BeiGene, Ltd.
Form 10-K
February 28, 2019
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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10 K

(Mark One)

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

For the fiscal year ended December 31, 2018

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 37686

BEIGENE, LTD.
(Exact Name of Registrant as Specified in its Charter)

Cayman Islands	98 1209416
(State or Other Jurisdiction of Incorporation or Organization)	(I.R.S. Employer Identification No.)
c/o Mourant Governance Services (Cayman) Limited 94 Solaris Avenue, Camana Bay Grand Cayman Cayman Islands (Address of Principal Executive Offices)	KY1 1108 (Zip Code)

+1 (345) 949 4123
(Registrant's Telephone Number, Including Area Code)

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

Title of each class	Name of each exchange on which registered
American Depositary Shares, each representing 13 Ordinary Shares, par value $0.0001 per share	The NASDAQ Global Select Market
Ordinary Shares, par value $0.0001 per share*	The Stock Exchange of Hong Kong Limited

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 T No £

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

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 T 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 during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes T No £

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10 K or any amendment to this Form 10 K. T

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

				Smaller reporting company £
Large accelerated filer T	Accelerated filer £	Non accelerated filer £	Emerging growth company £	

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

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

As of June 29, 2018, the last business day of the registrant's most recently completed second fiscal quarter, the aggregate market value of the ordinary shares, including in the form of American Depositary Shares, or ADSs, each representing 13 ordinary shares, held by non affiliates of the registrant was approximately $4.6 billion, based upon the closing price of the registrant's ADSs on the NASDAQ Global Select Market on June 29, 2018.

As of February 15, 2019, 776,113,184 ordinary shares, par value $0.0001 per share, were outstanding, of which 599,894,893 ordinary shares were held in the form of 46,145,761 ADSs.

DOCUMENTS INCORPORATED BY REFERENCE

The registrant intends to file a definitive proxy statement pursuant to Regulation 14A within 120 days of the end of the fiscal year ended December 31, 2018. Portions of such definitive proxy statement are incorporated by reference into Part III of this Annual Report on Form 10 K.

*Included in connection with the registration of the American Depositary Shares with the Securities and Exchange Commission. The ordinary shares are not registered or listed for trading in the United States but are listed for trading on The Stock Exchange of Hong Kong Limited.

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Forward Looking Statements and Market Data

This Annual Report on Form 10 K, or Annual Report, contains forward looking statements that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this Annual Report, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, objectives of management and expected growth, are forward looking statements. These statements 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 the forward looking statements.

Forward looking statements are often identified by the use of words such as, but not limited to, “anticipate,” “believe,” “can,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “project,” “seek,” “should,” “target,” “will,” “would expressions or variations intended to identify forward-looking statements, although not all forward-looking statements contain those identifying words. These forward looking statements include, among other things, statements about:

- the initiation, timing, progress and results of our preclinical studies and clinical trials and our research and development programs;
- our ability to advance our drug candidates into, and successfully complete, clinical trials;
- our reliance on the success of our clinical stage drug candidates;
- our plans, expected milestones and the timing or likelihood of regulatory filings and approvals;
- the commercialization of our drugs and drug candidates, if approved;
- our ability to further develop sales and marketing capabilities and launch new drugs, if approved;
- the pricing and reimbursement of our drugs and drug candidates, if approved;
- the implementation of our business model, strategic plans for our business, drugs, drug candidates and technology;
- the scope of protection we (or our licensors) are able to establish and maintain for intellectual property rights covering our drugs, drug candidates and technology;
- our ability to operate our business without infringing, misappropriating or otherwise violating the intellectual property rights and proprietary technology of third parties;
- costs associated with enforcing or defending against intellectual property infringement, misappropriation or violation, product liability and other claims;
- regulatory developments in the United States, China, the United Kingdom, the European Union and other jurisdictions;
- the accuracy of our estimates regarding expenses, revenues, capital requirements and our need for additional financing;
- the potential benefits of strategic collaboration and licensing agreements and our ability to enter into strategic arrangements;
- our ability to maintain and establish collaborations or licensing agreements;
- our reliance on third parties to conduct drug development, manufacturing and other services;
- our ability to manufacture and supply, or have manufactured and supplied, drug candidates for clinical development and drugs for commercial sale;
- the rate and degree of market access and acceptance and reimbursement of our drugs and drug candidates, if approved;

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- developments relating to our competitors and our industry, including competing therapies;
- the size of the potential markets for our drugs and drug candidates and our ability to serve those markets;
- our ability to effectively manage our growth;
- our ability to attract and retain qualified employees and key personnel;
- statements regarding future revenue, hiring plans, expenses, capital expenditures, capital requirements and share performance;
- the future trading price of our American Depositary Shares, or ADSs, and ordinary shares, and impact of securities analysts' reports on these prices; and
- other risks and uncertainties, including those listed under "Part I-Item 1A-Risk Factors."

These forward looking statements are only predictions and we may not actually achieve the plans, intentions or expectations disclosed in such statements, so you should not place undue reliance on them. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward looking statements we make. We have based these forward looking statements largely on our current expectations and projections about future events and trends that we believe may affect our business, financial condition and operating results. We have included important factors in the cautionary statements included in this Annual Report, particularly in "Part I-Item 1A-Risk Factors," that could cause actual future results or events to differ materially from the forward looking statements that we make. Our forward looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

You should read this Annual Report and the documents that we have filed as exhibits to the Annual Report with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward looking statements whether as a result of new information, future events or otherwise, except as required by applicable law.

This Annual Report includes statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties. Industry publications and third party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. While we believe these industry publications and third-party research, surveys and studies are reliable, you are cautioned not to give undue weight to this information.

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PART I

Unless the context requires otherwise, references in this report to "BeiGene," the "Company," "we," "us," and "our" refer to BeiGene, Ltd. and its subsidiaries, on a consolidated basis.

Item 1. Business

Overview

We are a commercial-stage biotechnology company focused on developing and commercializing innovative molecularly-targeted and immuno-oncology drugs for the treatment of cancer. Our internally-developed lead drug candidates are currently in late-stage clinical trials, including 21 registration or registration-enabling trials in 14 discrete cancer indications. We have submitted three new drug applications for regulatory approval in China and are planning for new drug launches and additional submissions in China and the United States in 2019 and 2020. In addition, we are marketing three in-licensed cancer drugs in China from which we have been generating product revenue since September 2017.

We started as a research and development company in Beijing in 2010, focusing on developing best-in-class oncology drugs. Over the last nine years, we have developed into a fully-integrated global biotechnology company with operations in China, the United States, Europe and Australia, including a more than 800-person global clinical development team running over 50 ongoing or planned clinical trials as of January 24, 2019. We also have a growing commercial team that is selling our existing in-licensed drugs in China and preparing for launches of our internally-developed drug candidates in China and the United States, as well as internal manufacturing capabilities in China that are operational or under construction for the clinical and commercial supply of our small molecule and biologic drug candidates.

Our lead internally-developed drug candidates include the following:

- Zanubrutinib (BGB-3111) - a potentially best-in-class investigational small molecule inhibitor of Bruton's tyrosine kinase, or BTK, designed to maximize BTK occupancy and minimize off-target effects, that is currently being evaluated in a broad pivotal clinical program in China and in other markets, including the United States, Europe and Australia, which we refer to as globally, for which we submitted for approval in China in 2018 initially for the treatment of patients with relapsed or refractory (R/R) mantle cell lymphoma, or MCL, and chronic lymphocytic leukemia or small lymphocytic lymphoma, or CLL/SLL. We subsequently received priority review in China for both R/R MCL and R/R CLL/SLL. We also plan to submit in 2019 or early 2020 a new drug application, or NDA, to the U.S. Food and Drug Administration, or the FDA, and an NDA in China for Waldenström's Macroglobulinemia, or WM. In the United States, the FDA has granted zanubrutinib Fast Track status in WM and Breakthrough Therapy designation for the treatment of adult patients with MCL who have received at least one prior therapy. We plan to launch zanubrutinib in China and the United States if we receive approval from the relevant regulatory authorities;
- Tislelizumab (BGB-A317) - an investigational humanized IgG4 monoclonal antibody against the immune checkpoint receptor programmed cell death protein 1, or PD-1, specifically designed to minimize binding to Fc R on macrophages, that is currently being evaluated in a broad pivotal clinical program for both solid tumor and hematological indications, both globally and in China, for which we submitted for approval in China in 2018 initially for the treatment of R/R classical Hodgkin's lymphoma, or cHL. We subsequently received priority review in China, and we plan to launch tislelizumab in China if we receive approval. We also plan to file an NDA in China for the treatment of urothelial bladder cancer, or UBC; and
- Pamiparib (BGB-290) - an investigational small molecule inhibitor of poly ADP-ribose polymerase 1, or PARP1, and PARP2 enzymes that is being evaluated in two pivotal clinical trials in China, a global Phase 3 trial, and earlier-stage trials in solid tumor cancers.

In addition to our three late-stage clinical drug candidates, our pipeline also includes three internally-developed drug candidates in early stage clinical development: lifirafenib (BGB-283), an investigational RAF dimer inhibitor; BGB-A333, an investigational humanized monoclonal antibody against the immune checkpoint receptor ligand PD-L1; and BGB-A425, an investigational humanized monoclonal antibody against TIM-3. We also pursue in-licensing opportunities that, among other things, allow us to help our collaborators by leveraging our capabilities in clinical development and commercialization in China and other Asia-Pacific countries. Our business development efforts have led to a development-stage portfolio that includes sitravatinib, an investigational, spectrum-selective

kinase inhibitor in clinical development by Mirati Therapeutics, Inc., or Mirati, for which we have in-licensed development and commercial rights in Asia (excluding Japan), Australia and New Zealand; and ZW25 and ZW49, two bispecific antibody-based biologic drug candidates targeting HER2, in clinical

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development by Zymeworks Inc., or Zymeworks, for which we have in-licensed development and commercial rights in Asia (excluding Japan), Australia and New Zealand.

We entered into a strategic collaboration with Celgene Corporation in August 2017, in which we obtained an exclusive license to market in China Celgene's approved cancer therapies ABRAXANE®, REVLIMID® and VIDAZA®, as well as rights in China to develop and commercialize avadomide (CC-122), an investigational next-generation Cereblon modulator currently in clinical development by Celgene outside of China for lymphoma and hepatocellular carcinomas, or HCC. As part of the collaboration, we also granted Celgene an exclusive right to develop and commercialize tislelizumab for solid tumors in the United States, Europe, Japan and the rest of the world other than Asia.

We believe that we are well-positioned to capture significant market opportunities in China for innovative cancer therapies, including those created by recent regulatory reforms and new reimbursement policies. China is the second largest pharmaceutical market in the world based on revenue. We believe that there is a large and growing opportunity for novel cancer therapeutics in China based on significant unmet medical need, a large target patient population, expanding reimbursement coverage, and increasing treatment affordability and willingness to pay. In addition, China's chief drug regulator, the National Medical Products Administration, or NMPA, has undertaken significant regulatory reforms that are designed to accelerate the development of new innovative drugs and allow China to be an integral part of global drug development. In addition, innovative oncology drugs have been included in the most recent National Reimbursement Drug List, or NRDL, reducing out-of-pocket expenses for patients. We believe that access to the large number of patients in China during clinical development as well as commercialization creates new opportunities for us. Leveraging our strong China presence and experience, as well as our commitment to global standards of innovation and quality, we believe that we have a unique ability to effectively take advantage of these opportunities.

Our Strategy

Our mission is to become a global leader in the discovery, development and commercialization of innovative therapies. In the near term, we plan to focus on pursuing what we believe are the following significant opportunities:

- Globally Develop and Commercialize Zanubrutinib, a Potentially Best-in-Class BTK Inhibitor. Zanubrutinib is an investigational small molecule inhibitor of BTK that is currently being evaluated both as a monotherapy and in combination with other therapies to treat various lymphomas. Our clinical experience to date suggests a potentially best-in-class profile. To pursue this opportunity, we are conducting a broad pivotal clinical program globally and in China. We have submitted for approval in China for two indications based on single-arm Phase 2 clinical trials in patients with R/R CLL/SLL and R/R MCL. Both applications have been accepted and are being reviewed under priority review status. In addition, we are conducting three global Phase 3 trials: head-to-head against ibrutinib, an approved BTK inhibitor, for patients with WM; against bendamustine plus rituximab for patients with treatment naïve, or TN, CLL/SLL; and head-to-head against ibrutinib for patients with R/R CLL/SLL. Further, we are conducting a global pivotal Phase 2 trial in combination with obinutuzumab in follicular lymphoma, or FL, a pivotal Phase 2 trial in China in WM, and we have recently begun a global study in R/R marginal zone lymphoma, or MZL. Subject to the successful completion and satisfactory results of these trials, we expect to submit for approval of zanubrutinib in the United States in 2019 or early 2020, where it has been granted Fast Track status for patients with WM and Breakthrough Therapy designation for patients with R/R MCL. We also plan to file an NDA in China for patients with WM.
- Develop and Commercialize Our Investigational Checkpoint Inhibitor, Tislelizumab, in a Rapidly and Favorably Evolving China Market and Other Markets. We believe that there is a large and growing opportunity for novel cancer therapeutics in China and that the market opportunity for PD-1/PD-L1 antibody therapies may be especially attractive, as this class of agents has demonstrated anti-tumor activity in all four of the most common tumors in China: lung cancer, gastric cancer (GC), liver cancer and esophageal cancer (EC). We believe that we are uniquely positioned to capture this opportunity with our strong presence and experience in China and our integrated global clinical development capabilities in China and other Asia-Pacific countries, the United States, Europe and Australia. We have submitted an NDA in China to market tislelizumab for the treatment of patients with R/R cHL, and the application has been accepted and is being reviewed under priority review status. We are currently running 11 registration or

potentially registration-enabling trials in six tumor types and expect to commence additional global pivotal trials in 2019 and 2020. We also plan to submit an NDA in China for patients with UBC. We have additional earlier stage exploratory studies ongoing, and we plan to initiate other studies.

- Establish a Leadership Position by Further Expanding Our Capabilities. Although we believe that we have significant integrated capabilities in research and clinical development, manufacturing and commercialization, we plan

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to continue to strengthen and expand our operations. In particular, we plan to significantly expand our commercial capabilities in China in preparation for the potential launch of our drug candidates and to support our existing marketed drugs. We have an established commercial team in China, which provides coverage of large hospitals and physician clients. As a result of the improving reimbursement environment in China, which is expected to provide access to innovative medicines for a significantly larger number of patients, we believe that the scale of our commercial organization and the breadth of our market coverage will become even more important. We plan to invest in expanding our teams of sales and marketing, market access, medical affairs, compliance, manufacturing, and other supporting functions. We aim to become a leading organization in the commercialization of oncology drugs in China. Outside of China, we are currently building commercial capabilities in the hematology-oncology area in the United States. In addition, we plan to continue to invest in building our global clinical development capabilities, which we believe will provide a competitive advantage in allowing us to conduct pivotal trials to support approvals globally and in China.

- Take Advantage of Significant Regulatory Reforms in China to Accelerate Global Drug Development. Historically, the regulatory environment in China has been considered highly challenging, with clinical development significantly delayed and regulatory approvals taking much longer than in the United States and Europe. To address these challenges, the NMPA has issued a series of reform policies and opinions, which, among many things, are expected to expand access to clinical patients and expedite development and approval by removing delays and creating an environment with international quality standards for drug development, manufacturing and commercialization in China. We expect that these regulatory reforms will allow clinical trials in China to play a major role in global drug development programs. We also believe that the ability to effectively operate in China and integrate trials conducted in China with those in the rest of the world will be of increasing strategic importance. We are already taking advantage of these opportunities by conducting and leading dual-purpose global / China registration trials.
- Expand Our Product Portfolio and Pipeline Through Collaborations with Other Biopharmaceutical Companies to Complement Our Internal Research. We expect to further expand our portfolio of drugs and drug candidates, in oncology as well as potentially in other therapeutic areas, through internal research and external collaborations, such as our collaborations with Celgene, Mirati and Zymeworks. We intend to pursue collaborations with other biopharmaceutical companies both in China and globally by leveraging our strong clinical development capabilities globally and our commercial capabilities in China. We have pursued and plan to continue to pursue business development opportunities in which development in China is expected to contribute to, and potentially accelerate, the global development program. We believe that there will be increasing interest by international biopharmaceutical companies in seeking collaborations in Asia, particularly in oncology, because clinical recruitment is a major bottleneck in new drug development.

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Our Pipeline and Commercial Products

The following table summarizes the status of our pipeline and commercial products as of February 20, 2019:

*Some indications will not require a non-pivotal Phase 2 clinical trial prior to beginning pivotal Phase 2 or Phase 3 clinical trials. **Confirmatory clinical trials post approval are required for accelerated approvals. ***REVLIMID® approved as a combination therapy with dexamethasone. 1. Celgene has the right to develop and commercialize tislelizumab in solid tumors in the U.S., EU, Japan and the rest-of-world outside of Asia. 2. Collaboration with Mirati Therapeutics, Inc.; APAC study. 3. Collaboration with Zymeworks.

Abbreviations: 1L = first line; 2L = second line; 3L = third line; AML = acute myeloid leukemia; CLL = chronic lymphocytic leukemia; CMMoL = chronic myelomonocytic leukemia; DLBCL = diffuse large B-cell lymphoma; Dose Esc = dose escalation; ESCC = esophageal squamous cell carcinoma; FL = follicular lymphoma; gBRCA = germline BRCA (Breast Cancer); GC = gastric cancer; HCC = hepatocellular carcinoma; HL = Hodgkin's lymphoma; IMiD = immunomodulatory drugs; MCL = mantle cell lymphoma; MDS = myelodysplastic syndrome; MM = multiple myeloma; MZL = marginal zone lymphoma; NSCLC = non-small cell lung cancer; ND = newly diagnosed; NDA = new drug application; NHL = non-Hodgkin's lymphoma; NK = natural killer; OC = ovarian cancer; PH = Phase; R/R = relapsed / refractory; RT = radiotherapy; SLL = small lymphocytic lymphoma; Sq = squamous; TMZ = temozolomide; UC = urothelial carcinoma; WM = Waldenström's macroglobulinemia

Our Clinical-Stage Drug Candidates

A description of our clinical-stage drug candidates, together with a summary of the most recently available publicly reported clinical data from key clinical trials as of the date of this Annual Report, is set forth below. We plan to make available subsequent clinical data from time to time in our press releases and/or filings with the U.S. Securities and Exchange Commission and Hong Kong Stock Exchange, copies of which are available on the Investors section of our website.

Zanubrutinib (BGB-3111), a BTK Inhibitor

Zanubrutinib is an investigational small molecule inhibitor of BTK that is currently being evaluated in a broad pivotal clinical program globally and in China as a monotherapy and in combination with other therapies to treat various lymphomas. Zanubrutinib has demonstrated higher selectivity against BTK than IMBRUVICA® (ibrutinib), an approved BTK inhibitor, based on our biochemical assays; higher exposure than ibrutinib based on their respective Phase 1 experience in separate studies; and sustained 24-hour BTK occupancy in both the peripheral blood and lymph node compartments.

Mechanism of Action

BTK is a key component of the B-cell receptor, or BCR, signaling pathway and is an important regulator of cell proliferation and cell survival in various lymphomas. BTK inhibitors block BCR-induced BTK activation and its downstream signaling, leading to growth inhibition and cell death in certain malignant white blood cells called B-cells. Zanubrutinib is an orally active inhibitor that covalently binds to BTK, resulting in irreversible inactivation of the enzyme.

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Market Opportunity and Competition

Lymphomas are blood-borne cancers involving lymphatic cells of the immune system. They can be broadly categorized into non-Hodgkin's lymphoma, or NHL, and Hodgkin's lymphoma, or HL. Depending on the origin of the cancer cells, lymphomas can also be characterized as B-cell or T-cell lymphomas. B-cell lymphomas make up approximately 85% of NHLs and comprise a variety of specific diseases involving B-cells at differing stages of maturation or differentiation. According to statistics from the Surveillance, Epidemiology and End Results, or SEER, program of the U.S. National Cancer Institute, there were 72,240 new NHL cases and 20,140 deaths, and 20,110 new CLL cases and 4,660 deaths in 2017 in the United States. Similar SEER analyses calculate U.S. incidence rates for MCL of 3,000 and 1,350 for WM. According to a published study (Chen et al., Cancer Statistics in China, 2015, CA Cancer J. Clin. 2016; 66(2):115-32), which we refer to as Chen et al. 2016, and GLOBOCAN's online Global Cancer Observatory analyses on cancer statistics in China, there are an estimated 88,200 to 93,097 new lymphoma cases and 52,100 to 50,865 deaths in China each year, and of the lymphoma cases, approximately 90% are NHL and approximately 4.5% of the NHL cases are CLL/SLL.

Conventional methods of treating lymphomas vary according to the specific disease or histology, but generally include chemotherapy, antibodies directed at CD20, a molecular marker found on the surface of B-cells, and, less frequently, radiation. Recently, significant progress has been made in the development of new therapies for lymphomas, including BTK inhibitors, the PI3K inhibitors, idelalisib, copanlisib and duvelisib, and the Bcl-2 inhibitor, venetoclax. Most recently, a cell-based therapy, YESCARTA® (axicabtagene ciloleucel) was approved for the treatment of adult patients with diffuse large B-cell lymphoma, or DLBCL, who have failed at least two other kinds of treatment. YESCARTA® is a genetically modified autologous T-cell immuno-oncology therapy directed at CD19.

The BTK inhibitor IMBRUVICA® (ibrutinib) was first approved by the FDA in 2013 for the treatment of patients with MCL who have received at least one prior therapy. Since that time, ibrutinib has received supplemental FDA approvals for the treatment of patients with CLL, CLL patients with 17p deletion, patients with WM, patients with MZL who have received at least one prior anti-CD20-based therapy, patients with chronic graft versus host disease after failure of one or more lines of systemic therapy, for use in combination with obinutuzumab in CLL, and in combination with rituximab in WM. Ibrutinib is also approved by the European Medicines Agency for the treatment of patients with MCL, CLL and WM. Ibrutinib has been approved in over 90 countries and regions, and it was approved and launched in China at the end of 2017. In 2018, global revenues for BTK inhibitors were approximately US$4.5 billion according to published reports. Another BTK inhibitor, CALQUENCE® (acalabrutinib) was approved by the FDA in 2017 under accelerated approval for the treatment of patients with MCL who have received at least one prior therapy. In late 2017, ibrutinib was the first BTK inhibitor approved and launched in China, for the treatment of patients with R/R CLL/SLL and R/R MCL. Subsequently, in July 2018, ibrutinib was also approved for first-line CLL.

Summary of Clinical Results

As of January 25, 2019, we had enrolled more than 1,300 patients in clinical trials of zanubrutinib, including trials of zanubrutinib in combination with other therapies, which we refer to as combination trials. A multi-center, open-label Phase 1 trial is being conducted in Australia, New Zealand, the United States, South Korea and European countries to assess the safety, tolerability, pharmacokinetic properties and preliminary activity of zanubrutinib as a monotherapy in patients with different subtypes of B-cell malignancies, such as WM, CLL/SLL, FL, and MCL. The initial results of the dose-escalation phase and dose-expansion phase of this trial demonstrated that, consistent with zanubrutinib's pharmacokinetic profile, complete and sustained 24-hour BTK occupancy in the blood was observed in all tested patients, starting at the lowest dose of 40 mg once daily. In addition, sustained full BTK occupancy was observed in the lymph nodes especially for the 160 mg twice daily dosing regimen. There is no guarantee that these results will be reproduced in pivotal trials.

