14 Business Day Requirements. If any notice or other action or omission is required to be taken by a Party under this Agreement on a day that is not a Business Day, then such notice or other action or omission will be deemed to be required to be taken on the next occurring Business Day.

17.15 Further Actions. Each Party agrees to execute, acknowledge, and deliver such further instruments, and to do all such other acts, as necessary or appropriate in order to carry out the purposes and intent of this Agreement.

17.16 Non-Solicitation of Employees. [****] each Party agrees that neither it nor any of its Affiliates will recruit, solicit, or induce any employee of the other Party [****] to terminate his or her employment with such other Party and become employed by or consult for such Party, whether or not such employee is a full-time employee of such other Party, and whether or not such employment is pursuant to a written agreement or is at-will. For purposes of the foregoing, "recruit," "solicit," or "induce" will not be deemed to mean (a) circumstances where an employee of a Party (i) initiates contact with the other Party or any of its Affiliates with regard to possible employment; or (ii) responds to general solicitations of employment not specifically targeted at employees of a Party or any of its Affiliates, including responses to general advertisements or postings, and (b) discussions, interviews, negotiations, offers, or acceptances of employment or similar activities that arise as a result of circumstances described in the foregoing clause (a).

17.17 Construction. Except where the context expressly requires otherwise, (a) the use of any gender herein will be deemed to encompass references to either or both genders, and the use of the singular will be deemed to include the plural (and vice versa), (b) the words "include," "includes," and "including" will be deemed to be followed by the phrase "without limitation," (c) the word "will" will be construed to have the same meaning and effect as the word "shall," (d) any definition of or reference to any agreement, instrument, or other document herein will be construed as referring to such agreement, instrument, or other document as from time to time amended, supplemented, or otherwise modified (subject to any restrictions on such amendments, supplements or modifications set forth herein), (e) any reference herein to any person will be construed to include the person's successors and assigns, (f) the words "herein," "hereof," and "hereunder" and words of similar import, will each be construed to refer to this Agreement in its entirety and not to any particular provision hereof, (g) all references herein to Articles, Sections, Schedules, or Exhibits will be construed to refer to Articles, Sections, Schedules, or Exhibits of this Agreement, and references to this Agreement include all Schedules hereto, (h) the word "notice" means notice in writing (whether or not specifically stated) and will include notices, consents, approvals and other written communications contemplated under this Agreement, (i) provisions that require that a Party, the Parties or any committee hereunder "agree," "consent," "approve," or the like will require that such agreement, consent, or approval be specific and in writing, whether by written agreement, letter, approved minutes, or otherwise (but excluding e-mail and instant messaging), (j) references to any specific law, rule or regulation, or section or other division thereof, will be deemed to include the then-current amendments thereto or any replacement or successor law, rule or regulation thereof, and (k) the term "or" will be interpreted in the inclusive sense commonly associated with the term "and/or."

17.18 Language; Translations. This Agreement is in the English language only, which language will be controlling in all respects, and all versions hereof in any other language will be for accommodation only and will not be binding upon the Parties. All communications and notices to be made or given by one Party to the other pursuant to this Agreement, and any dispute proceeding related to or arising hereunder, will be in the English language. If there is a discrepancy between this Agreement and any non-English translation of this Agreement, this Agreement will prevail. Upon Blueprint's request, Zai will provide to Blueprint any documentation in English already in Zai's possession. For other material data, information, documents or materials, Zai will provide to Blueprint [****] in English upon Blueprint's reasonable request. In addition, at Blueprint's request, Zai will provide a full English translation of such material data, information, or materials [****]. Zai will be responsible[****] for the translation to Chinese of any documentation provided by Blueprint. [****]

17.19 Counterparts. This Agreement may be executed in counterparts, all of which taken together will be regarded as one and the same instrument. Counterparts may be delivered via electronic mail, including Adobe™ Portable Document Format (PDF) or any electronic signature complying with the U.S. Federal ESIGN Act of 2000, and any counterpart so delivered will be deemed to be original signatures, will be valid and binding upon the Parties, and, upon delivery, will constitute due execution of this Agreement.

{Signature Page Follows}

IN WITNESS WHEREOF, the Parties intending to be bound have caused this License and Collaboration Agreement to be executed by their respective duly authorized representatives as of the Effective Date.

BLUEPRINT MEDICINES CORPORATION

By: /s/ Jeff Albers

Name: Jeff Albers

Title: CEO

ZAI LAB (SHANGHAI) CO., LTD

By: /s/ Samantha Du

Name: Samantha Du

Title: CEO

Exhibit 21.1

Subsidiaries of the Registrant

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

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

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

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

of our reports dated February 17, 2022, with respect to the consolidated financial statements of Blueprint Medicines Corporation and the effectiveness of internal control over financial reporting of Blueprint Medicines Corporation included in this Annual Report (Form 10-K) of Blueprint Medicines Corporation for the year ended December 31, 2021.

/s/ Ernst & Young LLP

Boston, Massachusetts
February 17, 2022

Exhibit 31.1

CERTIFICATIONS

I, Jeffrey W. Albers, certify that:

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

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

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

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

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

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

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

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

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

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

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

Date: February 17, 2022

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

Exhibit 31.2

CERTIFICATIONS

I, Michael Landsittel, certify that:

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

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

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

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

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

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

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

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

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

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

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

Date: February 17, 2022

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

Exhibit 32.1

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

In connection with the Annual Report on Form 10-K of Blueprint Medicines Corporation (the "Company") for the year ended December 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), each of the undersigned officers of the Company hereby certifies, pursuant to 18 U.S.C. Section 1350, that to his knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: February 17, 2022

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

Date: February 17, 2022

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