Waldenström's Macroglobulinemia

On October 12, 2018, data from our Phase 1 trial in patients with WM were presented at the 10th International Workshop on Waldenström's Macroglobulinemia (IWWM). As of the data cutoff of July 24, 2018, 77 patients with WM were enrolled in the study, and 62 patients remained on study treatment. Responses were determined according

to the modified Sixth International Workshop on WM Criteria.

Seventy-three patients were evaluable for efficacy in this analysis and the median follow-up time was 22.5 months (4.1-43.9). The median time to response (>PR, or partial response) was 85 days (55-749). At the time of the data cutoff, 62 patients remained on study treatment. The overall response rate, or ORR, was 92% (67/73), the major response rate, or MRR, was 82%, and 41% of patients achieved a very good partial response, or VGPR, defined as a >90% reduction in baseline IgM levels and improvement of extramedullary disease by CT scan. The 12-month progression-free survival, or PFS, was estimated

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at 89%. The median PFS had not yet been reached. The median IgM decreased from 32.7 g/L (5.3-91.9) at baseline to 8.2 g/L (0.3-57.8). The median hemoglobin increased from 8.85 g/dL (6.3-9.8) to 13.4 g/dL (7.7-17.0) among 32 patients with hemoglobin <10 g/dL at baseline.

MYD88 genotype was known in 63 patients. In the subset known to have the MYD88L265P mutation (n=54), the objective response rate was 94%, the major response rate was 89%, and the VGPR rate was 46%. In the nine patients known to be MYD88WT, a less common genotype that historically has had sub-optimal response to BTK inhibition, the ORR was 89%, the MRR was 67%, and the VGPR rate was 22%.

Zanubrutinib was observed to be generally well-tolerated with no discontinuation for zanubrutinib-related toxicity. The majority of adverse events, or AEs, were grade 1 or 2 in severity. The most frequent AEs of any attribution were petechia/purpura/contusion (43%), upper respiratory tract infection (42%), cough (17%), diarrhea (17%), constipation (16%), back pain (16%), and headache (16%). Grade 3-4 AEs of any attribution reported in three or more patients included neutropenia (9%), anemia (7%), hypertension (5%), basal cell carcinoma (5%), renal and urinary disorders (4%), and pneumonia (4%). Serious adverse events, or SAEs, were seen in 32 patients (42%), with events in five patients (7%) considered possibly related to zanubrutinib treatment: febrile neutropenia, colitis, atrial fibrillation, hemothorax, and pneumonia (n=1 each). Nine patients (12%) discontinued due to AEs: abdominal sepsis (fatal), septic shoulder, worsening bronchiectasis, scedosporium infection, gastric adenocarcinoma (fatal), prostate adenocarcinoma, metastatic neuroendocrine carcinoma, acute myeloid leukemia, or breast cancer (n=1 each, all considered by the investigator to be unrelated to treatment). Atrial fibrillation/flutter occurred in four patients (5%). Major hemorrhage was observed in two patients (3%). Four patients (5%) discontinued study treatment due to disease progression as assessed by investigator and one patient remains on treatment post-disease progression.

Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma

On October 24, 2018, we announced the acceptance by the NMPA of our NDA for zanubrutinib for the treatment of patients with R/R CLL/SLL, together with the top line clinical data that supported the filing. The trial was a 91-patient single-arm pivotal Phase 2 study in Chinese patients with R/R CLL/SLL treated with zanubrutinib, dosed at 160 mg orally twice daily, or BID. An independent review of response data from this study, with a data cut-off of June 15, 2018 and a median follow-up of 9.1 months, showed an ORR of 80%, inclusive of complete response, or CR, of 2%, PR of 39%, and partial response with lymphocytosis, or PR-L, of 40%. The median duration of response had not been reached, as a majority of the responders remained in a response. The safety profile results were consistent with previously reported clinical data for zanubrutinib, which are described below. We plan to submit updated data with additional follow-up of the patients in this trial in support of the NDA.

On June 14, 2017, at the 14th International Conference on Malignant Lymphoma in Lugano, Switzerland, data were presented from patients with CLL/SLL from the same Phase 1 trial that included WM patients described above. As of the data cutoff of March 31, 2017, 69 patients with CLL or SLL (18 TN, 51 R/R) were enrolled in the trial.

At the time of the data cutoff, 66 patients (16 TN and 50 R/R) had more than 12 weeks of follow-up and were evaluable for efficacy, and three other patients had less than 12 weeks of follow-up. After a median follow-up of 10.5 months (2.2-26.8 months), the ORR was 94% (62/66) with CRs in 3% (2/66), PRs in 82% (54/66), and PR-Ls in 9% (6/66) of patients. Stable disease, or SD, was observed in 5% (3/66) of patients. A patient with pleural effusion discontinued treatment prior to week 12 and was not evaluable for response. There was one instance of Hodgkin's transformation. In TN CLL/SLL, at a median follow-up time of 7.6 months (3.7-11.6 months), the ORR was 100% (16/16) with CRs in 6% (1/16), PRs in 81% (13/16) and PR-Ls in 13% (2/16) of patients. In R/R CLL/SLL, at a median follow-up time of 14.0 months (2.2-26.8 months), the ORR was 92% (46/50) with CRs in 2% (1/50), PRs in 82% (41/50) and PR-Ls in 8% (4/50) of patients. SD was observed in 6% (3/50) patients.

Zanubrutinib was shown to be generally well-tolerated in CLL/SLL. The most frequent AEs (≥10%) of any attribution were petechiae/purpura/contusion (46%), fatigue (29%), upper respiratory tract infection (28%), cough (23%), diarrhea (22%), headache (19%), hematuria (15%), nausea (13%), rash (13%), arthralgia (12%), muscle spasms (12%) and urinary tract infection (12%). All of these events were grade 1 or 2 except for one case of grade 3 purpura (subcutaneous hemorrhage), which was the only major bleeding event. Additional AEs of interest included one case of each grade 2 diarrhea and grade 2 atrial fibrillation. A total of 18 SAEs occurred in 13 patients, with no SAE occurring in more than one patient. Only one patient discontinued treatment due to an AE, a grade 2 pleural effusion.

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Mantle Cell Lymphoma

On December 1, 2018, at the 60th American Society of Hematology, or ASH, Annual Meeting, in San Diego, CA, two data sets were presented on zanubrutinib in MCL patients from our Phase 2 and Phase 1 studies.

The Phase 2 study was a single arm, open-label, multi-center, pivotal trial of zanubrutinib as a monotherapy in Chinese patients with R/R MCL that enrolled 86 patients who had received a median of two prior lines of therapy (range of 1-4). Patients were treated with zanubrutinib, dosed at 160 mg orally BID. The primary endpoint of the trial was ORR assessed by independent review committee, or IRC, using PET-based imaging according to the Lugano Classification 2014.

As of March 27, 2018, 85 patients with R/R MCL were evaluable for efficacy and 65 patients (75.6%) remained on study treatment. The median follow-up time for patients enrolled in the trial was 35.9 weeks (1.1-55.9). The IRC-assessed ORR was 83.5% (71/85); the CR rate was 58.8% (50/85); and the PR rate was 24.7% (21/85). The 24-week PFS was estimated at 82%. The median PFS had not yet been reached. With 24.1 weeks median follow-up (0.1-41.1), the median duration of response, or DOR, had not yet been reached and 90% of responders were still in response at 24 weeks.

Zanubrutinib tolerability was generally consistent with previous reports in patients with various B-cell malignancies and the majority of AEs were grade 1 or 2 in severity. The most frequent AEs of any attribution were neutrophil count decreased (31.4%), rash (29.1%), upper respiratory tract infection (29.1%), and platelet count decreased (22.1%). The most frequently reported (in >5% of patients) grade 3 or higher AEs were neutrophil count decreased (11.6%) and lung infection (5.8%). Four patients (4.7%) had treatment-emergent adverse events, or TEAEs, leading to death (one case each of traffic accident, cerebral hemorrhage, pneumonia, and unknown cause in the setting of infection). Among events of special interest for BTK inhibitors, diarrhea was observed in nine patients (10.5%), all grade 1-2. Major hemorrhage was observed in one patient (1.2%) with a blastoid variant of MCL who had intra-parenchymal CNS bleeding. No cases of atrial fibrillation/flutter were reported in this trial.

The Phase 1 study is an open-label trial of zanubrutinib as a monotherapy in patients with different subtypes of B-cell malignancies, including MCL, and is being conducted in Australia, New Zealand, the United States, Italy, and South Korea. As of July 24, 2018, 48 patients with TN (n=9) or R/R (n=39) MCL had been enrolled in the trial and the median follow-up time was 12.7 months (0.7-38.0). Forty-five patients including six with TN and 39 with R/R MCL, were evaluable for efficacy in this analysis, per the Lugano 2014 classification. At the time of the data cutoff, 26 patients remained on study treatment.

The investigator-assessed ORR was 88.9% (40/45); the CR rate was 26.7% (12/45); and the PR rate was 62.2% (28/45). The majority of patients were assessed via CT-scan; PET scans were optional per trial protocol. The median DOR was 16.2 months and the median PFS for R/R patients was 18.0 months (0.7-30.7).

Zanubrutinib tolerability was generally consistent with previous reports in patients with various B-cell malignancies and the majority of AEs were grade 1 or 2 in severity. The most frequent AEs of any attribution were petechia/purpura/contusion (33.3%), diarrhea (33.3%), upper respiratory tract infection (29.2%), fatigue (25.0%), and constipation (18.8%). Grade 3-5 AEs occurred in 56.3% of patients. Grade 3-5 AEs of any attribution reported in > three patients included anemia (8.3%), major hemorrhage (6.3%), cellulitis (6.3%), myalgia (6.3%), neutropenia (6.3%), pneumonia (6.3%); and thrombocytopenia (6.3%). Discontinuation due to AEs occurred in 18.8% of patients with all but one event (peripheral edema) determined to be unrelated to study drug. There were four deaths due to AEs, which were all determined by the investigators to be unrelated to zanubrutinib treatment.

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Other Lymphomas

We have a broad clinical program investigating zanubrutinib for the treatment of patients with several other lymphomas outside of the work detailed above. Efficacy results of those clinical trials reported to date are summarized in the table below.

Indication	MZL	FL	FL	DLBCL
Source	ASH 2017[1]	ASH 2017[1]	CSCO 2018[2]	ASH 2017[1]
n	9	17	26	26
Follow-up	7.0 mo	7.8 mo	9.5 mo	4.2 mo
Prior Lines	2 (1-8)	2 (1-8)	3 (1-9)	2 (1-10)
ORR	78%	41%	42%	31%
CR	—%	18%	8%	15%
VGPR	—	—	—	—
PR/PR-L	78%	24%	35%	15%
MR	—	—	—	—

Source: 1. Tam et al., ASH 2018 (poster 1592); 2. Press Release dated September 21, 2018

Pooled Analysis of Safety Data from Monotherapy Trials

At the 23rd Congress of the European Hematology Association, or EHA 2018, the pooled safety data were presented from patients with various B-cell lymphomas in four ongoing zanubrutinib monotherapy studies, totaling 476 patients with a median exposure of seven months. Overall, the data suggested that exposure levels of zanubrutinib resulting in complete and sustained BTK inhibition can be achieved and that zanubrutinib was generally well-tolerated. There were infrequent AEs of interest with BTK inhibitor therapy, such as atrial fibrillation/flutter (2%), major hemorrhage (2%), and grade 3 and above diarrhea (1%). Treatment discontinuation due to zanubrutinib-related AEs was uncommon (3%). The majority of patients (94%) experienced one or more AEs of any attribution, primarily grades 1 or 2. The most common grade 3 or higher AEs of any attribution were neutropenia/neutrophil count decreased/febrile neutropenia (14%), anemia (7%) and thrombocytopenia/platelet count decreased (7%). SAEs were reported in 116 patients (24%), with 38 patients (8%) assessed by the investigator as related to zanubrutinib. The most common SAEs were pneumonia/lung infection (6%), pleural effusion (1%), and febrile neutropenia (1%). The only treatment-related SAE reported in greater than 1% of patients was pneumonia/lung infection (2%). No cases of pneumocystis jiroveci pneumonia, or PJP, or cytomegalovirus, or CMV, reactivation were reported. The most common bleeding events observed included petechiae/purpura/contusion (26%) and hematuria (11%). Major hemorrhage (2%) included gastrointestinal hemorrhage/melena (n=3), intraparenchymal CNS hemorrhage grade 5, hematuria, purpura, hemorrhagic cystitis, renal hematoma, and hemothorax (one each). The median time to first major hemorrhage was 1.2 months. Among patients with emergent atrial fibrillation/flutter (n=8), a majority had known risk factors including hypertension (n=2), pre-existing cardiovascular disease (n=2), and concurrent infection (n=1). The cumulative rates of grade 3 or higher infections were 14% at six months, 19% at 12 months and 21% at 18 months. The exposure-adjusted incidence rate was 1.82 per 100 person-months. The most common second primary malignancies included basal cell carcinoma (3%) and squamous cell carcinoma of the skin (1%).

Clinical Development Plan

Based on the clinical data to date, we believe that zanubrutinib has a potentially best-in-class profile, and we are running a broad global pivotal program in multiple indications including seven registration or registration-enabling clinical trials.

Globally, we have an ongoing monotherapy head-to-head Phase 3 trial versus ibrutinib in WM, which has closed to new patient screening and completed enrollment having met the enrollment target. We are also conducting an ongoing Phase 3 trial compared to bendamustine and rituximab in patients with TN CLL/SLL and a head-to-head Phase 3 trial in R/R CLL/SLL versus ibrutinib. Additionally, we have an ongoing pivotal Phase 2 trial in combination with GAZYVA® (obinutuzumab) in patients with R/R FL, which is designed as a pivotal trial for accelerated or conditional approval and will require a confirmatory study, as well as a Phase 2 trial in patients with R/R MZL.

Zanubrutinib was granted, by the FDA, Fast Track designation for the treatment of patients with WM in July 2018, and was granted Breakthrough Therapy designation in January 2019 for the treatment of adult patients with MCL who

have

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received at least one prior therapy. We plan to submit in 2019 or early 2020 an NDA to pursue an approval of zanubrutinib in the United States.

In China, we are conducting three separate pivotal Phase 2 trials of zanubrutinib as monotherapy in patients with R/R MCL, R/R CLL/SLL, and WM. We have announced the acceptance of our filings for approval in MCL and CLL/SLL on August 26, 2018 and October 24, 2018, respectively.

If we receive conditional approval instead of full approval, we will be required to conduct one or more confirmatory studies after such conditional approvals. If approved, we plan to commercialize zanubrutinib shortly after approval. In addition, we are conducting a Phase 2 trial in China of zanubrutinib in patients with R/R DLBCL.

Tislelizumab (BGB-A317), an anti-PD-1 Antibody

Tislelizumab is an investigational humanized monoclonal antibody against the immune checkpoint receptor PD-1 that is currently being evaluated in pivotal clinical trials globally and in China and for which we plan to commence additional pivotal trials as a monotherapy and in combination with standard of care to treat various solid and hematological cancers. We have a global strategic collaboration with Celgene for tislelizumab for solid tumors outside of Asia (other than Japan) as further described in "--Celgene Collaboration."

Mechanism of Action

Cells called cytotoxic T-lymphocytes, or CTLs, provide an important self-defense mechanism against cancer, patrolling the body, recognizing cancer cells due to immunogenic features that differ from normal cells, and killing cancer cells by injecting deleterious proteins into them. T-lymphocytes have various mechanisms that prevent them from damaging normal cells, among which is a protein called PD-1 receptor, that is expressed on the surface of T-lymphocytes. PD-L1 is an important signaling protein that can engage PD-1. PD-L1 binding to PD-1 sends an inhibitory signal inside the T-lymphocyte and suppresses its cytotoxic effects. Many types of cancer cells have hijacked the PD-L1 expression system that normally exists in healthy cells. By expressing PD-L1, cancer cells protect themselves from being killed by CTLs. Anti-PD-1 therapies are designed to bind to and block downstream activity of PD-1, allowing the immune system to combat cancer cells.

Tislelizumab is a monoclonal antibody designed to specifically bind to PD-1, without activating the receptor, thereby blocking engagement of PD-1 by its ligands PD-L1 and PD-L2. Tislelizumab has demonstrated high affinity and specificity for PD-1 in preclinical studies. It is differentiated mechanistically from the currently approved PD-1 antibodies by an engineered Fc region designed to minimize binding to Fc R on macrophages, thereby abrogating antibody-dependent phagocytosis, a potential mechanism of T-cell clearance, which we believe may minimize potentially negative interactions with other immune cells based on preclinical data.

Market Opportunity and Competition

A number of PD-1 or PD-L1 antibody drugs have been approved by the FDA. These include Merck's KEYTRUDA® (pembrolizumab), Bristol-Myers Squibb's OPDIVO® (nivolumab), Roche's TECENTRIQ® (atezolizumab), AstraZeneca's IMFINZI® (durvalumab), Pfizer and Merck Sereno's BAVENCIO® (avelumab), and Regeneron and Sanofi's LIBTAYO® (cemiplimab). In the global setting, several PD-1 or PD-L1 antibody agents are in clinical development in addition to tislelizumab, such as Novartis' PDR-001, GlaxoSmithKline / Tesaro's TSR042, Pfizer's PF-06801591, and AstraZeneca's MEDI0680. In China, as of February 20, 2019, there are four approved PD-1 antibodies, OPDIVO® (nivolumab) and KEYTRUDA® (pembrolizumab), as well as Junshi's TUOYI (toripalimab) and Innovent's TYVYT (sintilimab), and there are no approved PD-L1 antibody agents yet. There are approximately six more PD-1 and PD-L1 agents in late stage development in China, of which one has filed for approval as of February 20, 2019.

Globally, the top four PD-1/PD-L1 antibody drugs had sales of approximately $15 billion in 2018 based on public reports. We believe that there is a large commercial opportunity in China for PD-1 and PD-L1 antibody drugs. Currently available clinical data suggest that some of the most prevalent cancers in China, such as lung cancer, GC, liver cancer and EC, are responsive to this class of agents. According to the World Health Organization's Globocan online database, China suffered 37%, 44%, 47%, and 54% of all deaths from lung cancer, GC, liver cancer and EC, respectively, in the world. Collectively, these four tumor types comprised over 2.3 million new cases in 2016 in China alone, according to Chen et al. 2016. In addition, China has a higher proportion of PD-1 responsive tumors in its total annual cancer incidence in comparison to other geographies like the United States and the European Union, or EU.

According to Chen et al. 2016, the annual incidence of the top ten PD-1 responsive tumors in China is estimated to be 3.0 million out of 4.3 million in total annual cancer incidence. In comparison, the estimated annual incidence of the top ten PD-1 responsive tumors is 0.9 million out of 1.7 million in total annual cancer

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incidence in the United States, and 0.9 million out of the 1.8 million total in the EU5 countries (United Kingdom, France, Germany, Spain and Italy) according to SEER program of the U.S. National Cancer Institute and the World Health Organization.

Summary of Clinical Results

As of December 8, 2018, we have enrolled over 2,200 patients in clinical trials of tislelizumab, including combination trials. Preliminary data from our monotherapy Phase 1 trials suggested that tislelizumab was generally well-tolerated and exhibited anti-tumor activity in a variety of tumor types. There is no guarantee that these results will be reproduced in pivotal trials.

Hodgkin's Lymphoma

On December 3, 2018, data from a pivotal Phase 2 clinical trial of tislelizumab in R/R cHL were presented at the ASH meeting. This single arm, open-label, multi-center, pivotal Phase 2 trial of tislelizumab as a monotherapy in Chinese patients with R/R cHL enrolled 70 patients who failed to achieve a response or progressed after autologous stem cell transplant, or ASCT, or received at least two prior lines of systemic therapy for cHL and were not an ASCT candidate. Patients were treated with tislelizumab, dosed at 200 mg intravenously every three weeks. The primary endpoint of the trial is ORR-assessed by IRC using PET-based imaging according to the Lugano Classification 2014.

As of May 25, 2018, 70 patients with R/R cHL were evaluable for efficacy and 53 patients (75.7%) remained on study treatment. Thirteen patients received prior ASCT, and the remaining 57 patients were ineligible for prior ASCT, including 53 for failure to achieve an objective response to salvage chemotherapy, two for inadequate stem cell collection or unable to collect stem cells, and two for co-morbidities. The patients had a median of three prior lines of systemic therapy with a range of two to eleven. The median study follow-up was 7.85 months (3.4-12.7).

The ORR assessed by IRC was 85.7% (60/70); the CR rate was 61.4% (43/70); and the PR rate was 24.4% (17/70). Among patients who had received prior ASCT, 92.3% (12/13) achieved an objective response, with nine patients (69.2%) achieving a CR. The DOR had not yet been reached. The estimated event-free rates at nine months were 84%. PFS data were preliminary and six-month PFS was estimated at 80%. The median PFS had not yet been reached.

The majority of AEs were grade 1 or 2 in severity. The most frequently reported TEAEs of any grade were pyrexia (52.9%), hypothyroidism (30.0%), weight increased (28.6%), upper respiratory tract infection (27.1%), cough (17.1%), white blood cell count decreased (14.3%), and pruritus (14.3%). Grade ≥3 TEAEs occurred in 21.4% of patients. The most frequently reported grade 3 or higher TEAEs were upper respiratory tract infection (2.9%) and pneumonitis (2.9%). Four patients (5.7%) discontinued study drug due to TEAEs, including pneumonitis (n=2), focal segmental glomerulosclerosis (n=1), and organizing pneumonia (n=1); there were no cases of TEAE leading to death. Immune-related AEs reported in more than five percent of patients included thyroid disorder (18.6%), pneumonitis (5.7%), and skin adverse reactions (5.7%).

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Other Tumor Types

In addition to cHL, we are evaluating tislelizumab for the treatment of patients with a broad array of tumor types. Efficacy results from those clinical trials reported to date are summarized in the table below.

Tumor Type	Gastric Cancer	Esophageal Cancer	Head & Neck SCC	Ovarian Cancer	Hepato-cellular Carcinoma	Urothelial Cancer	NSCLC	MSI-H / dMMR
Source	ESMO-IO 2018[1]	ESMO-IO 2018[1]	ESMO 2017[2]	ESMO 2017[3]	ESMO-IO 2018[1]	ESMO-IO 2018[4]	ESMO-IO 2018[1]	CSCO 2018[5]
Median Treatment Duration	—	—	104 days (30-339)	71 days (29-540)	—	4.1 mo (0.7-26.3)	—	2.2 mo (0.69-11.1)
Median Follow-up Time	4.9 mo (0.9-25.4)	5.2 mo (0.2-22.7)	—	—	10.8 mo (0.7-31.6)	—	11.2 mo (0.5-25.9)	4.4 mo (0.1-10.7)
Median Duration of Response	8.5 mo	NR	—	—	15.7 mo	18.7 mo (6.2-18.7)	NR	—
Evaluable Patients	N=54	N=54	N=17	N=50	N=49	N=17	N=46	N=14
CR (Confirmed)	—	1	—	—	—	1	—	—
PR	7	5	3	2	6	4	6	4
SD	9	14	6	20	19	3	23	4
Patients Remaining on Treatment *	3	3	3	6	5	2	7	9

* At the time of data cutoff.

Notes: 1. Phase 1A/1B data as of August 31, 2018, presented at the ESMO Immuno-Oncology 2018 Congress (Sanjeev et al); 2. Phase 1 data as of June 8, 2017, presented at the ESMO 2017 Congress (Horvath et al, Abstract 389P); 3. Phase 1 data as of June 8, 2017, presented at the ESMO 2017 Congress (Meniawy et al, Abstract 388P); 4. Phase 1/2 data as of August 31, 2018, presented at the ESMO Immuno-Oncology 2018 Congress (Shahneen et al); 5. Phase 1 data as of May 11, 2018, presented at CSCO 2018.

Safety Results

The safety results of tislelizumab in clinical trials to date are consistent with its therapeutic class, having a relatively low rate of drug-related grade 3 or above toxicity. Across the monotherapy studies, the safety results were consistent with our two Phase 1 studies, and our first-in-human Phase 1 study TEAE are indicated in the table below. Over half of the patients in our two Phase 1 studies experienced a tislelizumab-related TEAE, though ≥ grade 3 events were less frequent (8% to 10%).

System Organ Class Preferred Term	Phase 1a N=116 n (%)	Phase 1b N=335 n (%)	Total N=451 n (%)
Patients with at least one TEAE	114 (25.3)	322 (71.4)	436 (96.7)
Fatigue	47 (10.4)	78 (17.3)	125 (27.7)
Nausea	41 (9.1)	68 (15.1)	109 (24.2)
Decreased appetite	19 (4.2)	71 (15.7)	90 (20.0)
Diarrhea	32 (7.1)	49 (10.9)	81 (18.0)
Constipation	26 (5.8)	50 (11.1)	76 (16.9)
Abdominal pain	26 (5.8)	38 (8.4)	64 (14.2)
Vomiting	20 (4.4)	43 (9.5)	63 (14.0)
Back pain	22 (4.9)	40 (8.9)	62 (13.7)
Cough	15 (3.3)	45 (10.0)	60 (13.3)
Rash	23 (5.1)	37 (8.2)	60 (13.3)

Dyspnea	12 (2.7)	33 (7.3)	45 (10.0)

All grades, regardless of causality; Data cut-off April 27, 2018; 6 months after Last Patient Enrolled; Source: BGB-A317 IB v6.0. Of the 451 total patients in the Safety Population for Study BGB A317_001, 203 (45.0%) experienced at least 1 grade 3 or higher TEAE. The most commonly occurring grade 3 or higher TEAEs (≥ 2%; 9 or more patients overall incidence) were pneumonia (22 patients, 4.9%), anemia (18 patients, 3.2%), and hypokalemia (9 patients, 2.0%).

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Immune-Related Treatment-Emergent Adverse Events and Deaths

Immune-related TEAEs, or irTEAEs, of any grade were reported in approximately 25% of patients but were primarily low grade (3% to 5% ≥ grade 3). These irTEAEs, however, have well-established algorithms for treatment and are considered manageable.

Across the monotherapy studies, the rate of treatment emergent SAEs, or TESAEs, ranged from 16% to 37% in patients with a variety of different disease characteristics. TESAEs considered to be related to treatment with tislelizumab were notably lower, ranging from 6% to 13%.

There have been some deaths reported across the active studies with clinical data available (as of the cut-off dates ranging from April 25, 2018 to August 29, 2018), of which less than 0.5% of the total patient population were deemed to be related to treatment with tislelizumab.

Clinical Development Plan

We are running a broad development program for tislelizumab, including 11 registration or registration-enabling clinical trials. These include global pivotal trials in Asia-prevalent cancers, such as non-small cell lung cancer, or NSCLC, EC, GC and HCC, which are intended to support regulatory submissions globally and in China. We have initiated pivotal or Phase 3 trials to evaluate tislelizumab as a potential second- or third-line treatment compared to docetaxel in patients with NSCLC; as a potential first-line treatment compared to sorafenib in patients with HCC and in second or third line HCC used as a monotherapy; as a potential first-line treatment in GC in combination with platinum and fluoropyrimidine-based chemotherapy; and as a potential second-line treatment compared to investigator-chosen chemotherapy in patients with esophageal squamous cell carcinoma, or ESCC, and as a potential first-line treatment in advanced ESCC patients in combination with platinum and fluoropyrimidine-based chemotherapy. Under our collaboration with Celgene, Celgene has opened enrollment in its first Phase 3 trial in Stage 3 NSCLC examining tislelizumab in combination with chemoradiation. We have also recently initiated a global Phase 2 trial in patients with relapsed or refractory mature T- and NK-cell lymphomas.

We have four China pivotal trials ongoing, including two Phase 2 trials in patients with R/R cHL and in patients with PD-L1 positive second/third-line urothelial cancer, or UC, and two Phase 3 trials in combination with chemotherapy -- one in patients with non-squamous NSCLC and the second in patients with squamous NSCLC. We submitted for approval for tislelizumab in China to treat R/R cHL and announced that this submission had been accepted on August 31, 2018, and received priority review on November 15, 2018. We expect to submit for approval in China for the treatment of patients with UC based on the results of the pivotal Phase 2 trial. If we receive conditional approval instead of full approval, we will be required to conduct one or more confirmatory studies after such conditional approvals. We also expect to submit for approval in China for tislelizumab for the treatment of patients with NSCLC, ESCC, GC and HCC based on our China trials and, where appropriate, our global studies.

Pamiparib (BGB-290), a PARP Inhibitor

Pamiparib is an investigational small molecule inhibitor of PARP1 and PARP2 that is being evaluated as a potential monotherapy and in combinations for the treatment of various solid tumors. We believe that pamiparib has the potential to be differentiated from other PARP inhibitors because of its brain penetration, greater selectivity, strong DNA-trapping activity, and good oral bioavailability demonstrated in preclinical models.

Mechanism of Action

PARP family members PARP1 and PARP2 play essential roles in cell survival in response to DNA damage. PARP1 and PARP2 are key base-excision-repair proteins that function as DNA damage sensors by binding rapidly to the site of damaged DNA and modulating a variety of proteins in DNA repair processes. Inhibition of PARPs prevents the repair of common single-strand DNA breaks, which leads to formation of double-strand breaks during DNA replication. Double-strand DNA breaks in normal cells are repaired by homologous recombination, and normal cells are relatively tolerant of PARP inhibition. On the other hand, cancer cells with mutations in breast cancer susceptibility gene, or BRCA1/2 genes, which are key players in homologous recombination, are highly sensitive to PARP inhibition. This phenomenon is called “synthetic lethality” and is the foundation of the therapeutic utility of PARP inhibitors as a monotherapy for BRCA mutant cancers. In addition to hereditary BRCA1/2 mutations, the synthetic lethality concept has been broadened to include sporadic tumors that display homologous recombination deficiency, or HRD, a gene expression profile that resembles that of a BRCA deficient tumor. HRD can stem from

somatic mutation of BRCA1/2, epigenetic silencing of BRCA genes or genetic or epigenetic loss of function of other genes in homologous recombination DNA damage repair pathways. Third-party clinical studies have published results

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demonstrating that sensitivity to platinum-based chemotherapies confers sensitivity to PARP inhibitors in OC as well. Thus, the application of PARP inhibitors is likely broader than BRCA or HRD mutations, and there is additional possibility to identify and enrich patient populations for PARP inhibition.

Another potential therapeutic utility of PARP inhibitors is in combination therapy, which has strong scientific rational. PARP proteins are key factors in base-excision-repair, which is critical for the repair of DNA lesions caused by some chemotherapeutic agents and by radiation. PARP inhibitors are hypothesized to potentiate cytotoxicity of DNA-alkylating agents such as platinum compounds, temozolomide and ionizing radiation, and may be used in combination with these agents in treating various cancers.

PARP inhibitors are also considered good potential combination partners with checkpoint inhibitors in part due to increased mutations in tumor cells as a result of the blockade of DNA repair by PARP inhibitors as a higher mutational load in cancers has been shown in clinical studies to correlate with improved response to checkpoint inhibitors. In addition, preclinical data suggest that BRCA mutant tumors which are sensitive to PARP inhibition are likely to be immunogenic and responsive to PD-1 or PD-L1 antibodies.

Market Opportunity and Competition

We believe that the market opportunity for PARP inhibitors is large and expanding in various patient segments. Many tumor types have been shown to be responsive to PARP inhibitors, including OC, breast cancer, prostate cancer and GC. PARP inhibitors have demonstrated encouraging activity both in relapsed and refractory patients as well as in the maintenance setting. In the United States, in 2018 there were approximately 22,240 new cases of OC, 266,120 new cases of breast cancer, 164,690 new cases of prostate cancer, and 26,240 new cases of GC, according to the U.S. National Cancer Institute's SEER online database. In China, each year there are approximately 52,000 new cases of OC, 272,000 new cases of breast cancer, 60,000 new cases of prostate cancer, and 680,000 new cases of GC according to Chen et al. 2016.

A number of PARP inhibitors have been approved by the FDA. These include AstraZeneca’s LYNPARZA® (olaparib), Clovis Oncology’s RUBRACA® (rucaparib), GlaxoSmithKline / Tesaro’s ZEJULA® (niraparib), and Pfizer’s TALZENNA® (talazoparib). AbbVie’s veliparib is in late-stage development. In 2017, global sales of the PARP class exceeded US$461 million according to company reports. In China, AstraZeneca received approval for olaparib in August 2018 under priority review that utilized international multi-center data. Zai Labs obtained the development and commercial rights for niraparib in China, and its NDA to the NMPA was accepted in December 2018 for use as maintenance therapy in OC. There are some other PARP inhibitors being developed by domestic Chinese companies, including fluzoparib from Hengrui and Hansoh, but none have been submitted to the NMPA as of February 6, 2019.

Summary of Clinical Data

As of November 6, 2018, we have enrolled over 360 patients in clinical trials of pamiparib, including three registration or registration-enabling clinical trials.

A multi-center, open-label Phase 1/2 trial of pamiparib is being conducted in Australia in patients with advanced solid tumors. On September 8, 2017, preliminary clinical data from the ongoing Phase 1/2 trial of pamiparib in patients with advanced solid tumors were presented at ESMO. As of June 1, 2017, 68 patients were enrolled in the trial. The median duration of therapy for all patients was 79 days (range 1 to 926 days). At the time of the data cutoff, 20 patients remained on treatment.

At the time of the data cutoff, 39 patients with epithelial ovarian cancer, or EOC, or associated tumors such as fallopian tube or primary peritoneal cancers, were evaluable for efficacy. Among this group, there were three confirmed CRs, 10 confirmed PRs, and 21 cases of SD. Of the 23 evaluable patients with EOC or other associated tumors known to be BRCA-mutated, there were three CRs, seven PRs, and 10 cases of SD. Of the 13 evaluable patients whose BRCA gene types are wild type, there were two PRs. Of the three evaluable patients whose BRCA gene types were unknown, there was one PR. Complete and partial responses were observed in patients known to be platinum-resistant as well as patients with platinum-sensitive disease. There is no guarantee that these results will be reproduced in pivotal trials.

The safety analysis suggested that pamiparib was generally well-tolerated in patients with advanced solid tumors. AEs assessed to be treatment-related occurred in 78% of patients and were all grade 3 or lower in severity. The most common treatment-related AEs (≥10% of patients) were nausea (56%), fatigue (40%), anemia (25%), vomiting (21%),

diarrhea (21%), decreased appetite (15%), and neutropenia or neutrophil count decrease (12%). SAEs occurred in 46% of patients, and SAEs considered to be treatment-related and occurring in more than one patient included two cases each of nausea and anemia. Four

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patients reported dose-limiting toxicity, or DLT. Four patients had a TEAE with a fatal outcome; none were assessed as being treatment-related and all of which were associated with disease progression.

Ovarian Cancer

On April 16, 2018, preliminary clinical data from the open-label, multi-center Phase 1 dose-escalation trial of pamiparib in Chinese patients with locally advanced or metastatic high-grade non-mucinous ovarian cancer, or HGOC, including fallopian cancer, or triple-negative breast cancer, or TNBC, who had disease progression following at least one line of chemotherapy were presented at the 2018 American Association for Cancer Research Annual Meeting in Chicago, IL.

Patients were dosed at 20 mg, 40 mg, or 60 mg BID. As of September 25, 2017, 15 female patients were enrolled, nine with HGOC and six with TNBC. Nine patients had received four or more prior lines of therapies. All nine patients with HGOC were platinum-resistant (n=8) or refractory (n=1). Seven patients had a confirmed BRCA1/2 mutation (BRCAm), including five patients with HGOC and two patients with TNBC and the remaining patients had BRCA 1/2 wildtype (BRCA-WT). The median duration of treatment was 2.5 months (range: 8-260 days).

As of September 25, 2017, 13 of the 15 patients were evaluable for antitumor activity; five patients remained on treatment. Two of the nine HGOC patients achieved a confirmed PR including one platinum-refractory patient with BRCA wildtype status and one platinum-resistant patient with BRCA1/2 mutation, six HGOC patients had SD (BRCAm, n=4 and BRCA-WT, n=2) and one patient discontinued before the first radiographic assessment. Of the six treated TNBC patients, five (BRCAm, n=1, BRCA-WT, n=4) experienced disease progression and one patient (BRCAm) discontinued before the first radiographic assessment. Four of these evaluable TNBC patients were BRCA-WT and all experienced disease progression during the previous platinum-based chemotherapy.

The safety analysis suggested that pamiparib was generally well-tolerated. No dose-limiting toxicities were reported across the dose range, with the recommended Phase 2 dose, or RP2D, confirmed as 60 mg BID. Asthenia (n=12) and nausea (n=12) were the most commonly reported TEAE. Severity of all AEs was grade 3 or less. Overall, three patients experienced a serious AE (grade 2 abdominal infection, n=1; grade 3 pleural effusion, n=1; grade 3 ileus, n=1), none of which were considered related to treatment. Two of the SAEs led to treatment withdrawal (abdominal infection, n=1; pleural effusion, n=1).

Glioblastoma Multiforme

On November 16, 2018, we announced data from an open-label, multi-center global Phase 1b/2 multiple-dose and dose-escalation trial of pamiparib plus radiation therapy, or RT, and/or temozolomide, or TMZ, in patients with newly diagnosed or R/R glioblastoma multiforme, or GBM, at the 23rd Annual Scientific Meeting and Education Day of the Society for Neuro-Oncology (SNO). This study was designed to evaluate the safety, efficacy and clinical activity of the combination. Patients with newly diagnosed GBM with unmethylated MGMT (O6-methylguanine-DNA methyltransferase) promoter status (Arm A) received pamiparib (60 mg BID) over escalating time periods (two, four, or six weeks) in combination with RT over six to seven weeks. Patients with R/R GBM (Arm C) received pamiparib (60 mg BID) continuously plus TMZ administered on Days 1 to 21 of each 28-day cycle. After evaluation of safety and tolerability from Arm A and C, Arm B will enroll patients with newly diagnosed GBM and treat them with the triple combination of RT, pamiparib, and TMZ.

As of September 14, 2018, a total of 18 patients with newly diagnosed GBM were enrolled in Arm A (n=3, 6 and 9 in the two-, four-, and six-week cohorts respectively). The median study follow-up duration was 19 weeks (2-54). As of the data cutoff date, 15 of the 18 patients were evaluable for response per modified response assessment in neuro-oncology (mRANO) criteria. Two of 15 patients achieved a PR (one was confirmed) and six patients achieved stable disease (SD); the disease control rate was 53.3% (95% CI: 26.6-78.7). Five grade >3 AE (chills, diarrhea, fatigue, nausea, vertigo, one each, or 5.6%) were considered related to pamiparib or RT. Dose-limiting toxicities of fatigue, vertigo, and chills (one each) were reported. In Arm C, eight patients received TMZ at a fixed dose of 40 mg for 21 of 28 days and seven patients received 20 mg TMZ. The median study follow-up duration was 12.9 weeks (0.3-31.4). Ten of the 15 patients were evaluable per mRANO criteria and there were two PRs (one unconfirmed and one confirmed after data cutoff) and three SD. Grade >3 AEs included anemia (20%), fatigue (13.3%), and decreased lymphocyte count (13.3%), which were considered related to pamiparib or TMZ. Dose-limiting toxicities of nausea and neutropenia were reported. The combination of 21 days of 40 mg TMZ with pamiparib was not tolerable; a lower

20 mg TMZ dose evaluation in combination with pamiparib is ongoing.

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Clinical Development Plan

In addition to the above trials, our global program includes a Phase 3 maintenance trial in patients with platinum-sensitive GC. In China, we are conducting a Phase 3 trial as a maintenance therapy in patients with platinum-sensitive recurrent OC in addition to an ongoing pivotal Phase 2 study in OC.

Lifirafenib (BGB-283), a RAF Dimer Inhibitor

Lifirafenib is an investigational novel small molecule inhibitor with RAF monomer and dimer inhibition activities. Lifirafenib has shown antitumor activities in preclinical models and in cancer patients with tumors harboring BRAF V600E mutations, non-V600E BRAF mutations or KRAS/NRAS mutations. We have been developing lifirafenib for the treatment of cancers with aberrations in the mitogen-activated protein kinase, or MAPK, pathway, including BRAF gene mutations and KRAS/NRAS gene mutations where first generation BRAF inhibitors are not effective. The MAPK pathway consists of proteins in the cell that transmit a signal from a receptor on the surface of the cell to the DNA in the nucleus of the cell. This pathway plays an essential role in regulating cell proliferation and survival. We believe that lifirafenib as monotherapy or in combination with other agents may have potential for treating various malignancies, such as melanoma, NSCLC and endometrial cancer. In October 2018, we formed a collaboration with SpringWorks Therapeutics to investigate the combination of lifirafenib and their MEK inhibitor, PD-0325901, in patients with advanced solid tumors that harbor RAS, RAF mutations and other MAPK pathway aberrations. This study is planned to commence in the first quarter of 2019.

Currently approved BRAF inhibitors include Roche's ZELBORAF® (vemurafenib), Novartis' TAFINLAR® (dabrafenib) and Array BioPharma's BRAFTOVI® (encorafenib). The combination of BRAF and MEK inhibitors is approved in patients with BRAF V600E/K mutation-positive metastatic melanoma, such as Novartis' dabrafenib and MEKINIST® (trametinib), Genentech's vemurafenib and COTELLIC® (cobimetinib), and Array Biopharma's encorafenib and MEKTOVI® (binimetinib). We are aware of several other BRAF inhibitors in clinical development, such as Roche's belvarafenib and Novartis' LXH254.

Lifirafenib was evaluated in a multi-center, open-label Phase 1 trial conducted in Australia and New Zealand comprised of two parts - dose escalation and dose expansion - in patients with BRAF or KRAS/NRAS mutated solid tumors or patients with pancreatic cancer. Lifirafenib demonstrated antitumor activity in both BRAF and KRAS-mutated tumors in preclinical studies and in the dose-escalation portion of this Phase 1 trial.

Data from the dose-expansion portion of the trial were presented at the 2017 American Association for Cancer Research, or AACR, Annual Meeting. The dose-expansion portion of the trial was designed to evaluate the safety and efficacy of lifirafenib at the recommended Phase 2 dose of 30 mg once daily established in the dose-escalation part of the trial. In the dose-expansion portion, lifirafenib was generally well-tolerated at a dose of 30 mg once daily and continued to show antitumor activity in patients with BRAF V600-mutated solid tumors and patients with KRAS-mutated solid tumors. The safety analysis, which included 96 patients as of the September 12, 2016 cutoff, suggested that lifirafenib was generally well-tolerated at 30 mg once daily, with most drug-related AEs being grades 1 or 2 in severity. The most frequent drug-related AEs (≥10%) of any grade were fatigue (38.5%), dysphonia (26.0%), decreased appetite (21.9%), palmar-plantar erythrodysesthesia syndrome (21.9%), thrombocytopenia (19.8%), dermatitis acneiform (17.7%), diarrhea (16.7%), rash (16.7%), nausea (15.6%), hypertension (11.5%) and glossodynia (10.4%). The most frequent drug-related grade 3 and 4 AEs (≥ 2%, two patients or more) included fatigue (7.3%), hypertension (6.3%), thrombocytopenia (6.3%), pyrexia (3.1%), hyponatremia (2.1%), anemia (2.1%), neutropenia (2.1%), febrile neutropenia (2.1%), decreased platelet count (2.1%), increased alanine aminotransferase (2.1%), increased GGT (2.1%) and sepsis (2.1%).

The cutoff for the efficacy analysis was September 17, 2016. In seven patients with BRAF V600-mutated melanoma (including one V600K and one V600R) who were naïve to BRAF or MEK inhibitors, there were three PRs and three cases of SD. In three patients with BRAF V600-mutated PTC, there was one PR and two cases of SD. In six patients with KRAS-mutated NSCLC, there was one PR and two cases of SD. In ten patients with solid tumors with BRAF non-V600 mutations or solid tumors with BRAF V600 mutations that are not included in other cohorts, there were two PRs, in one patient with BRAF V600E-mutated melanoma and one with BRAF V600E-mutated OC, and three cases of SD. In two patients with BRAF V600-mutated NSCLC, there was one unconfirmed PR and one case of SD. Additional cases of SD were observed in four of six melanoma patients with BRAF V600-mutated melanoma who had

responses to, but developed resistance against, BRAF or MEK inhibitors, nine of 13 patients with BRAF V600-mutated CRC, five of five patients with KRAS-mutated endometrial cancer, 12 of 20 patients with KRAS/NRAS-mutated CRC, and 10 of 21 patients with other KRAS/NRAS-mutated solid tumors or pancreatic cancer. In the Phase 1a portion of the trial, confirmed objective responses included a CR in a patient with BRAF V600E-mutated melanoma and two PRs, one in a patient with BRAF V600E-mutated thyroid cancer and one in a patient with KRAS-mutated endometrial cancer.

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BGB-A333, a PD-L1 Inhibitor

BGB-A333 is an investigational humanized IgG1-variant monoclonal antibody against PD-L1, the ligand of PD-1. We intend to develop BGB-A333 either as a monotherapy or in combination with other cancer therapies, such as tislelizumab, to treat various cancers and potentially other areas of unmet need. BGB-A333 is currently being evaluated in a Phase 1 clinical trial in Australia to assess the safety and antitumor effect of BGB-A333 alone and in combination with tislelizumab in patients with advanced solid tumors.

BGB-A425, a TIM-3 Inhibitor

BGB-A425 is an investigational humanized IgG1-variant monoclonal antibody against T-cell immunoglobulin and mucin-domain containing-3, or TIM-3. We began a Phase 1/2 trial of BGB-A433 in combination with tislelizumab in various solid tumors in the fourth quarter of 2018.

Sitravatinib (MGCD-0516), a Multi-Kinase Inhibitor

In January 2018, we entered into an exclusive license agreement with Mirati for the development, manufacturing and commercialization of Mirati's sitravatinib in Asia (excluding Japan and certain other countries), Australia and New Zealand. Sitravatinib is an investigational spectrum-selective kinase inhibitor which potently inhibits receptor tyrosine kinases, including RET, TAM family receptors (TYRO3, Axl, MER), and split family receptors (VEGFR2, KIT). Sitravatinib is being evaluated by Mirati in multiple clinical trials to treat patients who are refractory to prior immune checkpoint inhibitor therapy, including a potentially registration-enabling Phase 3 trial of sitravatinib in non-small cell lung cancer projected to initiate in the first half of 2019. Sitravatinib is also being evaluated as a single agent in patients with NSCLC, melanoma and other solid tumor types whose tumors harbor specific genetic alterations in CBL. In recent data readouts by Mirati, sitravatinib has demonstrated durable responses in lung cancer patients who progressed after treatment with checkpoint inhibitors. We began a Phase 1 study of sitravatinib in combination with tislelizumab in various solid tumors in Australia and China in the third quarter of 2018.

Avadomide (CC-122), a Cereblon Modulator

Avadomide (CC-122) is an investigational next-generation Cereblon modulator currently in clinical development by Celgene. It is in multiple Phase 1 and Phase 1/2 clinical trials, both as a single agent and in combination, for hematological and solid tumor cancers outside of China. Avadomide (CC-122) has been differentiated from previous compounds (such as thalidomide, lenalidomide and pomalidomide) and has been developed based on the scientific understanding of Cereblon-mediated protein homeostasis. We have rights to develop and commercialize avadomide (CC-122) in China under our exclusive license agreement with Celgene. See "-Celgene Collaboration."

Our Commercial Products

We commercialize the following cancer drugs in China under an exclusive license from Celgene. Historically, the fourth quarter sales of many oncology drug sales in China are lower than sales levels in the third quarter. Our product ABRAXANE®'s fourth quarter sales were lower than the third quarter in 2018.

ABRAXANE®

ABRAXANE® (paclitaxel albumin-bound particles for injectable suspension) is a solvent-free chemotherapy product which was developed using Celgene's proprietary nab® technology platform. This protein-bound chemotherapy agent combines paclitaxel with albumin. Globally, ABRAXANE® is approved for uses in breast cancer, NSCLC, pancreatic cancer and GC with geographic differences in labeling. In China, ABRAXANE® is approved for metastatic breast cancer after failure of combination chemotherapy for metastatic disease or relapse within six months of adjuvant chemotherapy. Prior therapy should have included an anthracycline unless clinically contraindicated.

According to Chen et al. 2016, there were approximately 4.3 million new cancer cases and 2.8 million cancer deaths in China in 2015, with breast cancer as the most common tumor type in Chinese women. It is estimated that in 2015 breast cancer affected 268,600 women and resulted in 69,500 deaths. Targeted therapy, hormone therapy and chemotherapy are three main strategies to treat different types of breast cancer.

Taxanes are the backbone chemotherapy to treat triple negative breast cancer, Her2+ or aggressive estrogen-receptor-positive and/or progesterone-receptor-positive breast cancer patients. ABRAXANE® is the only currently approved taxane that does not need pre-medication with dexamethasone to prevent hypersensitivity reactions, and several Phase 3 trials have

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demonstrated its efficacy and safety compared to solvent-based taxanes in both metastatic breast cancer and neo-adjuvant settings. Unlike other taxanes, ABRAXANE® has demonstrated unique and strong efficacy in pancreatic cancer and has become the backbone of first line standard of care for metastatic pancreatic cancer globally.

The taxanes marketed in China include two branded solvent-based paclitaxel (TAXOL® and ANZATAX) formulations, one branded docetaxel (TAXOTERE®) formulation, one paclitaxel liposome (LIPUSU®), one albumin-bound paclitaxel (ABRAXANE®) and dozens of generic taxanes. LIPUSU® is currently the market leader with approximately one-third of the market share.

In February 2018, an albumin-bound paclitaxel from CSPC Pharmaceutical Group was approved by the NMPA. Another form of albumin-bound paclitaxel from Hengrui was approved by the NMPA in September 2018.

In 2019, we plan to seek to differentiate and defend ABRAXANE® against growing generic competition in China, expand our sales force footprint and hospital coverage, and improve patient access through critical illness insurance negotiations and provincial reimbursement listings. As of September 1, 2018, ABRAXANE® is listed on provincial reimbursement drug lists of Fujian, Hubei, Ningxia, Jiangsu and Hunan, as well as in critical illness insurance program in Zhejiang and Shandong.

REVLIMID®

REVLIMID® (lenalidomide) is an oral immunomodulatory drug that was approved by the NMPA in China in 2013 for the treatment of multiple myeloma, or MM, in combination with dexamethasone in adult patients who have received at least one prior therapy. On February 2, 2018, REVLIMID® received NMPA approval of a new indication for the treatment of MM in combination with dexamethasone in adult patients with previously untreated MM who are not eligible for transplant.

MM is a malignant disease whose tumor cells originate in plasma cells in the bone marrow, which are cells in which B-lymphocytes develop to the final functional phase. The World Health Organization currently classifies it as a B-cell lymphoma, also known as plasma cell myeloma/plasmacytoma. MM is characterized by abnormal proliferation of bone marrow plasma cells accompanied by overproduction of monoclonal immunoglobulin. MM is often accompanied by multiple osteolytic lesions, hypercalcemia, anemia, and kidney damage. Due to the inhibition of normal immunoglobulin production, patients are prone to a variety of bacterial infections.

At present, MM is one of the most common malignant tumors in the blood system and occurs frequently in the elderly. The actual incidence increases with age, peaking from 60 to 70 years of age. Men suffer slightly more than women. Globally, the incidence was estimated at two to three per 100,000, with a male-to-female ratio of 1.6:1, and most patients are over 40 years old, according to Siegel et al., 2011 and IMS analysis. It is estimated that the incidence rate of MM is approximately one to two per 100,000 people in China, or approximately 18,000 new patients in 2017, out of which 10,000 are in urban populations, according to Lu et al., 2014, IMS analysis, and local market research. With a growing aging population and improving diagnosis, China has seen a steady increase in MM incidence.

Although MM cannot be cured, the progression of the disease can be controlled. The purpose of treatment is to extend patients' survival and improve quality of life. The main treatments for MM in China include VELCADE®, which is a proteasome inhibitor marketed by Johnson & Johnson in China since 2006, generic thalidomide and REVLIMID®. VELCADE® currently dominates the market in first-line MM treatment in China, while VELCADE® and REVLIMID® share the market in the second line. Chinese guidelines recommend lenalidomide as a standard of care for the treatment of R/R and newly diagnosed MM as well as in the maintenance setting. The first lenalidomide generic and first bortezomib generic in China were approved in November 2017. Another new agent for R/R MM, NINLARO® (ixazomib), an oral proteasome inhibitor developed by Takeda, received marketing approval from the NMPA on April 12, 2018. In February 2018, generic lenalidomide from ShuangLu Pharmaceutical Company was approved by the NMPA, and a third generic from Yangtze River is under review.

REVLIMID® was listed on the NRDL in June 2017.

VIDAZA®

VIDAZA® (azacitidine for injection) is a pyrimidine nucleoside analog that has been shown to reverse the effects of DNA hypermethylation and promote subsequent gene re-expression. VIDAZA® was approved in China in April 2017 for the treatment of intermediate-2 and high-risk myelodysplastic syndromes, or MDS, chronic myelomonocyte leukemia, or CMML, and acute myeloid leukemia, or AML, with 20% to 30% blasts and multi-lineage dysplasia. In

January 2018, VIDAZA® became commercially available in China.

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MDS are a group of cancers in which immature blood cells in the bone marrow do not mature and therefore do not become healthy blood cells. Approximately seven per 100,000 people are affected with approximately four per 100,000 people newly acquiring the condition each year globally according to Germing et al., 2013. The typical age of onset is 70 years. The higher-risk MDS (intermediate-2 and high-risk MDS) is considered fatal because the median overall survival rate is only 0.4-1.1 years and nearly 30% of these patients progress to AML, according to the U.S. National Comprehensive Cancer Network, or NCCN, MDS guideline 2013 and MDS Foundation. DNA methylation is an important mechanism of epigenetic gene regulation, but aberrant DNA hypermethylation can result in gene silencing. Silencing of tumor suppressor genes promotes cancer development and progression. MDS patients display aberrant DNA methylation of thousands of genes, which increases with advanced disease and is a poor prognostic factor.

In China, the main treatments for intermediate-2 and high-risk MDS are conventional care regimen, or CCR (best supportive care, low-dose cytarabine and intensive chemotherapy), and hypomethylating agents, or HMAs. DACOGEN® (decitabine) marketed by Johnson & Johnson was the first HMA agent approved in China in 2009. In the past several years, at least six decitabine generics have become available. In 2017, decitabine was listed in the NRDL. Nevertheless, there are still over 50% of higher-risk MDS patients treated by CCR and the unmet need remains large.

VIDAZA® is the only approved HMA shown to prolong survival for patients with MDS. Besides reversing the effects of DNA hypermethylation, VIDAZA® inhibits protein synthesis via RNA incorporation. VIDAZA® is a Category 1 recommended treatment for patients with intermediate-2 and high-risk MDS, according to the U.S. NCCN guideline. It is also a first-line recommended treatment for patients with intermediate-2 and high-risk MDS, according to the Chinese MDS treatment guidelines, and was listed on the NRDL in October 2018.

Our Preclinical Programs

We have a proprietary cancer biology platform that has also allowed us to develop our clinical-stage drug candidates and several additional preclinical-stage drug candidates in potentially important areas. These currently consist of targeted therapies and immuno-oncology agents. We anticipate advancing one or more of our preclinical assets into the clinic in the next 12 months. We believe we have the opportunity to combine tislelizumab with our preclinical candidates to target multiple points in the cancer immunity cycle. We also may seek to develop companion diagnostics that will help identify patients who are most likely to benefit from the use of our drug candidates.

Manufacturing and Supply

We currently have manufacturing capabilities at our research and development center in Beijing and at our manufacturing site in Suzhou, China that may be used for process development and clinical-scale small molecule drugs and biologics, as well as commercial scale production of small molecule drugs at our Suzhou facility. We are also constructing a commercial-scale biologics facility in Guangzhou, China. However, we have not yet begun to manufacture or process, either on our own or through a third-party, our drug candidates on a commercial scale. We currently rely on, and expect to continue to rely on, third-party contract research organization, or CROs, and contract manufacturing organizations, or CMOs, for the supply of raw materials and production of our drug candidates, as described below.

Raw Materials

We obtain raw materials for our manufacturing activities from multiple suppliers who we believe have sufficient capacity to meet our demands. Raw materials and starting materials used at our facilities in Beijing and Suzhou include active pharmaceutical ingredients custom-made by our CROs and excipients, which are commercially available from well-known vendors that meet the requirements of the relevant regulatory agencies. The core raw material to be used in manufacturing at our Guangzhou facility under construction is expected to be a genetically modified cell line that we co-developed and licensed from Boehringer Ingelheim.

We typically order raw materials on a purchase order basis and do not enter into long-term dedicated capacity or minimum supply arrangements. We pay for our purchases of raw materials on credit. Credit periods granted to us by our suppliers generally range from 30 to 60 days. Our suppliers are generally not responsible for the defects of our finished products.

Production

We have an approximately 11,000 square meter manufacturing facility in Suzhou, China, where we produce small molecule and biologics drug candidates for clinical supply and which we plan to use for commercial supply of our small molecule drug candidates, if approved. This facility consists of one oral-solid-dosage production line for small molecule drug

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products and one pilot plant for monoclonal antibody drug substances. In January 2018, the facility received a manufacturing license from the Jiangsu Food and Drug Administration, which is required for the commercial manufacture of zanubrutinib in China following NDA approval.

In addition, we have formed a joint venture with Guangzhou GET Technology Development Co., Ltd., an affiliate of Guangzhou Development District, to build a 24,000-liter commercial-scale biologics manufacturing facility in Guangzhou, China. Approximately US$300 million in funding has been committed for the construction of the 100,000 square meter manufacturing site. We contracted with General Electric to acquire its state-of-the-art KUBio™ prefabricated biomanufacturing equipment and commenced construction in 2017. We expect the first phase of the facility to be completed in 2019, and, following regulatory inspection and approval, to be used for commercial-scale production of tislelizumab, if approved.

We also have an approximately 140-square meter manufacturing facility at our research and development facilities in Beijing, China, which produces preclinical and clinical trial materials for some of our small molecule drug candidates.

Manufacturing is subject to extensive regulations that impose various procedural and documentation requirements governing recordkeeping, manufacturing processes and controls, personnel, quality control and quality assurance, among others. Our manufacturing facilities and the CMOs we use to manufacture our drugs and drug candidates operate under current good manufacturing practice regulations, or cGMP conditions. cGMP are regulatory requirements for the production of pharmaceuticals that will be used in humans.

Contract Manufacturing Organizations

We outsource to a limited number of external contract manufacturers the production of some drug substances and drug products, and we expect to continue to do so to meet the preclinical, clinical and potential commercial requirements of our drugs and drug candidates. We have adopted procedures to ensure that the production qualifications, facilities and processes of our third-party outsourced suppliers comply with the relevant regulatory requirements and our internal guidelines. We select our third-party suppliers carefully by considering a number of factors, including their qualifications, relevant expertise, production capacity, geographic proximity, reputation, track record, product quality, reliability in meeting delivery schedules, and terms offered by such third-party outsourced suppliers.

We have framework agreements with most of our external service providers, under which they generally provide services to us on a short-term and project-by-project basis. For example, we have an agreement with a contract manufacturer for clinical supply of zanubrutinib and expect to enter into a commercial supply agreement for zanubrutinib in the future. We have entered into a commercial supply agreement with Boehringer Ingelheim Biopharmaceuticals (China) Ltd., or Boehringer Ingelheim, for our investigational anti-PD-1 antibody therapy, tislelizumab, which will be manufactured at Boehringer Ingelheim's facility in Shanghai, China as part of a marketing authorization holder, or MAH, trial project pioneered by us and Boehringer Ingelheim. We believe the MAH status will be maintained after the expiration of the MAH pilot program in November 2019, based on confirmation from the relevant governmental authority, and therefore we believe that the expiration of the MAH pilot program will not impact our drug candidates. Under the terms of the commercial supply agreement, Boehringer Ingelheim will manufacture tislelizumab in China under an exclusive multi-year arrangement, with contract extension possible. In addition, we obtained certain preferred rights for future capacity expansion by Boehringer Ingelheim in China. For our commercial products licensed from Celgene, we rely on Celgene and its contract manufacturers outside of China for the supply of those drugs.

Agreements with outsourced suppliers generally set out terms, including product quality or service details, technical standards or methods, delivery terms, agreed price and payment, and product inspection and acceptance criteria. We are generally allowed to return any products that fail to meet our quality standards. Our outsourced suppliers procure raw materials themselves. Typically, outsourced suppliers request settlement of payment within 30 days from the date of invoice. Either party may terminate the agreements by serving notice to the other party under certain circumstances.

Celgene Collaboration

Exclusive License and Collaboration Agreement

On July 5, 2017, we entered into an Exclusive License and Collaboration Agreement, as amended and restated, with Celgene and its wholly-owned subsidiary, Celgene Switzerland LLC, or Celgene Switzerland, which became effective on August 31, 2017, pursuant to which we granted the Celgene parties an exclusive right to develop and

commercialize tislelizumab in all fields of treatment, other than hematology, in the United States, Europe, Japan and the rest of world other than Asia, which we refer to as the PD-1 License Agreement.

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Pursuant to the terms of the PD-1 License Agreement, the Celgene parties made upfront payments of US$263 million to us. In addition, pursuant to a share subscription agreement with Celgene Switzerland dated July 5, 2017, or the Share Subscription Agreement, we issued approximately 32.7 million of our ordinary shares on August 31, 2017 for an aggregate purchase price of US$150 million at $4.58 per ordinary share, or $59.55 per ADS, representing a 35% premium to an 11-day volume-weighted average price of our ADSs. The agreement also provides for up to US$980 million in potential development, regulatory and sales milestone payments and tiered royalties based on percentages of annual net sales, depending on specified terms, in the low double digit to mid-twenties, with customary reductions in specified circumstances. Royalties are payable on a licensed product-by-product and country-by-country basis until the latest of the expiration of the last valid patent claim, the expiration of regulatory exclusivity, or 12 years after the first commercial sale of such licensed product in the country of sale.

Each party has the right to develop and commercialize tislelizumab in its respective field and territory, and has also agreed to collaborate through a joint steering committee comprised of an equal number of representatives from each party on, among other things, the conduct of up to eight global pivotal clinical trials, or the Basket Studies. Each Basket Study will be conducted and funded by either us or Celgene in accordance with a mutually agreed development plan and study design. For any Basket Studies conducted and funded by us, Celgene has the right to opt into such program, at which time it will reimburse us for agreed upon development costs based on a multiple of such costs that varies according to the stage of development at which Celgene opts into the program. Celgene has committed to use commercially reasonable efforts to develop at least one licensed product, to seek specified regulatory approvals and to spend at least US$100 million on development for the Basket Studies led by Celgene, subject to specified conditions. In addition, we retain the right to develop tislelizumab in combination therapies with our portfolio compounds, and Celgene has a right of first negotiation for tislelizumab in the hematology field and in our territory, subject to specified conditions.

The PD-1 License Agreement contains customary representations, warranties and covenants by us and Celgene. Unless earlier terminated, the agreement will expire on a licensed product-by-product and country-by-country basis upon the expiration of the royalty term in such country for such licensed product. The agreement may be terminated by Celgene upon 30 days' prior written notice, or by either party upon the other party's bankruptcy or uncured material breach. In addition, the agreement includes standard exclusivity obligations and provisions that are triggered in the event that Celgene acquires or is acquired by a third party with a competing product.

In January 2019, Celgene and Bristol-Myers Squibb, or BMS, announced the proposed acquisition of Celgene by BMS, which is expected to close in the third quarter of 2019, subject to receipt of required approvals. BMS markets the anti-PD-1 inhibitor OPDIVO® (nivolumab). Assuming that the BMS-Celgene transaction closes, we expect that a likely outcome will be that the PD-1 License Agreement will be terminated under the exclusivity and related provisions, and we will regain the full rights to tislelizumab with a termination fee from Celgene. Prior to that time, we expect to continue to conduct the agreed upon development plans under the existing terms of the agreement, including receipt from Celgene of development funding for the Basket Studies that it has agreed to fund. In the event that the PD-1 License Agreement is terminated, we believe that we are operationally and financially capable of continuing to advance tislelizumab on our own with minimal disruption.

Celgene China Agreements

On July 5, 2017, we and a wholly-owned subsidiary of Celgene, Celgene Logistics Sàrl, or Celgene Logistics, entered into a License and Supply Agreement, which we refer to as the China License Agreement and which became effective on August 31, 2017, pursuant to which we were granted the right to exclusively distribute and promote Celgene's approved cancer therapies, ABRAXANE®, REVLIMID® and VIDAZA®, and its investigational agent avadomide (CC-122) in clinical development in China, excluding Hong Kong, Macau and Taiwan. In addition, if Celgene decides to commercialize a new oncology product through a third-party in the licensed territory during the first five years of the term, we have a right of first negotiation to obtain the right to commercialize the product, subject to certain conditions. We paid an aggregate of US$4.5 million in cash for the license and our acquisition of Celgene Shanghai, as described below.

The term of the China License Agreement is 10 years and may be terminated by either party upon written notice in the event of uncured material breach or bankruptcy of the other party, or if the underlying regulatory approvals for the

covered products are revoked. Celgene Logistics also has the right to terminate the agreement with respect to REVLIMID® at any time upon written notice to the Company under certain circumstances.

In the event of an acquisition of Celgene Logistics by another party, the China License Agreement provides that Celgene Logistics shall provide notice to us, and within a specified period of time, requires that the parties discuss in good faith any changes in the supply requirements of the China License Agreement that Celgene Logistics may request as a result of the acquisition. During that period, the China License Agreement requires us to conduct business in the ordinary course and provides that Celgene Logistics is not required to supply more than a specified amount more than the amount of our forecasted

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demand. We expect to be able to continue to market ABRAXANE®, REVLIMID® and VIDAZA® in China under the China License Agreement following the closing of the announced BMS acquisition of Celgene, if that transaction occurs.

The China License Agreement contains customary representations and warranties and confidentiality and mutual indemnification provisions.

On August 31, 2017, our wholly owned subsidiary, BeiGene (Hong Kong) Co., Ltd., acquired 100% of the equity interests of Celgene Pharmaceutical (Shanghai) Co., Ltd., or Celgene Shanghai, a wholly-owned subsidiary of Celgene Holdings East Corporation established under the laws of China. The purchase price of Celgene Shanghai was determined to be approximately US$28.1 million from an accounting perspective, and comprised of a cash consideration of US$4.5 million and non-cash consideration of US$23.6 million. The amount allocated to non-cash consideration, related to the discount on ordinary shares issued to Celgene in connection with the Share Subscription Agreement and was a result of the increase in fair value of our shares between the fixed price of US$59.55 per ADS specified in the Share Subscription Agreement and the fair value per ADS on August 31, 2017, the date the transaction closed. This company, which we subsequently renamed BeiGene Pharmaceutical (Shanghai) Co., Ltd., is in the business of, among other things, providing marketing and promotional services for the pharmaceutical products that we license from Celgene. Prior to closing, Celgene separated out certain business functions, including regulatory and drug safety, that continue to support the business acquired by us.

Intellectual Property

The proprietary nature of, and protection for, our drug candidates and their methods of use are an important part of our strategy to develop and commercialize novel medicines, as described in more detail below. We have obtained patents and filed patent applications in the United States and other countries and regions, such as China and Europe, relating to certain of our drug candidates, and are pursuing additional patent protection for them and for our other drug candidates and technologies. We rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection including our manufacturing processes. We also rely on know-how, continuing technological innovation and in-licensing opportunities to develop, strengthen and support our development programs.

As of February 11, 2019, we owned 18 issued U.S. patents, 10 issued China patents, a number of pending U.S. and China patent applications, and corresponding patents and patent applications internationally. In addition, we owned pending international patent applications under the Patent Cooperation Treaty, or PCT, which we plan to file nationally in the United States and other jurisdictions, as well as additional priority PCT applications. With respect to any issued patents in the United States and Europe, we may be entitled to obtain a patent term extension to extend the patent expiration date, provided that we meet the applicable requirements for obtaining such patent term extensions. For example, in the United States, we can apply for a patent term extension of up to five years for one of the patents covering a drug product once the product is approved by the FDA. The exact duration of the extension depends on the time that we spend in clinical studies as well as getting approval from the FDA.

The patent portfolios for our later-stage clinical drug candidates as of February 11, 2019, are summarized below:

Zanubrutinib. We own two issued U.S. patents, one issued China patent, a number of pending PCT and U.S. patent applications, and corresponding patent applications in other jurisdictions directed to zanubrutinib, a small molecule BTK inhibitor, combinations of zanubrutinib with other therapeutic agents, and its use for the treatment of hematological malignancies or autoimmune disease. The expected expiration for the issued U.S. patents and the issued China patent is 2034, excluding any additional term for patent term extensions. We intend to pursue marketing exclusivity periods that are available under regulatory provisions in certain countries.

Tislelizumab. We own three issued U.S. patents, one issued China patent, pending PCT, U.S. and China patent applications, and corresponding pending patent applications in other jurisdictions directed to tislelizumab, a humanized monoclonal antibody against PD-1, and its use for the treatment of cancer. The expected expiration for the issued U.S. patents and the issued China patent is 2033, excluding any additional term for patent term extensions. We intend to pursue marketing exclusivity periods that are available under regulatory provisions in certain countries.

Pamiparib. We own three issued U.S. patents, one issued China patent, a number of pending PCT, U.S. and China patent applications, and corresponding pending patent applications in other jurisdictions directed to pamiparib, a small

molecule PARP1/2 inhibitor, and its use for the treatment of cancer, including glioblastomas and breast cancer. The expected expiration for the issued U.S. patents and the issued China patent is 2031, excluding any additional term for patent term extensions. We intend to pursue marketing exclusivity periods that are available under regulatory provisions in certain countries.

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Lifirafenib. We own two issued U.S. patents, two issued China patents, a number of pending PCT, U.S. and China patent applications, and corresponding pending patent applications in other jurisdictions directed to lifirafenib, a small molecule BRAF inhibitor, and its use for the treatment of cancer, including BRAF mutated cancers. The expected expiration for the issued U.S. patents and the issued China patents is 2031, excluding any additional term for patent term extensions. We intend to pursue marketing exclusivity periods that are available under regulatory provisions in certain countries.

The patent portfolios for our three in-licensed commercial products in China are summarized below:

ABRAXANE®. We are the exclusive licensee of five issued Chinese patents and a number of pending Chinese patent applications directed to ABRAXANE®, a nanoparticle albumin-bound paclitaxel, covering its composition, liquid formulation, and use for the treatment of cancer. Two of the five issued Chinese patents expired in 2018. The expected expirations for the other three issued Chinese patents are 2021, 2026 and 2031, respectively, excluding any additional term for patent term extensions. However, generic versions of albumin-bound palclitaxel have been approved in China and are being commercialized.

REVLIMID®. We are the exclusive licensee of seven issued Chinese patents directed to REVLIMID® (lenalidomide), covering its use for the treatment of cancer, including MM. The expected expirations for the issued Chinese patents are 2023 and 2027, respectively, excluding any additional term for patent term extensions. However, generic versions of lenalidomide have been approved in China and are being commercialized.

VIDAZA®. We do not have any rights in any issued China patent or pending China patent applications directed to VIDAZA®, a chemical analog of cytidine, and its use for the treatment of cancer. We are aware of third parties who are seeking to develop and obtain approval for generic forms of this drug.

Furthermore, although various extensions may be available, the life of a patent and the protection it affords, is limited. As noted above, ABRAXANE®, REVLIMID® and VIDAZA® face or are expected to face competition from generic medications, and we may face similar competition for any approved drug candidates even if we successfully obtain patent protection once the patent life has expired for the drug. The scope, validity or enforceability of our patents may be challenged in court, and we may not be successful in enforcing or defending those intellectual property rights and, as a result, may not be able to develop or market the relevant product exclusively, which would have a material adverse effect on any potential sales of that product. Under our license agreement with Celgene, Celgene retains the responsibility for, but is not obligated, to prosecute, defend and enforce the patents for these in-licensed products. As such, any issued patents may not protect us from generic competition for these drugs.

The term of individual patents may vary based on the countries in which they are obtained. In most countries in which we file, including the United States and China, the term of an issued patent is generally 20 years from the earliest claimed filing date of a non-provisional patent application in the applicable country. In the United States, a patent's term may be lengthened in some cases by a patent term adjustment, which extends the term of a patent to account for administrative delays by the United States Patent and Trademark Office, or USPTO, in excess of a patent applicant's own delays during the prosecution process, or may be shortened if a patent is terminally disclaimed over a commonly owned patent having an earlier expiration date. In addition, in certain instances, a patent term can be extended to recapture a portion of the term effectively lost as a result of the FDA regulatory review period. However, the restoration period cannot be longer than five years and the total patent term including the restoration period must not exceed 14 years following FDA approval.

In certain foreign jurisdictions similar extensions as compensation for regulatory delays are also available. The actual protection afforded by a patent varies on a claim by claim and country by country basis and depends upon many factors, including the type of patent, the scope of its coverage, the availability of any patent term extensions or adjustments, the availability of legal remedies in a particular country and the validity and enforceability of the patent.

We may rely, in some circumstances, on trade secrets and unpatented know-how to protect aspects of our technology. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with employees, consultants, scientific advisors and contractors and invention assignment agreements with our employees. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems.

Additionally, we currently own a number of registered trademarks and pending trademark applications. We currently have registered trademarks for BeiGene and our corporate logo in China, the European Union and other jurisdictions and are seeking trademark protection for BeiGene, our corporate logo, product names and logos, and other marks in the United States and other countries where available and appropriate.

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Government Regulation

Government authorities in the United States 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, pricing and export and import of drugs such as those we are developing and commercializing. 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.

U.S. Regulation

U.S. Government Regulation and Product Approval

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations, and biologics under the FDCA, its implementing regulations, and the Public Health Service Act, or PHSA, and its implementing regulations.

Cancer therapies are sometimes characterized as first line, second line or third line, and the FDA often approves new therapies initially only for second or third line use. When cancer is detected early enough, first line therapy is sometimes adequate to cure the cancer or prolong life without a cure. Whenever first line therapy, usually chemotherapy, hormone therapy, surgery or a combination of these, proves unsuccessful, second line therapy may be administered. Second line therapies often consist of more chemotherapy, radiation, antibody drugs, tumor targeted small molecule drugs or a combination of these. Third line therapies can include bone marrow transplantation, antibody and small molecule targeted therapies, more invasive forms of surgery and new technologies.

U.S. Drug Development Process

The process required by the FDA before a drug or biologic may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests, animal studies and formulation studies according to Good Laboratory Practices, or GLP, regulations;
- submission to the FDA of an investigational new drug, or IND, application, which must become effective before human clinical trials may begin;
- performance of adequate and well-controlled human clinical trials according to GCP, to establish the safety and efficacy of the proposed drug or safety, purity and potency of the proposed biologic, for the intended use;
- preparation and submission to the FDA of an NDA for a drug or a BLA for a biologic;
- a determination by the FDA within 60 days of its receipt of an NDA or BLA to file the application for review;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with cGMP;
- FDA audits of some clinical trial sites to ensure compliance with GCPs; and
- FDA review and approval of the NDA or licensing of the BLA.

Once a product candidate is identified for development, it enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, toxicity, formulation and stability, as well as animal studies. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data and any available clinical data or literature, to the FDA as part of the IND. The sponsor must also include a protocol detailing, among other things, the objectives of the initial clinical trial, dosing procedures, subject selection and exclusion criteria, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated if the initial clinical trial lends itself to an efficacy evaluation. Some preclinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA raises concerns or questions related to the proposed clinical trial and places the trial on a clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding

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concerns before the clinical trial can begin. Clinical holds also may be imposed by the FDA at any time before or during clinical trials due to safety concerns or noncompliance and may be imposed on all products within a certain class of products. The FDA also can impose partial clinical holds, for example, prohibiting the initiation of clinical trials of a certain duration or for a certain dose.

All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with GCP regulations. These regulations include the requirement that all research subjects provide informed consent in writing before their participation in any clinical trial. Further, an institutional review board, or IRB, must review and approve the plan for any clinical trial before it commences at any institution, and the IRB must conduct continuing review and reapprove the study at least annually. An IRB considers, among other things, whether the risks to individuals participating in the clinical trial are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the information regarding the clinical trial and the 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.

Each new clinical protocol and any amendments to the protocol must be filed with the FDA as an IND amendment and submitted to the IRBs for approval.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- Phase 1. The product is initially introduced into a small number of healthy human subjects or patients and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion and, if possible, to gain early evidence on effectiveness. In the case of some products for severe or life-threatening diseases, especially when the product is suspected or known to be unavoidably toxic, the initial human testing may be conducted in patients.
- Phase 2. Involves clinical trials in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage and schedule.
- Phase 3. Clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population. These clinical trials are intended to evaluate the overall risk/benefit relationship of the product and provide an adequate basis for product labeling.

We refer to our Phase 1 programs as dose-escalation and dose-expansion trials. In addition, we refer to some of our Phase 2 programs as pivotal or registrational programs, where the results can be used to support regulatory approval in specific jurisdictions without the need to conduct a Phase 3 trial.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and safety reports must be submitted to the FDA and the investigators for serious and unexpected suspected AEs, any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator's brochure, or any findings from other studies or animal or in vitro testing that suggest a significant risk in humans exposed to the product drug. Phase 1, Phase 2 and Phase 3 studies may not be completed successfully within any specified period, or at all. The FDA or the 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 product has been associated with unexpected serious harm to subjects.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the product and finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the product does not undergo unacceptable deterioration over its shelf life.

U.S. Review and Approval Processes

The results of product development, preclinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the product, proposed labeling and other relevant information, are submitted to the FDA as part of an NDA for a new drug or a BLA for a biologic, requesting approval to market the

product. The submission of an

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NDA or BLA is subject to the payment of a substantial user fee; although a waiver of such fee may be obtained under certain limited circumstances. The sponsor of an approved NDA or BLA is also subject to an annual prescription drug product program fee.

The FDA reviews all NDAs and BLAs submitted to ensure that they are sufficiently complete for substantive review before it accepts them for filing. The FDA may request additional information rather than accept an NDA or BLA for filing. In this event, the NDA or BLA must be re-submitted with the additional information. The re-submitted application also is subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use, and a BLA to determine whether the biologic is safe, pure, and potent for its intended use. The FDA also evaluates whether the product's manufacturing is cGMP-compliant to assure the product's identity, strength, quality and purity. Before approving an NDA or BLA, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications.

The approval process is lengthy and difficult, and the FDA may refuse to approve an NDA or BLA if the applicable regulatory criteria are not satisfied or may require additional clinical data or other data and information. Even if such data and information are submitted, the FDA may ultimately decide that the NDA or BLA 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. The FDA will issue a complete response letter if the agency decides not to approve the NDA or BLA in its present form. The complete response letter usually describes all of the specific deficiencies that the FDA identified in the NDA or BLA that must be satisfactorily addressed before it can be approved. The deficiencies identified may be minor, for example, requiring labeling changes, or major, for example, requiring additional clinical trials. Additionally, the complete response letter may include recommended actions that the applicant might take to place the application in a condition for approval. If a complete response letter is issued, the applicant may either resubmit the NDA or BLA, addressing all of the deficiencies identified in the letter, or withdraw the application or request an opportunity for a hearing.

If a product receives regulatory 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 product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. In addition, the FDA may require post-approval studies, including Phase 4 clinical trials, to further assess a product's safety and effectiveness after NDA or BLA approval and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized. The FDA may also approve an NDA or BLA with 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.

Regulation of Combination Products in the United States

Certain products may be comprised of components that would normally be regulated under different types of regulatory authorities in certain jurisdictions, and in the United States by different centers at the FDA. These products are known as combination products. Under the FDCA, the FDA is charged with assigning a center with primary jurisdiction, or a lead center, for review of a combination product. That determination is based on the "primary mode of action" of the combination product. We are developing combination products using our own drug candidates and third-party drugs.

Expedited Programs

Fast Track Designation

The FDA has a fast track program that is intended to expedite or facilitate the process for reviewing new drugs, including biologics that meet certain criteria. Specifically, new drugs are eligible for Fast Track designation if they are intended to treat a serious or life-threatening disease or condition for which there is no effective treatment and demonstrate the potential to address unmet medical needs for the condition. Fast track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a new drug may

request the FDA to designate the drug as a fast track product concurrently with, or at any time after, submission of an IND, and the FDA must determine if the drug candidate qualifies for fast track designation within 60 days of receipt of the sponsor's request.

In addition to other benefits, such as the ability to engage in more frequent interactions with the FDA, the FDA may initiate review of sections of a fast track drug's NDA or BLA before the application is complete. This rolling review is available

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if the applicant provides, and the FDA approves, a schedule for the submission of each portion of the NDA or BLA and the applicant pays the applicable user fee. However, the FDA's time period goal for reviewing an application does not begin until the last section of the NDA or BLA is submitted. Additionally, the fast track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Accelerated Approval

Under FDA's accelerated approval regulations, the FDA may approve a drug, including a biologic, for a serious or life-threatening illness that provides meaningful therapeutic benefit to patients over existing treatments based upon 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. In clinical trials, a surrogate endpoint is a marker, such as a laboratory measurement or clinical signs of a disease or condition that is thought to predict clinical benefit but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. A drug candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of post-approval clinical trials sometimes referred to as Phase 4 trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or to confirm a clinical benefit during post-marketing studies, will allow the FDA to withdraw the drug from the market on an expedited basis. All promotional materials for drug candidates approved under accelerated regulations are subject to prior review by the FDA.

Breakthrough Designation

Breakthrough therapy designation is intended to expedite the development and review of a breakthrough therapy. A drug or biologic product can be designated as a breakthrough therapy if it is intended to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that it may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. A sponsor may request that a product be designated as a breakthrough therapy concurrently with, or at any time after, the submission of an IND, and the FDA must determine if the candidate qualifies for breakthrough therapy designation within 60 days of receipt of the sponsor's request. If so designated, the FDA shall act to expedite the development and review of the product's marketing application, including by meeting with the sponsor throughout the product's development, providing timely advice to the sponsor to ensure that the development program to gather preclinical and clinical data is as efficient as practicable, involving senior managers and experienced review staff in a cross-disciplinary review, and assigning a cross-disciplinary project lead for the FDA review team to facilitate an efficient review of the development program and to serve as a scientific liaison between the review team and the sponsor. The designation may be rescinded if the drug candidate does not continue to meet the criteria for breakthrough therapy designation.

Priority Review

The FDA may grant an NDA for a new molecular entity or BLA a priority review designation, which sets the target date for FDA action on the application at six months after the FDA accepts the application for filing. Priority review is granted where there is evidence that the proposed product would be a significant improvement in the safety or effectiveness of the treatment, diagnosis, or prevention of a serious condition. If criteria are not met for priority review, the application is subject to the standard FDA review period of ten months after FDA accepts the application for filing. Priority review designation does not change the scientific/medical standard for approval or the quality of evidence necessary to support approval.

Post-Approval Requirements

Any products for which we receive FDA approval are subject to continuing regulation by the FDA, including, among other things, record-keeping requirements, reporting of adverse experiences with the product, providing the FDA with updated safety and efficacy information, product sampling and distribution requirements, complying with certain electronic records and signature requirements and complying with FDA promotion and advertising requirements. The FDA strictly regulates labeling, advertising, promotion and other types of information on products that are placed on the market. Products may be promoted only for the approved indications and in accordance with the provisions of the

approved label. Further, manufacturers must continue to comply with cGMP requirements, which are extensive and require considerable time, resources and ongoing investment to ensure compliance. In addition, changes to the manufacturing process generally require prior FDA approval before being implemented and other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval.

Manufacturers and other entities involved in the manufacturing and distribution of approved products are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by

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the FDA and certain state agencies for compliance with cGMP and other laws. The cGMP requirements apply to all stages of the manufacturing process, including the production, processing, sterilization, packaging, labeling, storage and shipment of the product. Manufacturers must establish validated systems to ensure that products meet specifications and regulatory requirements and test each product batch or lot prior to its release.

The FDA may withdraw a product approval or revoke a biologics license if compliance with regulatory requirements is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market. Further, the failure to maintain compliance with regulatory requirements may result in administrative or judicial actions, such as fines, untitled or warning letters, holds on clinical trials, product seizures, product detention or refusal to permit the import or export of products, refusal to approve pending applications or supplements, restrictions on marketing or manufacturing, injunctions or civil or criminal penalties. We may undertake or be required to undertake a product recall.

Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of FDA approval of the use 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 or BLA plus the time between the submission date of an NDA or BLA and the approval of that application, except that this review period is reduced by any time during which the applicant failed to exercise due diligence. Only one patent applicable to an approved product 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, if available, we intend to apply for restorations of patent term for some of our currently owned patents beyond their current expiration dates, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant NDA or BLA; however, there can be no assurance that any such extension will be granted to us.

Market exclusivity provisions under the FDCA can also delay the submission or the approval of certain applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to gain 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 NDA, or ANDA, or a 505(b)(2) NDA submitted by another company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, such an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) 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, for new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the conditions of use associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active agent. 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. Pediatric exclusivity is another type of exclusivity in the United States. Pediatric exclusivity, if granted, provides an additional six months of exclusivity, which runs from the end of other exclusivity or patent periods.

Biosimilars and Exclusivity

The PHSA includes an abbreviated approval pathway for biological products shown to be similar to, or interchangeable with, an FDA-licensed reference biological product. Biosimilarity, which requires that there be no

clinically meaningful differences between the biological product and the reference product in terms of safety, purity and potency, can be shown through analytical studies, animal studies, and a clinical trial or trials. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product and, for products administered multiple times, the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic.

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A reference biologic is granted 12 years of exclusivity from the time of first licensure of the reference product. The first biologic product submitted under the abbreviated approval pathway that is determined to be interchangeable with the reference product has exclusivity against other biologics submitting under the abbreviated approval pathway for the lesser of (i) one year after the first commercial marketing, (ii) 18 months after approval if there is no legal challenge, (iii) 18 months after the resolution in the applicant's favor of a lawsuit challenging the biologic's patents if an application has been submitted, or (iv) 42 months after the application has been approved if a lawsuit is ongoing within the 42-month period.

Orphan Drugs

Under the Orphan Drug Act, the FDA may grant orphan drug designation, or ODD, to drugs, including biologics, intended to treat a rare disease or condition-generally a disease or condition that affects fewer than 200,000 individuals in the United States or that affects more than 200,000 individuals in the U.S. and for which there is no reasonable expectation that costs of research and development of the product for the indication can be recovered by sales of the product in the United States. Orphan drug designation must be requested before submitting an NDA or BLA.

After the FDA grants orphan drug designation, the generic identity of the drug or biologic and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. The first NDA or BLA applicant to receive FDA approval for a particular active ingredient to treat a particular disease or condition with FDA orphan drug designation is entitled to a seven-year exclusive marketing period in the United States for that product, for that indication. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the NDA or BLA application user fee.

During the exclusivity period, the FDA may not approve any other applications to market the same drug for the same disease or condition, except in limited circumstances, such as if the second applicant demonstrates the clinical superiority of its product to the product with orphan drug exclusivity through a demonstration of superior safety, superior efficacy, or a major contribution to patient care. "Same drug" means a drug that contains the same active moiety if it is a drug composed of small molecules, or the same principal molecular structural features if it is composed of macromolecules and is intended for the same use as a previously approved drug, except that if the subsequent drug can be shown to be clinically superior to the first drug, it will not be considered to be the same drug. Orphan drug exclusivity does not prevent the FDA from approving a different drug for the same disease or condition, or the same drug for a different disease or condition.

Zanubrutinib was granted ODD status by the FDA for the treatment of WM, CLL and MCL on June 29, 2016, July 20, 2016, and June 23, 2016, respectively.

Disclosure of Clinical Trial Information

Sponsors of clinical trials of FDA-regulated products, including drugs and biologics, are required to register and disclose certain clinical trial information, which is publicly available at www.clinicaltrials.gov. Information related to the product, patient population, phase of investigation, study sites and investigators, and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to disclose the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed until the new product or new indication being studied has been approved. Competitors may use this publicly available information to gain knowledge regarding the progress of development programs.

Pharmaceutical Coverage, Pricing and Reimbursement

In the United States, sales of any products for which we may receive regulatory approval for commercial sale will depend in part on the availability of coverage and reimbursement from third-party payors, including government authorities, managed care providers, private health insurers and other organizations. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the reimbursement rate that the payor will pay for the product. Third-party payors may limit coverage to specific products on an approved list which might not include all of the FDA-approved products for a particular indication. Moreover, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an

appropriate return on our investment in product development.

Third-party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. In order to obtain coverage and reimbursement for any product that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of any products, in addition to the costs required to obtain regulatory approvals. If third-party payors do not consider a product to be cost-effective or medically-necessary compared to other available therapies,

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they may not cover the product after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow a company to sell its products at a profit.

The U.S. government and state legislatures have shown significant interest in implementing cost containment programs to limit the growth of government-paid health care costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. For example, the Affordable Care Act, or ACA, contains provisions that may reduce the profitability of drug products, including, for example, increased rebates for drugs reimbursed by Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies' share of sales to federal health care programs. Adoption of government controls and measures and tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceuticals.

The current U.S. president's administration's budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. Additionally, the current administration released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out of pocket costs of drug products paid by consumers. The U.S. Department of Health and Human Services, or HHS, has already started the process of soliciting feedback on some of these measures and, at the same time, is immediately implementing others under its existing authority. For example, in September 2018, CMS announced that it will allow Medicare Advantage Plans the option to use step therapy for Part B drugs beginning January 1, 2019, and in October 2018, CMS proposed a new rule that would require direct-to-consumer television advertisements of prescription drugs and biological products, for which payment is available through or under Medicare or Medicaid, to include in the advertisement the Wholesale Acquisition Cost, or list price, of that drug or biological product. In addition, CMS issued an Advanced Notice of Proposed Rulemaking, or ANPRM, in October 2018 indicating it is considering issuing a proposed rule in the spring of 2019 on a model called the International Pricing Index, or IPI. This model would utilize a basket of other countries' prices as a reference for the Medicare program to use in reimbursing for drugs covered under Part B. The ANPRM also included an updated version of the Competitive Acquisition Program, or CAP, as an alternative to current "buy and bill" payment methods for Part B drugs. Such a proposed rule could limit our product pricing and have material adverse effects on our business. Although a number of these, and other proposed measures will require authorization through additional legislation to become effective, Congress and the current administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. 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.

Other U.S. Healthcare Laws and Compliance Requirements

If we obtain regulatory approval of our product candidates, we may be subject to various federal and state laws targeting fraud and abuse in the healthcare industry. These laws may impact, among other things, our proposed sales, marketing and education programs. In addition, we may be subject to patient privacy regulation by both the federal government and the states in which we conduct our business prior to and after receiving regulatory approval of our product candidates. The laws that may affect our ability to operate include:

- the federal Anti-Kickback Statute, which prohibits, among other things, knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, either the referral of an individual, or the purchase, lease, order or recommendation of any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs;

federal civil and criminal false claims and civil monetary penalty laws, such as the federal False Claims Act, which impose criminal and civil penalties and authorize civil whistleblower or qui tam actions, against individuals or entities for, among other things: knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent; making a false statement or record material to a false or fraudulent claim or obligation to pay or transmit money or property to the federal government; or knowingly concealing or knowingly and improperly avoiding or decreasing an obligation to pay money to the federal government. In addition, the government

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may assert that a claim including items and services resulting from a violation of the federal Anti-Kickback Statute constitutes a false of fraudulent claim for purposes of the False Claims Act;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which prohibits knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, and their respective implementing regulations, which impose requirements on certain covered healthcare providers, health plans and healthcare clearinghouses as well as their respective business associates who perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information;
- the federal transparency requirements under the ACA, including the provision commonly referred to as the Physician Payments Sunshine Act, which require manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program to report annually to the U.S. Department of Health and Human Services information related to payments or other transfers of value made to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers.

The ACA broadened the reach of the fraud and abuse laws by, among other things, amending the intent requirement of the federal Anti-Kickback Statute and the applicable criminal healthcare fraud statutes contained within 42 U.S.C. § 1320a-7b. Pursuant to the statutory amendment, a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, the ACA provides 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 civil False Claims Act or the civil monetary penalties statute. Many states have adopted laws similar to the federal Anti-Kickback Statute and False Claims Act, some of which apply to claims for, and referral of patients for, healthcare items or services reimbursed by any source, not only the Medicare and Medicaid programs. Similarly, state privacy laws may be broader and require greater protections than HIPAA. Violations of fraud and abuse laws may be punishable by criminal and/or civil sanctions, including penalties, fines and/or exclusion or suspension from federal and state healthcare programs such as Medicare and Medicaid and debarment from contracting with the U.S. government. In addition, private individuals have the ability to bring actions on behalf of the U.S. government under the federal False Claims Act as well as under the false claims laws of several states.

European Data Collection

The collection and use of personal health data in the European Union are governed by the provisions of the Data Protection Directive, and as of May 2018 the General Data Protection Regulation, or GDPR. This directive imposes several requirements relating to the consent of the individuals to whom the personal data relates, the information provided to the individuals, notification of data processing obligations to the competent national data protection authorities, and the security and confidentiality of the personal data. The Data Protection Directive and GDPR also impose strict rules on the transfer of personal data out of the European Union to the United States. Failure to comply with the requirements of the Data Protection Directive, the GDPR, and the related national data protection laws of the European Union Member States may result in fines and other administrative penalties. The GDPR introduces new data protection requirements in the European Union and substantial fines for breaches of the data protection rules. The GDPR regulations may impose additional responsibility and liability in relation to personal data that we process, and we may be required to put in place additional mechanisms ensuring compliance with the new data protection rules. This may be onerous and adversely affect our business, financial condition, results of operations, and prospects.

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PRC Regulation

In the People's Republic of China, or PRC, we operate in an increasingly complex legal and regulatory environment. We are subject to a variety of PRC laws, rules and regulations affecting many aspects of our business. This section summarizes the principal PRC laws, rules and regulations that we believe are relevant to our business and operations.

PRC Drug Regulation

Introduction

China heavily regulates the development, approval, manufacturing and distribution of drugs, including biologics. The specific regulatory requirements applicable depend on whether the drug is made and finished in China, which is referred to as a domestically manufactured drug, or made abroad and imported into China in finished form, which is referred to as an imported drug, as well as the approval or “registration” category of the drug. For both imported and domestically manufactured drugs, China typically requires regulatory approval for a clinical trial, or CTA, prior to submitting an application for marketing approval. For a domestically manufactured drug, there is also a requirement to have a drug manufacturing license for a facility in China.

In 2017, the drug regulatory system entered a new and significant period of reform. The State Council and the China Communist Party jointly issued the Opinion on Deepening the Reform of the Regulatory Approval System to Encourage Innovation in Drugs and Medical Devices, or the Innovation Opinion. The expedited programs and other advantages under this and other recent reforms encourage drug manufacturers to seek marketing approval in China first, manufacture domestically, and develop drugs in high priority disease areas, such as oncology.

To implement the regulatory reform introduced by the Innovation Opinion, the NMPA has been revising the fundamental laws, regulations and rules regulating pharmaceutical products and the industry, which include the framework law known as the PRC Drug Administration Law, or DAL. The DAL is also generally implemented by a set of regulations issued by the State Council referred to as the DAL Implementing Regulation. The NMPA has its own set of regulations implementing the DAL; the primary one governing clinical trial applications, marketing approval, and license renewal and amendment is known as the Drug Registration Regulation. Although the NMPA made progress in 2018 on different proposals, finalizing several guidelines and documents, as of January 2019 final implementing regulations for many of the reforms in the Innovation Opinion had not been announced, and therefore, the details regarding the implementation of the regulatory changes remained uncertain in some respects.

Regulatory Authorities and Recent Government Reorganization

In the PRC, the NMPA is the primary regulator for pharmaceutical products and businesses. The agency was newly formed from the prior China Food and Drug Administration, or CFDA, in 2018 as part of a complete government reorganization. NMPA is no longer an independent agency. Its parent agency is now the newly organized State Administration for Market Regulation (SAMR), into which agencies responsible for, among other areas, consumer protection, advertising, anticorruption, pricing, fair competition and intellectual property have been merged.

Like the CFDA, the NMPA is still the chief drug regulatory agency and implements the same laws, regulations, rules, and guidelines as the CFDA, and it regulates almost all of the key stages of the life-cycle of pharmaceutical products, including nonclinical studies, clinical trials, marketing approvals, manufacturing, advertising and promotion, distribution, and pharmacovigilance (i.e., post-marketing safety reporting obligations). The Center for Drug Evaluation, or CDE, which remains under the NMPA, conducts the technical evaluation of each drug and biologic application for safety and effectiveness.

The National Health Commission, or NHC, (formerly known by the names: the Ministry of Health (MOH) and National Health and Family Planning Commission (NHFPC)), is China’s chief healthcare regulator. It is primarily responsible for overseeing the operation of medical institutions, which also serve as clinical trial sites, and regulating the licensure of hospitals and other medical personnel. NHC plays a significant role in drug reimbursement. Furthermore, the NHC and its local counterparts at or below the provincial-level of local government also oversee and organize public medical institutions’ centralized bidding and procurement process for pharmaceutical products. This is the chief way that public hospitals and their internal pharmacies acquire drugs.

Also, as part of the 2018 reorganization, the PRC government formed a new State Medical Insurance Bureau which focuses on regulating reimbursement under the state-sponsored insurance plans.

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Preclinical and Clinical Development

The NMPA requires preclinical data to support registration applications for imported and domestic drugs. Preclinical work, including pharmacology and toxicology studies, must meet the GLP, issued in July 2017. The NMPA accredits GLP labs and requires that nonclinical studies on chemical drug substances and preparations and biologics that are not yet marketed in China be conducted there. There are no approvals required from the NMPA to conduct preclinical studies.

Registration Categories

Prior to engaging with the NMPA on research and development and approval, an applicant will need to determine the registration category for its drug candidate (which will ultimately need to be confirmed with the NMPA), which will determine the requirements for its clinical trial and marketing application. There are five categories for small molecule drugs: Category 1 (“innovative drugs”) refers to drugs that have a new chemical entity that has not been marketed anywhere in the world, Category 2 (“improved new drugs”) refers to drugs with a new indication, dosage form, route of administration, combination, or certain formulation changes not approved in the world, Categories 3 and 4 are for generics that reference an innovator drug (or certain well-known generic drugs) marketed either abroad or in China, respectively, and Category 5 refers to innovative or generic drugs that have already been marketed abroad but are not yet approved in China (i.e., many imported drugs).

Therapeutic biologics follow a similar categorization, with Category 1 being new to the world, but with fifteen product-specific categories. Like with small molecule drugs, Category 1 is for innovative biologics that have not been approved inside or outside of China. A clear regulatory pathway for biosimilars does not yet exist, but something was proposed in a draft revision to an NMPA regulation in 2017. Each of zanubrutinib, tislelizumab, pamiparib and lifirafenib is classified as Category 1 based on the respective clinical trial approval from the NMPA, which is a favored category for CTA and marketing approval.

Expedited Programs

Priority Evaluation and Approval Programs to Encourage Innovation

The NMPA has adopted several expedited review and approval mechanisms since 2009 and created additional expedited programs in recent years that are intended to encourage innovation. Applications for these expedited programs can be submitted after the CTA is admitted for review by the CDE. Some of the current categories of drugs eligible for priority status that may be particularly relevant for us include: (1) Category 1 innovative drugs that have not been approved inside or outside of China; (2) oncology drugs; (3) drugs using advanced technology, innovative treatment methods, and having clear therapeutic benefit; and (4) new drugs for which clinical trials are already approved in the United States or European Union, or for which marketing authorization applications have been filed simultaneously in China and in the United States or European Union and are manufactured in China using the same production line that passed FDA or EMA inspection.

If admitted to one of these expedited programs, an applicant will be entitled to more frequent and timely communication with reviewers at the CDE, expedited review and approval, and more agency resources throughout the approval process. Each of our drug candidates, zanubrutinib, tislelizumab, pamiparib and lifirafenib, is classified as Category 1 based on the respective clinical trial approval from the NMPA.

NMPA also permits conditional approval of certain medicines based on early phase data. Post-approval the applicant may need to conduct a post-market study. The agency has done this for drugs that meet unmet clinical needs for life-threatening illnesses and also for drugs that treat orphan indications. In 2018, NMPA established a conditional approval program for drugs designated by the CDE that have been approved in the US, EU and Japan within the last 10 years and that meet one of three criteria (1) orphan indications, (2) drugs that treat life threatening illnesses for which there are not effective treatment or preventive methods, and (3) drugs that treat life threatening illnesses and that have a clear clinical advantage over other clinical therapies.

CDE Guideline on PD-1/L1 NDA

In addition to the programs and proposals above, the CDE has recently stated that it will permit applicants for PD-1/L1 agents to submit data on a rolling basis based on the current high unmet medical need for PD-1/L1 agents. In February 2018, the CDE released the Guideline on the Basic Requirements of Information and Data for NDA Submissions of anti-PD-1/L1 Monoclonal Antibody Products on recurrent and refractory advanced cancers without

standard-of-care therapies. Under the guideline, the sponsor must have a pre-NDA meeting with the CDE regarding the data and the NDA submission. The CDE will permit the following submission for these applicants: (1) an initial NDA submission with full preliminary safety data and effectiveness data, including the results of at least two independent therapeutic efficacy assessments of all patients who are

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currently enrolled pursuant to all of the protocol's requirements; (2) during the CDE's substantive technical review of the NDA, submission on a rolling basis of follow-up safety and effectiveness data from at least six months from the time of the last enrolled patient showing the duration of the response; and (3) submission of all efficacy and safety data as provided for under the protocol before final approval is granted by the NMPA. Sponsors may also apply for priority review and approval for their NDA to accelerate the progress. If granted, priority status will be applied to various stages of the approval process, including testing, manufacturing site inspection, technical review, and clinical site inspection.

New Policies on Expediting Approval of Imported Oncology Drugs

The PRC government continues to establish measures and incentives to promote the development and swifter approval of marketing for oncology and other innovative drugs. Beginning in May 2018, the PRC eliminated tariffs on a significant number of imported innovative drugs, including oncology drugs, making the importation process more efficient. The PRC government has also stated that it will explore ways to expand access to reimbursement under the state health plans for innovative drugs (particularly for urgently needed oncology drugs).

Clinical Trials and Marketing Approval

Upon completion of preclinical studies, a sponsor typically needs to conduct clinical trials in China for registering a new drug. The materials required for this application and the data requirements are determined by the registration category. The NMPA has taken a number of steps to increase efficiency for approving CTAs, and it has also significantly increased monitoring and enforcement of GCP to ensure data integrity.

Trial Approval

All clinical trials conducted in China must be approved and conducted at hospitals accredited by the NMPA. For imported drugs, proof of foreign approval is required prior to the trial, unless the drug has never been approved anywhere in the world. In addition to a standalone China trial to support development, imported drug applicants may establish a site in China that is part of an international multicenter trial, or IMCT, at the outset of the global trial. Domestically manufactured drugs are not subject to foreign approval requirements, and in contrast to prior practice, the NMPA has recently decided to permit those drugs to conduct development via an IMCT as well.

In 2015, the NMPA began to issue an umbrella approval for all phases (typically three) of a new drug clinical trial, instead of issuing approval phase by phase. For certain types of new drug candidates, clinical trial applications may be prioritized over other applications, and put in a separate expedited queue for approval. Category 1 drugs are new drug trials which would qualify for this expedited umbrella approval status. Other trials that are not part of these expedited lines could still wait up to a year for approval to conduct the trial.

The NMPA has now also adopted a notification system for clinical trials of new drugs. Trials can proceed if after 60 business days, the applicant has not received any objections from the CDE, as opposed to the lengthier previous clinical trial pre-approval process in which the applicant had to wait for affirmative approval. China is also expanding the number of trial sites by truncating the timeline for accreditation by converting it from a pre-approval procedure into a notification procedure.

Human Genetic Resources Approval

According to the Interim Measures for the Administration of Human Genetic Resources, an additional approval is required for any foreign companies or foreign affiliates that conduct trials in China. Prior to entering into a clinical trial agreement and beginning a trial, the foreign sponsor and the Chinese clinical trial site are required to obtain human genetic resources, or HGR, approval to collect any biological samples that contain the genetic material of Chinese human subjects from the Ministry of Science and Technology, and any cross-border transfer of the samples or associated data requires additional approval. Furthermore, one of the key review points for the HGR review and approval process is the IP sharing arrangement between Chinese and foreign parties. The parties are required to share patent rights to inventions arising from the samples. Conducting a clinical trial in China without obtaining the relevant HGR preapproval will subject the sponsor and trial site to administrative liability, including confiscation of HGR samples and associated data, and administrative fines.

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Trial Exemptions and Acceptance of Foreign Data

The NMPA may reduce requirements for trials and data, depending on the drug and the existing data. The NMPA has granted waivers for all or part of trials, and has stated that it will accept data generated abroad (even if not part of a global study), including early phase data, that meets its requirements. On July 6, 2018, the NMPA issued the Technical Guidance Principles on Accepting Foreign Drug Clinical Trial Data, or the Guidance Principles, as one of the implementing rules for the Innovation Opinion. According to the Guidance Principles, the data of foreign clinical trials must meet the authenticity, completeness and accuracy requirements and such data must be obtained consistent with the relevant requirements under the Good Clinical Trial Practice (GCP) of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). Sponsors must be attentive to potentially meaningful ethnic differences in the subject population.

The NMPA now officially permits, and its predecessor agencies have permitted on a case-by-case basis in the past, drugs approved outside of China to be approved in China on a conditional basis without the need for pre-approval clinical trials inside China. Specifically, in 2018, the NMPA established a program permitting drugs that have been approved within the last ten years in the United States, EU or Japan and that i) prevent or treat orphan diseases, ii) prevent or treat serious life-threatening illnesses for which there is either no effective therapy in China, or for which the foreign-approved drug would have clear clinical advantages. Applicants will be required to establish a risk mitigation plan and may be required to complete trials in China after the drug is marketed. The CDE has developed a list of qualifying drugs that meet this criteria.

Clinical Trial Process and Good Clinical Practices

Typically drug clinical trials in China have three phases. Phase 1 refers to the initial clinical pharmacology and human safety evaluation studies. Phase 2 refers to the preliminary evaluation of a drug candidate's therapeutic efficacy and safety for target indication(s) in patients. Phase 3 (often the pivotal study) refers to clinical trials to further verify the drug candidate's therapeutic efficacy and safety on patients with target indication(s) and ultimately provide sufficient evidence for the review of a drug registration application. The NMPA requires that the different phases of clinical trials in China receive ethics committee approval prior to approval of the CTA and comply with GCP. The NMPA conducts inspections to assess GCP compliance and will cancel the CTA if it finds substantial issues.

Generic small molecule drugs are required to conduct a bioequivalence trial, in vitro studies or in some cases a clinical trial to demonstrate therapeutic equivalence to an innovator drug marketed either in China or abroad or an internationally accepted generic drug. The NMPA has released catalogues of reference products, and it released a first installment of a Marketed Drug List (China's "Orange Book") with information about drugs that may serve as reference products.

New Drug Application (NDA) and Approval

Upon completion of clinical trials, a sponsor may submit clinical trial data to support marketing approval for the drug. For imported drugs, this means issuance of an import license. Again, the applicant must submit evidence of foreign approval, unless it is an innovative drug that has never been approved anywhere in the world.

NDA sponsors must submit data derived from domestically manufactured drugs in support of a drug approval. Under the current regime, upon approval of the registration application, the NMPA will first issue a new drug certificate to the applicant. Only when the applicant is equipped with relevant manufacturing capability will the NMPA issue a Drug Approval Serial Number, which is effectively the marketing approval allowing the holder to market/commercialize the drug in China.

China has recently implemented a Drug Marketing Authorization Holder Mechanism. The MAH pilot program permits research institutions and individual entities to develop and hold the marketing approvals for drugs without holding a drug manufacturing license. Domestically established research institutions (including domestic companies) can apply through an MAH pilot program if they are established in one of 10 designated provinces (including Beijing and Shanghai), which is now being expanded nationwide in China. The MAHs may engage contract manufacturers and distributors.

The MAH program was originally set up as a pilot program until November 2018. China has now that stated it will expand the program nationwide and make it permanent. Implementing legislation has been proposed, and the MAH pilot has been renewed for one more year until November 2019 in the interim. The Innovation Opinion indicates that

China will strive to implement the MAH system nationally as soon as possible by amending the DAL. The NMPA has proposed revisions to accomplish this purpose, but the timeline to finalize these proposals is still unclear.

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Manufacturing and Distribution

According to the DAL, all facilities that make drugs in China must receive a drug manufacturing license with an appropriate "scope of manufacturing" from the local drug regulatory authority. This license must be renewed every five years. A separate certification of compliance with GMP is also required.

Similarly, to conduct sales, importation, shipping and storage ("distribution activities") a company must obtain a Drug Distribution License from the local drug regulatory authority, subject to renewal every five years. Like with GMPs, a separate certification of compliance with NMPA's drug good supply practice, or GSP, is required.

China has formed a "Two Invoice System" to control distribution of prescription drugs. The "Two-Invoice System" generally requires that no more than two invoices may be issued throughout the distribution chain, with one from the manufacturer to a distributor and another from the distributor to the end-user hospital. This excludes the sale of products invoiced from the manufacturer to its wholly owned or controlled distributors, or for imported drugs, to their exclusive distributor, or from a distributor to its wholly owned or controlled subsidiary (or between the wholly owned or controlled subsidiaries). However, the system still significantly limits the options for companies to use multiple distributors to reach a larger geographic area in China. Compliance with the Two-Invoice System will become a prerequisite for pharmaceutical companies to participate in procurement processes with public hospitals, which currently provide most of China's healthcare. Manufacturers and distributors that fail to implement the Two-Invoice System may lose their qualifications to participate in the bidding process. Non-compliant manufacturers may also be blacklisted from engaging in drug sales to public hospitals in a locality.

The Two-Invoice System was first implemented in 11 provinces that are involved in pilot comprehensive medical reforms, but the program has expanded to nearly all provinces, which have their own individual rules for the program.

Post-Marketing Surveillance

The manufacturer or marketing authorization holder of a drug is primarily responsible for pharmacovigilance, including quality assurance, adverse reaction reporting and monitoring, and product recalls. Distributors and user entities (e.g., hospitals) are also required to report, in their respective roles, adverse reactions of the products they sell or use, and assist with the manufacturer of the product recall. A drug that is currently under the new drug monitoring period has to report all adverse drug reactions (as opposed to just serious adverse reactions) for that period.

Advertising and Promotion of Pharmaceutical Products

China has a strict regime for the advertising of approved medicines. No unapproved medicines may be advertised. The definition of an advertisement is very broad, and does not exclude scientific exchange. It can be any media that directly or indirectly introduces the product to end users. There is no clear line between advertising and any other type of promotion.

An enterprise seeking to advertise a prescription drug may do so only in medical journals jointly approved by NMPA and the NHC, and each advertisement requires approval from a local drug regulatory authority. The content of an approved advertisement may not be altered without filing a new application for approval.

Prescription drug advertisements are subject to strict content restrictions, which prohibit recommendations by doctors and hospitals and guarantees of effectiveness. Advertising that includes content that is outside of the drug's approval documentation ("off-label content") is prohibited. False advertising can result in civil suits from end users and administrative liability, including fines. In addition to advertisements, non-promotional websites that convey information about a drug must go through a separate approval process by a local drug regulatory authority.

Regulatory Intellectual Property Protections

Non-patent exclusivities

New Drug Monitoring Period

Currently, new varieties of domestically produced drugs approved under Categories 1 or 2 in China may be placed under a monitoring period for three to five years. Category 1 innovative drugs will be monitored for five years. During the monitoring period, the NMPA will not approve another CTA from another applicant for the same type of drug, except if another sponsor

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has an approved CTA at the time that the monitoring period is initiated it may proceed with its trial and once approved become another drug that is part of the monitoring period.

Regulatory Data Protection

The Innovation Opinion also lays the foundation for the establishment of a system for regulatory data protection to protect innovators. This protection will be available to the undisclosed clinical trial data of drugs falling into the following categories: innovative drugs, innovative therapeutic biologics, drugs that treat orphan diseases, pediatric drugs, and drugs for which there has been a successful patent challenge.

NMPA published a draft on Implementing Regulations for Pharmaceutical Study Data Protection for public comment that would set regulatory data protection for innovative small molecule drugs at six years and for innovative therapeutic biologics at 12 years; pediatric and orphan drugs would receive six years to run concurrently from their approval dates. Full terms of protection would require reliance on local trials or sites of multi-center trials in China and simultaneous submissions of marketing applications in China and other countries. Submissions in China that are up to six years later than those abroad would result in the term being reduced to 1-5 years. Submissions over six years later in China may not receive protection.

There is also a reduction if the marketing application is filed in China based solely on overseas clinical data with no Chinese subjects (75% reduction) or based on supplemental “China clinical trial data” (50% reduction). Information about the exclusivity term will be included in a Marketed Drug List (similar to the Orange Book in the US) at the time of approval. Some mechanics of these proposed rules are not yet clear, and it is not certain when the proposed rules will be finalized.

Patent-Related Protections

Patent Linkage

The Innovation Opinion also sets forth the basic elements of a patent linkage system to protect innovators, in which a follow-on applicant will be required to specify patents that are relevant to its application and notify relevant patent holders (including, innovators) within a specified period after filing its application, permitting them to sue to protect their rights. The system will require that the NMPA continue to review the potentially infringing follow-on application during any lawsuit by the innovator. However, the NMPA may not approve the follow-on application pending resolution of the patent litigation in favor of the follow-on application or for a specified period of time, whichever is shorter. This reform will require implementing regulations. To date, the NMPA has not issued the relevant implementing regulations.

Patent Term Extension

In early 2019, pursuant to the Innovation Opinion, the National People’s Congress issued a proposal for patent term extension as part of a proposed amendment to the Patent Law. Under this proposal, the State Council may grant a patent term extension of up to five years to compensate for delays in the review process for innovative drugs that are applying simultaneously for marketing approval in both China and abroad. The patent term may not be extended to more than 14 years post-marketing. It is not clear when this will be finalized.

Reimbursement and Pricing

China’s national medical insurance program was adopted pursuant to the Decision of the State Council on the Establishment of the Urban Employee Basic Medical Insurance Program issued by the State Council in 1998, under which all employers in urban cities are required to enroll their employees in the basic medical insurance program. The insurance premium is jointly contributed by the employers and employees. In 2007, the State Council promulgated Guiding Opinions of the State Council about the Pilot Urban Resident Basic Medical Insurance , under which urban residents of the pilot district, rather than urban employees, may voluntarily join Urban Resident Basic Medical Insurance. Participants of the national medical insurance program and their employers, if any, are required to contribute to the payment of insurance premiums on a monthly basis. Program participants are eligible for full or partial reimbursement of the cost of medicines included in the National Reimbursement Drug List, or NRDL. A pharmaceutical product listed in the NRDL must be clinically needed, safe, effective, reasonably priced, easy to use, and available in sufficient quantity.

Factors that affect the inclusion of a pharmaceutical product in the NRDL include whether the product is consumed in large volumes and commonly prescribed for clinical use in the PRC and whether it is considered to be important in

meeting the basic healthcare needs of the general public. Since 2016, special consideration has been given to, among others, innovative drugs with high clinical value and drugs for serious diseases. In addition, the PRC Ministry of Human Resources and Social Security

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has also been negotiating with manufacturers of expensive drugs with high clinical demands and proven effectiveness for price cuts in exchange for inclusion into the NRDL. The version of the NRDL released in 2017 covers 2,535 drugs in total, including 339 new additions, with an emphasis on innovative drugs and drugs that treat cancer and other serious diseases. China has been pursuing a policy of expediting the addition of innovative oncology drugs to this list. In 2018, 17 more oncology drugs were added into the NRDL by the State Medical Insurance Bureau.

Government price controls

The Chinese government has abolished the 15-year-old government-led pricing system for drugs, and lifted the maximum retail price for most drugs, including drugs reimbursed by government medical insurance funds, patented drugs, and some other drugs. The government regulates prices mainly by establishing a consolidated procurement mechanism, restructuring medical insurance reimbursement standards and strengthening regulation of medical and pricing practices as discussed below.

Centralized procurement and tenders

Under current regulations, public medical institutions owned by the government or owned by state-owned or controlled enterprises are required to purchase pharmaceutical products through centralized online procurement processes. There are exceptions for drugs on the National List of Essential Drugs, which must comply with their own procurement rules, and for certain drugs subject to the central government's special control such as toxic, radioactive and narcotic drugs, and traditional Chinese medicines.

The centralized procurement process takes the form of public tenders operated by provincial or municipal-level government agencies. The centralized tender process is typically conducted once every year. The bids are assessed by a committee randomly selected from a database of experts. The committee members assess the bids based on a number of factors, including but not limited to bid price, product quality, clinical effectiveness, product safety, level of technology, qualifications and reputation of the manufacturer, after-sale services and innovation.

Over the last decade, the government has been using various methods to ensure that drugs are offered at affordable prices. In 2009, the central government announced a campaign to implement a "zero markup" policy on essential drugs among basic healthcare institutions, which has been fully implemented nationwide. In addition, some local government have begun to allow medical institutions to collectively negotiate with manufacturers for a second price to further lower the already agreed bid price. The newly adopted Two-Invoice System is also aimed to reduce price mark-ups brought about by multi-tier distribution chains.

Other PRC national- and provincial-level laws and regulations

We are subject to changing regulations under many other laws and regulations administered by governmental authorities at the national, provincial and municipal levels, some of which are or may become applicable to our business. For example, regulations control the confidentiality of patients' medical information and the circumstances under which patient medical information may be released for inclusion in our databases or released by us to third parties. The privacy of human subjects in clinical trials is also protected under regulations. For example, the case report forms must avoid disclosing names of the human subjects.

These laws and regulations governing both the disclosure and the use of confidential patient medical information may become more restrictive in the future, including restrictions on transfer of healthcare data. The Cybersecurity Law that took effect in 2017 designates healthcare as a priority area that is part of critical information infrastructure, and China's cyberspace administration is working to finalize a draft rule on cross-border transfer of personal information.

PRC Regulation of Foreign Investment

Investment activities in China by foreign investors are principally governed by the Guidance Catalogue of Industries for Foreign Investment, or the Catalogue, which was promulgated and is amended from time to time by the MOFCOM and the National Development and Reform Commission. Pursuant to the latest Catalogue which came into effect in July 2017 with the latest amendment being effective as of July 2018, or the 2017 Catalogue, industries are divided into two categories: encouraged industries and the industries within the catalogue of special management measures, or the Negative List. The Negative List is further divided into two sub-categories: restricted industries and prohibited industries. Establishment of wholly foreign-owned enterprises is generally allowed in industries outside of the Negative List. For the restricted industries within the Negative List, some are limited to equity or contractual joint ventures, while in some cases Chinese partners are required to hold the majority interests in such joint ventures. In

addition, restricted category projects are subject to government approvals and certain special

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requirements. Foreign investors are not allowed to invest in industries in the prohibited category. Industries not listed in the Catalogue are generally open to foreign investment unless specifically restricted by other PRC regulations. Pursuant to the 2017 Catalogue, the manufacture of innovative oncology drugs and certain other kinds of pharmaceutical products falls in the encouraged industries for foreign investment.

Regulations Relating to Foreign Exchange

The Foreign Exchange Administration Regulations are the principal regulations governing foreign currency exchange in China. Under the PRC foreign exchange regulations, payments of current account items, such as profit distributions and trade and service-related foreign exchange transactions, may be made in foreign currencies without prior approval from the State Administration of Foreign Exchange, or SAFE, by complying with certain procedural requirements. In contrast, approval from or registration with appropriate government authorities or designated banks is required when RMB is to be converted into a foreign currency and remitted out of China to pay capital expenses such as the repayment of foreign currency-denominated loans.

Under current regulations, the capital of a foreign-invested enterprise and capital in RMB obtained by the foreign-invested enterprise from foreign exchange settlement must not be used for the following purposes: directly or indirectly used for the payment beyond the business scope of the enterprises or the payment prohibited by relevant laws and regulations; directly or indirectly used for investment in securities, unless otherwise provided by relevant laws and regulations; extending loans to non-related parties, unless permitted by the scope of business; and/or paying the expenses related to the purchase of real estate that is not for self-use, except for the real estate enterprises.

In 2017, new regulations were adopted which, among other things, relax the policy restriction on foreign exchange inflow to further enhance trade and investment facilitation and tighten genuineness and compliance verification of cross-border transactions and cross-border capital flows.

Regulations Relating to Dividend Distributions

The principal laws, rules and regulations governing dividend distributions by foreign-invested enterprises in the PRC are the PRC Company Law, as amended, the Wholly Foreign-owned Enterprise Law and its implementating regulations, and the Sino-foreign Joint Venture Law and its implementing regulations. Under these requirements, foreign-invested enterprises may pay dividends only out of their accumulated profit, if any, as determined in accordance with PRC accounting standards and regulations. Both PRC domestic companies and wholly-foreign owned PRC enterprises are required to allocate at least 10% of their respective accumulated after-tax profits each year, if any, to fund certain capital reserve funds until the aggregate amount of these reserve funds have reached 50% of the registered capital of the enterprises. A PRC company is not permitted to distribute any profits until any losses from prior fiscal years have been offset. Profits retained from prior fiscal years may be distributed together with distributable profits from the current fiscal year.

Labor Laws and Social Insurance

Pursuant to the PRC Labor Law and the PRC Labor Contract Law, employers must execute written labor contracts with full-time employees. All employers must comply with local minimum wage standards. Employers must establish a comprehensive management system to protect the rights of their employees, including a system governing occupational health and safety to provide employees with occupational training to prevent occupational injury, and employers are required to truthfully inform prospective employees of the job description, working conditions, location, occupational hazards and status of safe production as well as remuneration and other conditions. Violations of the PRC Labor Contract Law and the PRC Labor Law may result in the imposition of fines and other administrative and criminal liability in the case of serious violations.

In addition, according to the PRC Social Insurance Law, employers like our PRC subsidiaries in China must provide employees with welfare schemes covering pension insurance, unemployment insurance, maternity insurance, work-related injury insurance, medical insurance and housing funds.

Rest of World Regulation

For other countries outside of the United States and the PRC, 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 having their origin in the Declaration of Helsinki.

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Employees

As of January 31, 2019, we had approximately 2,200 employees. We have also engaged and may continue to engage independent contractors to assist us with our operations. None of our employees are represented by a labor union or covered by a collective bargaining agreement. We have never experienced any employment-related work stoppages, and we consider our relations with our employees to be good.

Financial Information

The financial information required under this Item 1 is incorporated herein by reference to the section of this Annual Report titled “Part II-Item 8-Financial Statements and Supplementary Data.” For financial information regarding our business, see “Part II-Item 7-Management’s Discussion and Analysis of Financial Condition and Results of Operations” of this Annual Report and our consolidated audited financial statements and related notes included elsewhere in this Annual Report.

Corporate Information

We are an exempted company incorporated in the Cayman Islands with limited liability on October 28, 2010. Any company that is registered in the Cayman Islands but conducts business mainly outside of the Cayman Islands may apply to be registered as an exempted company. The principal executive office of our research and development operations is located at No. 30 Science Park Road, Zhong-Guan-Cun Life Science Park, Changping District, Beijing 102206, People’s Republic of China. Our telephone number at this address is +86 10 58958000. Our current registered office in the Cayman Islands is located at the offices of Mourant Governance Services (Cayman) Limited, 94 Solaris Avenue, Camana Bay, Grand Cayman KY1-1108, Cayman Islands. Our website address is www.beigene.com. We do not incorporate the information on or accessible through our website into this Annual Report, and you should not consider any information on, or that can be accessed through, our website as part of this Annual Report.

We own various applications and unregistered trademarks and servicemarks, including the name "BeiGene", and our corporate logo. All other trade names, trademarks and service marks of other companies appearing in this Annual Report are the property of their respective holders. Solely for convenience, some of the trademarks and trade names in this document are referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. We do not intend our use or display of other companies’ trademarks and trade names to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

Available Information

We make available on or through our website certain reports and amendments to those reports that we file with or furnish to the U.S. Securities and Exchange Commission, or SEC, in accordance with the Securities Exchange Act of 1934, as amended, or the Exchange Act. These include our annual reports on Form 10-K, our quarterly reports on Form 10-Q, and our current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act. We also make available, free of charge on our website, the reports filed with the SEC by our executive officers, directors and 10% shareholders pursuant to Section 16 under the Exchange Act. Additionally, we make available on our website our Hong Kong securities filings. We make this information available on or through our website free of charge as soon as reasonably practicable after we electronically file the information with, or furnish it to, the SEC and the Hong Kong Exchanges and Clearing Limited. We use our website as a means of disclosing material non-public information and for complying with our disclosure obligations under Regulation FD.

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Item 1A. Risk Factors

The following section includes the most significant factors that we believe may adversely affect our business and operations. You should carefully consider the risks and uncertainties described below and all information contained in this Annual Report, including our financial statements and the related notes and "Part II-Item 7-Management's Discussion and Analysis of Financial Condition and Results of Operations," before deciding to invest in our ADSs or ordinary shares. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and growth prospects. In such an event, the market price of our ADSs and ordinary shares could decline, and you may lose all or part of your investment. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations.

Risks Related to Clinical Development and Regulatory Approval of Our Drug Candidates

We depend substantially on the success of our drug candidates, which are in clinical development. If we are unable to successfully complete clinical development, obtain regulatory approval and commercialize our drug candidates, or experience significant delays in doing so, our business will be materially harmed.

Our business will depend on the successful development, regulatory approval and commercialization of our drug candidates for the treatment of patients with cancer, which are still in clinical development, and other drug candidates we may develop. We have invested a significant portion of our efforts and financial resources in the development of our existing drug candidates. The success of our drug candidates will depend on several factors, including:

- successful enrollment in, and completion of, clinical trials, as well as completion of preclinical studies;
- favorable safety and efficacy data from our clinical trials and other studies;
- receipt of regulatory approvals;
- establishing commercial manufacturing capabilities, either by building facilities ourselves or making arrangements with third-party manufacturers;
- the performance by contract research organizations, or CROs, or other third parties we may retain of their duties to us in a manner that complies with our protocols and applicable laws and that protects the integrity of the resulting data;
- obtaining and maintaining patent, trade secret and other intellectual property protection and regulatory exclusivity;
- ensuring we do not infringe, misappropriate or otherwise violate the patent, trade secret or other intellectual property rights of third parties;
- successfully launching our drug candidates, if and when approved;
- obtaining favorable reimbursement from third-party payors for drugs, if and when approved;
- competition with other products;
- continued acceptable safety profile following regulatory approval; and
- manufacturing or obtaining sufficient supplies of our drugs, drug candidates and any competitor drug products that may be necessary for use in clinical trials for evaluation of our drug candidates and commercialization of our drugs.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays in our ability or be unable to obtain approval for and/or to successfully commercialize our drugs and drug candidates, which would materially harm our business and we may not be able to generate sufficient revenues and cash flows to continue our operations.

If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the trial until its conclusion. We may experience difficulties in patient

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enrollment in our clinical trials for a variety of reasons, including the size and nature of the patient population and the patient eligibility criteria defined in the protocol.

Our clinical trials will likely compete with other clinical trials for drug candidates that are in the same therapeutic areas as our drug candidates, and this competition will reduce the number and types of patients available to us, because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. Because the number of qualified clinical investigators and clinical trial sites is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials at such clinical trial sites. Even if we are able to enroll a sufficient number of patients in our clinical trials, delays in patient enrollment may result in increased costs or may affect the timing or outcome of the planned clinical trials, which could prevent completion of these trials and adversely affect our ability to advance the development of our drug candidates.

Clinical drug development involves a lengthy and expensive process with an uncertain outcome, and results of earlier studies and trials may not be predictive of future trial results.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. 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, and initial or interim results of a trial may not be predictive of the final results. Drug candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical trials. In some instances, there can be significant variability in safety and/or efficacy results between different trials of the same drug candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, including genetic differences, patient adherence to the dosing regimen and other trial protocol elements and the rate of dropout among clinical trial participants. In the case of any trials we conduct, results may differ from earlier trials due to the larger number of clinical trial sites and additional countries and languages involved in such trials. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. Our future clinical trial results may not be favorable.

Even if our future clinical trial results show favorable efficacy and impressive durability of antitumor responses, not all patients may benefit. For certain drugs, including checkpoint inhibitors, and in certain indications, it is likely that the majority of patients may not respond to the agents at all, some responders may relapse after a period of response and certain tumor types may appear particularly resistant.

If clinical trials of our drug candidates fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our drug candidates.

Before obtaining regulatory approval for the sale of our drug candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of our drug candidates in humans. We may experience numerous unexpected events during, or as a result of, clinical trials that could delay or prevent our ability to receive regulatory approval or commercialize our drug candidates, including but not limited to: regulators, institutional review boards, or IRBs, or ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site; our inability to reach agreements on acceptable terms with prospective CROs and trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites; manufacturing issues, including problems with manufacturing, supply quality, compliance with China's drug Good Manufacturing Practice, current good manufacturing practice, or GMP, or obtaining from third parties sufficient quantities of a drug candidate for use in a clinical trial or for commercialization; clinical trials of our drug candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon drug development programs; the number of patients required for clinical trials of our drug candidates may be larger than we anticipate, enrollment may be insufficient or slower than we anticipate or patients may drop out at a higher rate than we anticipate; our third-party contractors, including clinical investigators, may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all; we might have to suspend or terminate clinical trials of our drug candidates for various reasons, including a finding of a

lack of clinical response or other unexpected characteristics or a finding that participants are being exposed to unacceptable health risks; regulators, IRBs or ethics committees may require that we or our investigators suspend or terminate clinical research or not rely on the results of clinical research for various reasons, including noncompliance with regulatory requirements; the cost of clinical trials of our drug candidates may be greater than we anticipate; and the supply or quality of our drugs and drug candidates, companion diagnostics or other materials necessary to conduct clinical trials of our drug candidates or commercialization of our drugs may be insufficient or inadequate.

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If we are required to conduct additional clinical trials or other testing of our drug candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our drug candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if they raise safety concerns, we may:

- be delayed in obtaining regulatory approval for our drug candidates;
- not obtain regulatory approval at all;
- obtain approval for indications that are not as broad as intended;
- have the drug removed from the market after obtaining regulatory approval;
- be subject to additional post-marketing testing requirements;
- be subject to warning labels or restrictions on how the drug is distributed or used; or
- be unable to obtain reimbursement for use of the drug.

Significant clinical trial or regulatory delays may also increase our development costs and could shorten any periods during which we have the exclusive right to commercialize our drug candidates or allow our competitors to bring drugs to market before we do. This could impair our ability to commercialize our drug candidates and may harm our business and results of operations.

Risks Related to Extensive Government Regulation

All material aspects of the research, development, manufacturing and commercialization of pharmaceutical products are heavily regulated.

All jurisdictions in which we intend to conduct our pharmaceutical-industry activities regulate these activities in great depth and detail. We initially intend to focus our activities in the major markets of the United States, China and other Asian countries, and the European Union. These geopolitical areas all strictly regulate the pharmaceutical industry, and in doing so they employ broadly similar regulatory strategies, including regulation of product development and approval, manufacturing, and marketing, sales and distribution of products. However, there are differences in the regulatory regimes-some minor, some significant-that make for a more complex and costly regulatory compliance burden for a company like ours that plans to operate in each of these regions.

The process of obtaining regulatory approvals and compliance with appropriate laws and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable 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 a regulator’s refusal to approve pending applications, withdrawal of an approval, license revocation, a clinical hold, voluntary or mandatory product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties. The failure to comply with these regulations could have a material adverse effect on our business. For example, although we received a Breakthrough Therapy designation for zanubrutinib for the treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy in January 2019, the FDA may later decide that such drug candidate no longer meets the conditions for qualification and may rescind 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 drugs considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA.

The regulatory approval processes of the regulatory authorities in the United States, China, Europe and other comparable regulatory authorities are lengthy, time consuming and inherently unpredictable. If we are ultimately unable to obtain regulatory approval for our drug candidates, our business will be substantially harmed.

The time required to obtain approval by the U.S. Food and Drug Administration, or FDA, the National Medical Products Administration of China, or NMPA (formerly known as the China Food and Drug Administration or China Drug Administration), the European Medicines Agency, or EMA, and other comparable regulatory authorities is unpredictable and typically takes many years following the commencement of preclinical studies and clinical trials and depends on numerous factors, including the substantial discretion of the regulatory authorities.

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

- failure to begin or complete clinical trials due to disagreements with regulatory authorities;
- failure to demonstrate that a drug candidate is safe and effective or that a biologic candidate is safe, pure, and potent for its proposed indication;
- failure of clinical trial results to meet the level of statistical significance required for approval;
- reporting or data integrity issues related to our clinical trials;
- disagreement with our interpretation of data from preclinical studies or clinical trials;
- changes in approval policies or regulations that render our preclinical and clinical data insufficient for approval or require us to amend our clinical trial protocols;
- regulatory requests for additional analyses, reports, data, nonclinical studies and clinical trials, or questions regarding interpretations of data and results and the emergence of new information regarding our drug candidates or other products;
- failure to satisfy regulatory conditions regarding endpoints, patient population, available therapies and other requirements for our clinical trials in order to support marketing approval on an accelerated basis or at all;
- our failure to conduct a clinical trial in accordance with regulatory requirements or our clinical trial protocols; and
- clinical sites, investigators or other participants in our clinical trials deviating from a trial protocol, failing to conduct the trial in accordance with regulatory requirements, or dropping out of a trial.

The FDA, NMPA, EMA or a comparable regulatory authority may require more information, including additional preclinical, chemistry, manufacturing and controls, or CMC, and/or clinical data, to support approval, which may delay or prevent approval and our commercialization plans, or we may decide to abandon the development program. Changes in regulatory requirements and guidance may also occur, and we may need to amend clinical trial protocols submitted to applicable regulatory authorities to reflect these changes. Amendments may require us to resubmit clinical trial protocols to IRBs or ethics committees for re-examination, which may impact the costs, timing or successful completion of a clinical trial.

If we experience delays in the completion of, or the termination of, a clinical trial of any of our drug candidates, the commercial prospects of that drug candidate will be harmed, and our ability to generate product sales revenues from any of those drug candidates will be delayed. In addition, any delays in completing our clinical trials will increase our costs, slow down our drug candidate development and approval process, and jeopardize our ability to commence product sales and generate related revenues for that candidate. Any of these occurrences may harm our business, financial condition and prospects significantly. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our drug candidates.

Our development activities also could be harmed or delayed by a shutdown of the U.S. government, including the FDA.

We believe that our drug candidates' designation in China as Category 1 products should confer certain regulatory advantages on us. These advantages may not result in commercial benefits to us as we expect, and they might be changed in the future in a manner adverse to us.

In China, prior to seeking approval from the NMPA, a pharmaceutical company needs to determine the drug's registration category, which will determine the requirements for its clinical trial and marketing application. These categories range from Category 1, for drugs incorporating a new chemical entity that has not previously been marketed anywhere in the world, to Category 2, for drugs with new indications, dosage forms or routes of administration and the like, to Categories 3 and 4, for certain generic drugs, to Category 5, for "originator" (what would be known elsewhere as innovative) or generic drugs previously marketed abroad but not yet approved for marketing in China. Therapeutic biologics follow a similar classification system. All of our internally developed drug candidates are classified as Category 1 based on the respective clinical trial approval from the NMPA, which is a favored category for regulatory review and approval.

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The NMPA has adopted several mechanisms for expedited review and approval for drug candidates that apply to Category 1 drug candidates. While we believe that the Category 1 designation of our internally developed clinical stage drug candidates should provide us with a significant regulatory, and therefore commercial, advantage over non-Chinese companies seeking to market products in China, we cannot be sure that this will be the case. The pharmaceutical regulatory environment is evolving quickly, and changes in laws, regulations, enforcement and internal policies could result in the "favored" status of Category 1 products changing, or being eliminated altogether or our products classification in Category 1 changing. We cannot be certain that the advantages we believe will be conferred by our Category 1 classifications will be realized or result in any material development or commercial advantage.

The absence of patent-linkage, patent-term extension and data and market exclusivity for NMPA-approved pharmaceutical products could increase the risk of early generic competition with our products in China.

In the United States, the Federal Food, Drug, and Cosmetic Act, as amended by the law generally referred to as the "Hatch-Waxman Amendments," provides the opportunity for patent-term restoration of up to five years to reflect patent term lost during certain portions of product development and the FDA regulatory review process. The Hatch-Waxman Amendments also have a process for patent linkage, pursuant to which FDA will stay approval of certain follow-on applications during the pendency of litigation between the follow-on applicant and the patent holder or licensee, generally for a period of 30 months. Finally, the Hatch-Waxman Amendments provide for statutory exclusivities that can prevent submission or approval of certain follow-on marketing applications. For example, federal law provides a five-year period of exclusivity within the United States to the first applicant to obtain approval of a new chemical entity (as defined) and three years of exclusivity protecting certain innovations to previously approved active ingredients where the applicant was required to conduct new clinical investigations to obtain approval for the modification. Similarly, the Orphan Drug Act provides seven years of market exclusivity for certain drugs to treat rare diseases, where FDA designates the drug candidate as an orphan drug and the drug is approved for the designated orphan indication. These provisions, designed to promote innovation, can prevent competing products from entering the market for a certain period of time after FDA grants marketing approval for the innovative product.

In China, however, there is no currently effective law or regulation providing patent term extension, patent linkage, or data exclusivity (referred to as regulatory data protection). Therefore, a lower-cost generic drug can emerge onto the market much more quickly. Chinese regulators have set forth a framework for integrating patent linkage and data exclusivity into the Chinese regulatory regime, as well as for establishing a pilot program for patent term extension. To be implemented, this framework will require adoption of regulations. To date, the NMPA has issued several draft implementing regulations in this regard for public comment but no regulations have been formally issued. These factors result in weaker protection for us against generic competition in China than could be available to us in the United States until the relevant implementing regulations for extension, patent linkage, or data exclusivity are put into effect officially in China.

Chinese manufacturing facilities have historically experienced issues operating in line with established cGMPs and international best practices, and passing FDA and NMPA inspections, which may result in a longer and costlier current good manufacturing practice inspection and approval process by the FDA or NMPA for our Chinese manufacturing processes and third party contract manufacturers.

To obtain FDA and NMPA approval for our products in the United States and China, respectively, we will need to undergo strict pre approval inspections of our manufacturing facilities, which we have located in China, or the manufacturing facilities of our contract manufacturers located in China and elsewhere. Historically, some manufacturing facilities in China have had difficulty meeting the FDA's or NMPA's standards. When inspecting our or our contractors' Chinese manufacturing facilities, the FDA or NMPA might cite cGMP deficiencies, both minor and significant, which we may not be required to disclose. Remediating deficiencies can be laborious and costly and consume significant periods of time. Moreover, if the FDA or NMPA notes deficiencies as a result of its inspection, it will generally reinspect the facility to determine if the deficiency was remediated to its satisfaction. The FDA or NMPA may note further deficiencies as a result of its reinspection, either related to the previously identified deficiency or otherwise. If we cannot satisfy the FDA and NMPA as to our compliance with cGMP in a timely basis, FDA or NMPA marketing approval for our products could be seriously delayed, which in turn would delay

commercialization of our drug candidates.

Undesirable adverse events caused by our drugs and drug candidates could interrupt, delay or halt clinical trials, delay or prevent regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following any regulatory approval.

Undesirable adverse events, or AEs, caused by our drugs and drug candidates 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, NMPA, EMA or other comparable regulatory authorities, or could result in limitations or withdrawal following

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approvals. If the conduct or results of our trials or patient experience following approval reveal a high and unacceptable severity or prevalence of AEs, our trials could be suspended or terminated and the FDA, NMPA, EMA or other comparable regulatory authorities could order us to cease further development of, or deny approval of, our drug candidates or require us to cease commercialization following approval.

Numerous drug-related AEs and serious AEs, or SAEs, have been reported in our clinical trials. Some of these events have led to patient death. Drug-related AEs or SAEs could affect patient recruitment or the ability of enrolled subjects to complete the trial, and could result in product liability claims. Any of these occurrences may harm our reputation, business, financial condition and prospects significantly. In our periodic and current reports filed with the SEC and our press releases and scientific and medical presentations released from time to time we disclose clinical results for our drug candidates, including the occurrence of AEs and SAEs. Each such disclosure speaks only as of the date of the data cutoff used in such report, and we undertake no duty to update such information unless required by applicable law. Also, a number of immune-related adverse events, or IRAEs, have been associated with treatment with checkpoint inhibitors such as our investigational PD-1 inhibitor tislelizumab, including immune-mediated pneumonitis, colitis, hepatitis, endocrinopathies, nephritis and renal dysfunction, skin adverse reactions, and encephalitis. These IRAEs may be more common in certain patient populations (potentially including elderly patients) and may be exacerbated when checkpoint inhibitors are combined with other therapies.

Additionally, undesirable side effects caused by our drugs and drug candidates, or caused by our drugs and drug candidates when used in combination with other drugs, could potentially cause significant negative consequences, including:

- regulatory authorities could delay or halt pending clinical trials;
- we may suspend, delay or alter development of the drug candidate or marketing of the drug;
- regulatory authorities may withdraw approvals or revoke licenses of the drug, or we may determine to do so even if not required;
- regulatory authorities may require additional warnings on the label;
- we may be required to develop a Risk Evaluation Mitigation Strategy, or REMS, for the drug, as is the case with REVLIMID®, or, if a REMS is already in place, to incorporate additional requirements under the REMS, or to develop a similar strategy as required by a comparable regulatory authority;
- we may be required to conduct post-market studies; and
- we could be sued and held liable for harm caused to subjects or patients.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular drug or drug candidate, and could significantly harm our business, results of operations and prospects.

Our drugs and any future approved drug candidates will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our drug candidates.

Our drugs and any additional drug candidates that are approved will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies, and submission of safety, efficacy, and other post-market information, including both federal and state requirements in the United States and requirements of comparable regulatory authorities in China and other countries.

Manufacturers and manufacturers' facilities are required to comply with extensive FDA, NMPA, EMA and comparable regulatory authority requirements, including, in the United States, ensuring that quality control and manufacturing procedures conform to cGMP regulations. As such, we and our contract manufacturers are and will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any New Drug Application, or NDA, or Biologics License Application, or BLA, other marketing application, and previous responses to any inspection observations. Accordingly, we and others with whom we work must continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production and quality control.

The regulatory approvals for our drugs and any approvals that we receive for our drug candidates are and may be subject to limitations on the approved indicated uses for which the drug may be marketed or to the conditions of approval, which could

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adversely affect the drug's commercial potential or contain requirements for potentially costly post-marketing testing and surveillance to monitor the safety and efficacy of the drug or drug candidate. The FDA, NMPA, EMA or comparable regulatory authorities may also require a REMS program or comparable program as a condition of approval of our drug candidates or following approval, as is the case with REVLIMID®. In addition, if the FDA, NMPA, EMA or a comparable regulatory authority approves our drug candidates, we will have to comply with requirements including, for example, submissions of safety and other post-marketing information and reports, establishment registration, as well as continued compliance with cGMP and Good Clinical Practice, or GCP, for any clinical trials that we conduct post-approval.

The FDA, NMPA, EMA or comparable regulatory authorities may seek to impose a consent decree or withdraw marketing approval if compliance with regulatory requirements is not maintained or if problems occur after the drug reaches the market. Later discovery of previously unknown problems with our drugs or drug candidates or with our drug's manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical studies to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of our drugs, withdrawal of the product from the market, or voluntary or mandatory product recalls;
- fines, untitled or warning letters, or holds on clinical trials;
- refusal by the FDA, NMPA, EMA or comparable regulatory authorities to approve pending applications or supplements to approved applications filed by us or suspension or revocation of license approvals or withdrawal of approvals;
- product seizure or detention, or refusal to permit the import or export of our drugs and drug candidates; and
- injunctions or the imposition of civil or criminal penalties.

The FDA, NMPA, EMA and other regulatory authorities strictly regulate the marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for their approved indications and for use in accordance with the provisions of the approved label. The FDA, NMPA, EMA and other regulatory authorities actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability. The policies of the FDA, NMPA, EMA and of other regulatory authorities may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our drug candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad, particularly in China, where the regulatory environment is constantly evolving. 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 regulatory approval that we may have obtained and we may not achieve or sustain profitability.

In addition, if we were able to obtain accelerated approval of any of our drug candidates, the FDA would require us to conduct a confirmatory study to verify the predicted clinical benefit and may also require post-marketing safety studies. Other comparable regulatory authorities outside the United States, such as the NMPA or EMA, may have similar requirements. The results from the confirmatory study may not support the clinical benefit, which would result in the approval being withdrawn. While operating under accelerated approval, we will be subject to certain restrictions that we would not be subject to upon receiving regular approval.

If safety, efficacy, or other issues arise with any medical product that is used in combination with our drugs, we may be unable to market such drug or may experience significant regulatory delays or supply shortages, and our business could be materially harmed.

We plan to develop certain of our drug candidates for use as a combination therapy. If the FDA, NMPA, EMA or another comparable regulatory agency revokes its approval of another therapeutic we use in combination with our drug candidates, we will not be able to market our drug candidates in combination with such revoked therapeutic. If safety or efficacy issues arise with these or other therapeutics that we seek to combine with our drug candidates in the future, we may experience significant regulatory delays, and we may be required to redesign or terminate the

applicable clinical trials. In addition, if manufacturing or other issues result in a supply shortage of any component of our combination drug candidates, we may not be able to complete clinical development of our drug candidates on our current timeline or at all, or we may experience disruptions in the commercialization of our approved drugs.

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Reimbursement may not be available for our drug candidates. Even if we are able to commercialize our drugs and any approved drug candidates, the drugs may become subject to unfavorable pricing regulations or third-party reimbursement practices, which could harm our business.

The regulations that govern regulatory approvals, pricing and reimbursement for new therapeutic products 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 or licensing approval is granted. In some non-U.S. markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain regulatory approval for a drug in a particular country, but then be subject to price regulations that delay our commercial launch of the drug and negatively impact our revenues.

Our ability to commercialize any drugs successfully also will depend in part on the extent to which reimbursement for these drugs and related treatments will be available from government health administration authorities, private health insurers and other organizations.

A primary trend in the global healthcare industry is cost containment. Government authorities and these third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications.

In the United States, no uniform policy of coverage and reimbursement for drugs exists among third-party payors. As a result, obtaining coverage and reimbursement approval of a drug from a government or other third-party payor is a time-consuming and costly process that could require us to provide to each payor supporting scientific, clinical and cost-effectiveness data for the use of our drugs on a payor-by-payor basis, with no assurance that coverage and adequate reimbursement will be obtained. Even if we obtain coverage for a given drug, the resulting reimbursement rates might not be adequate for us to achieve or sustain profitability or may require co-payments that patients find unacceptably high. Additionally, third-party payors may not cover, or provide adequate reimbursement for, long-term follow-up evaluations required following the use of our genetically modified drugs. Patients are unlikely to use our drugs and any approved drug candidates unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of the drug. Because some of our drugs and drug candidates have a higher cost of goods than conventional therapies, and may require long-term follow up evaluations, the risk that coverage and reimbursement rates may be inadequate for us to achieve profitability may be greater.

In China, the Ministry of Human Resources and Social Security of China or provincial or local human resources and social security authorities, together with other government authorities, review the inclusion or removal of drugs from China's National Drug Catalog for Basic Medical Insurance, Work-related Injury Insurance and Maternity Insurance, or the National Reimbursement Drug List, or the NRDL, or provincial or local medical insurance catalogues for the National Medical Insurance Program regularly, and the tier under which a drug will be classified, both of which affect the amounts reimbursable to program participants for their purchases of those drugs. There can be no assurance that our drugs and any approved drug candidates will be included in the NRDL. Products included in the NRDL have been typically generic and essential drugs. Innovative drugs similar to our drug candidates have historically been more limited on their inclusion in the NRDL due to the affordability of the government's Basic Medical Insurance, although this has been changing in recent years.

Increasingly, third-party payors are requiring that companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any drug that we commercialize and, if reimbursement is available, what the level of reimbursement will be. Reimbursement may impact the demand for, or the price of, any drug which we commercialize. Obtaining or maintaining reimbursement for our drugs may be particularly difficult because of the higher prices often associated with drugs administered under the supervision of a physician. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any drug candidate that we in-license or successfully develop.

There may be significant delays in obtaining reimbursement for approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or other comparable regulatory authorities outside the United States. 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 payments for

new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Payment rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on payments allowed for lower cost drugs that are already reimbursed, 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 weakening of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Our inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for

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our drugs and any new drugs that we develop could have a material adverse effect on our business, our operating results, and our overall financial condition.

We intend to seek approval to market our drug candidates in the United States, China, Europe and in other jurisdictions. In some non-U.S. countries, particularly those in the European Union, the pricing of drugs and biologics is subject to governmental control, which can take considerable time even after obtaining regulatory approval. Market acceptance and sales of our drugs will depend significantly on the availability of adequate coverage and reimbursement from third-party payors for drugs and may be affected by existing and future health care reform measures.

Recently enacted and future legislation may increase the difficulty and cost for us to obtain regulatory approval of and commercialize our drug candidates and affect the prices we may obtain.

In the United States, China, the European Union and some other jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding healthcare that could prevent or delay regulatory approval of our drug candidates, restrict or regulate post-approval activities and affect our ability to profitably sell our drugs and any drug candidates for which we obtain regulatory approval. We expect that healthcare reform measures may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved drug. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our drugs.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the regulatory approvals of our drug candidates, if any, may be.

In recent years, there have been and will likely continue to be efforts to enact administrative or legislative changes to healthcare laws and policies, including modification, repeal, or replacement of all, or certain provisions of, the Affordable Care Act, or ACA. The implications of the ACA, its possible repeal, any legislation that may be proposed to replace the ACA, modifications to the implementation of the ACA, and the political uncertainty surrounding any repeal or replacement legislation for our business and financial condition, if any, are not yet clear.

Risks Related to Commercialization of Our Drugs and Drug Candidates

If we are not able to obtain, or experience delays in obtaining, required regulatory approvals, we will not be able to commercialize our drug candidates, and our ability to generate revenue will be materially impaired.

Before obtaining regulatory approvals for the commercial sale of any drug candidate for a target indication, we must demonstrate in preclinical studies and well-controlled clinical trials, and, with respect to approval in the United States, to the satisfaction of the FDA, that the drug candidate is safe and effective, or the biologic drug candidate is safe, pure, and potent, for use for that target indication and that the manufacturing facilities, processes and controls are adequate. In addition to preclinical and clinical data, the NDA or BLA must include significant information regarding the chemistry, manufacturing and controls for the drug candidate. Obtaining approval of an NDA or BLA is a lengthy, expensive and uncertain process, and approval may not be obtained. If we submit an NDA or BLA to the FDA, the FDA decides whether to accept or reject the submission for filing. We cannot be certain that any submissions will be accepted for filing and review by the FDA.

We have not yet demonstrated an ability to receive regulatory approval for our drug candidates. For example, we have limited experience in preparing the required materials for regulatory submission and do not have experience navigating the regulatory approval process. As a result, our ability to successfully submit an NDA or BLA and obtain regulatory approval for our drug candidates may involve more inherent risk, take longer, and cost more than it would if we were a company with experience in obtaining regulatory approvals.

Regulatory authorities outside of the United States, such as the NMPA and EMA, also have requirements for approval of drugs for commercial sale with which we must comply prior to marketing in those areas. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our drug candidates. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and obtaining regulatory approval in one country does not mean that regulatory approval will be obtained in any other country.

Approval processes vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking non-U.S. regulatory approval could require additional nonclinical studies or clinical trials, which could be costly and time consuming. The non-U.S.

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regulatory approval process may include all of the risks associated with obtaining FDA approval. For all of these reasons, we may not obtain non-U.S. regulatory approvals on a timely basis, if at all.

The process to develop, obtain regulatory approval for and commercialize drug candidates is long, complex and costly both inside and outside the United States and China, and approval is never guaranteed. Even if our drug candidates were to successfully obtain approval from the regulatory authorities, any approval might significantly limit the approved indications for use, or require that precautions, contraindications or warnings be included on the product labeling, or require expensive and time-consuming post-approval clinical trials or surveillance as conditions of approval. Following any approval for commercial sale of our drug candidates, certain changes to the drug, such as changes in manufacturing processes and additional labeling claims, may be subject to additional review and approval by the FDA, NMPA and EMA and comparable regulatory authorities. Also, regulatory approval for any of our drug candidates may be withdrawn. If we are unable to obtain regulatory approval for our drug candidates in one or more jurisdictions, or any approval contains significant limitations, our target market will be reduced and our ability to realize the full market potential of our drug candidates will be harmed. Furthermore, we may not be able to obtain sufficient funding or generate sufficient revenue and cash flows to continue the development of any other drug candidate in the future.

We have limited manufacturing capability and must rely on third-party manufacturers to manufacture our clinical supplies and commercial products, if and when approved, and if they fail to meet their obligations, the development and commercialization of our products could be adversely affected.

We have limited manufacturing capabilities and experience. Our drug candidates are composed of multiple components and require specialized formulations for which scale-up and manufacturing could be difficult. We have limited experience in such scale-up and manufacturing requiring us to depend on a limited number of third parties, who may not be able to deliver in a timely manner, or at all. In order to develop products, apply for regulatory approvals, and commercialize our products, we will need to develop, contract for, or otherwise arrange for the necessary manufacturing capabilities. There are risks inherent in pharmaceutical manufacturing that could affect the ability of our contract manufacturers to meet our delivery time requirements or provide adequate amounts of material to meet our needs.

Additionally, our internally-developed drug candidates have not yet been manufactured for commercial use. If any of our drug candidates become approved for commercial sale, we will need to establish either internal or third-party manufacturing capacity. Manufacturing partner requirements may require us to fund capital improvements, perhaps on behalf of third parties, to support the scale-up of manufacturing and related activities. We may not be able to establish scaled manufacturing capacity for an approved drug in a timely or economic manner, if at all. If we or our third-party manufacturers are unable to provide commercial quantities of such an approved drug, we will have to successfully transfer manufacturing technology to a different manufacturer. Engaging a new manufacturer for such an approved drug could require us to conduct comparative studies or utilize other means to determine bioequivalence of the new and prior manufacturers' products, which could delay or prevent our ability to commercialize such an approved drug. If we or any of these manufacturers is unable or unwilling to increase its manufacturing capacity or if we are unable to establish alternative arrangements on a timely basis or on acceptable terms, the development and commercialization of such an approved drug may be delayed or there may be a shortage in supply. Any inability to manufacture our drug candidates or future approved drugs in sufficient quantities when needed would seriously harm our business.

Manufacturers of our approved drugs, if any, must comply with cGMP requirements enforced by the FDA, NMPA and other comparable foreign health authorities through facilities inspection programs. These requirements include quality control, quality assurance, and the maintenance of records and documentation. Manufacturers of our approved drugs, if any, may be unable to comply with these cGMP requirements and with other FDA, NMPA, state, and foreign regulatory requirements. A failure to comply with these requirements may result in fines and civil penalties, suspension of production, suspension or delay in product approval, product seizure or recall, or withdrawal of product approval. If the safety of any quantities supplied is compromised due to a manufacturer's failure to adhere to applicable laws or for other reasons, we may not be able to obtain regulatory approval for or successfully commercialize our products, which would seriously harm our business.

Our drugs and any future approved drug candidates may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.
Our drugs and any future approved drug candidates may fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. For example, current cancer treatments like chemotherapy and radiation therapy are well established in the medical community, and doctors may continue to rely on these treatments to the exclusion of our drugs and drug candidates. In addition, physicians, patients and third-party payors may prefer other novel products to ours. If our drugs and drug candidates do not achieve an adequate level of acceptance, we may not generate

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significant product revenues and we may not become profitable. The degree of market acceptance of our drugs and drug candidates, if approved for commercial sale, will depend on a number of factors, including:

- the clinical indications for which our drugs and drug candidates are approved;
- physicians, hospitals, cancer treatment centers and patients considering our drugs and drug candidates as a safe and effective treatment;
- the potential and perceived advantages of our drugs and drug candidates over alternative treatments;
- the prevalence and severity of any side effects;
- product labeling or product insert requirements of regulatory authorities;
- limitations or warnings contained in the labeling approved by regulatory authorities;
- the timing of market introduction of our drugs and drug candidates as well as competitive drugs;
- the cost of treatment in relation to alternative treatments;
- the availability of adequate coverage, reimbursement and pricing by third-party payors and government authorities;
- the willingness of patients to pay out-of-pocket in the absence of coverage and reimbursement by third-party payors and government authorities; and
- the effectiveness of our sales and marketing efforts.

If any drugs that we commercialize fail to achieve market acceptance among physicians, patients, hospitals, cancer treatment centers or others in the medical community, we will not be able to generate significant revenue. Even if our drugs achieve market acceptance, we may not be able to maintain that market acceptance over time if new products or technologies are introduced that are more favorably received than our drugs, are more cost effective or render our drugs obsolete.

We have limited experience in marketing third-party drugs and no experience in launching an internally-developed drug candidate. If we are unable to further develop marketing and sales capabilities or enter into agreements with third parties to market and sell our drug candidates and third-party drugs, we may not be able to generate product sales revenue.

In connection with our strategic collaboration with Celgene, we were granted an exclusive license in China, excluding Hong Kong, Macau and Taiwan, to commercialize Celgene's approved cancer therapies, ABRAXANE®, REVLIMID®, and VIDAZA®, and Celgene's investigational agent avadomide (CC-122) in clinical development, and acquired Celgene's commercial operations in China, excluding certain functions. We started marketing Celgene's approved drugs in September 2017. We continue to build our salesforce in China to market these drugs and our drug candidates, in the event they receive commercial approval, and any additional drugs or drug candidates that we may in-license, which will require significant capital expenditures, management resources and time.

We have not yet demonstrated an ability to launch and commercialize any of our drug candidates. For example, we do not have experience in building a commercial team, conducting a comprehensive market analysis, obtaining state licenses and reimbursement, or managing distributors and a sales force for our internally-developed drug candidates. As a result, our ability to successfully commercialize our drug candidates may involve more inherent risk, take longer, and cost more than it would if we were a company with experience launching drug candidates.

We will have to compete with other pharmaceutical and biotechnology companies to recruit, hire, train and retain marketing and sales personnel. If we are unable to, or decide not to, further develop internal sales, marketing and commercial distribution capabilities for any or all of our drugs, we will likely pursue collaborative arrangements regarding the sales and marketing of our drugs. However, there can be no assurance that we will be able to establish or maintain such collaborative arrangements, or if we are able to do so, that they will have effective sales forces. Any revenue we receive will depend upon the efforts of such third parties. We would have little or no control over the marketing and sales efforts of such third parties, and our revenue from product sales may be lower than if we had commercialized our drugs ourselves. We also face competition in our search for third parties to assist us with the sales and marketing efforts for our drugs.

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There can be no assurance that we will be able to further develop and successfully maintain in-house sales and commercial distribution capabilities or establish or maintain relationships with third-party collaborators to successfully commercialize any product, and as a result, we may not be able to generate product sales revenue.

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

The development and commercialization of new drugs is highly competitive. We face competition 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 drugs for the treatment of cancer for which we are commercializing our drugs or developing our drug candidates. 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.

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 commercialize or may develop. Our competitors also may obtain approval from the FDA, NMPA, EMA or other comparable regulatory authorities 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 are able to enter the market and or slow our regulatory approval.

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 and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

The market opportunities for our drugs and drug candidates may be limited to those patients who are ineligible for or have failed prior treatments and may be small.

In markets with approved therapies, we expect to initially seek approval of our drug candidates as a later stage therapy for patients who have failed other approved treatments. Subsequently, for those drugs that prove to be sufficiently beneficial, if any, we would expect to seek approval as a second line therapy and potentially as a first line therapy, but there is no guarantee that our drug candidates, even if approved, would be approved for second line or first line therapy.

Our projections of both the number of people who have the cancers we are targeting, as well as the subset of people with these cancers in a position to receive later stage therapy and who have the potential to benefit from treatment with our drug candidates, are based on our beliefs and estimates and may prove to be inaccurate or based on imprecise data. Further, new studies may change the estimated incidence or prevalence of these cancers. The number of patients may turn out to be lower than expected. Additionally, the potentially addressable patient population for our drugs and drug candidates may be limited or may not be amenable to treatment with our drugs and drug candidates. Even if we obtain significant market share for our drug candidates, because the potential target populations are small, we may never achieve profitability without obtaining regulatory approval for additional indications, including use as a first or second line therapy.

We may be subject, directly or indirectly, to applicable anti-kickback, false claims laws, physician payment transparency laws, fraud and abuse laws or similar healthcare and security laws and regulations in the United States and other jurisdictions, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and others play a primary role in the recommendation and prescription of any products for which we obtain regulatory approval. If we obtain FDA approval for any of our drug candidates and

begin commercializing those drugs in the United States, our operations may be subject to various federal and state fraud and abuse laws, including, without limitation, the federal Anti-Kickback Statute, the federal False Claims Act, and physician payment sunshine laws and regulations. These laws may impact, among other things, our proposed sales, marketing and education programs. In addition, we may be subject to patient privacy regulation by both the federal government and the states in which we conduct our business.

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Additionally, we are subject to state and non-U.S. equivalents of each of the healthcare laws described above, among others, some of which may be broader in scope and may apply to healthcare services reimbursed by any source, not just governmental payors, including private insurers. In addition, some states have passed laws that require pharmaceutical companies to comply with the April 2003 Office of Inspector General Compliance Program Guidance for Pharmaceutical Manufacturers and/or other voluntary industry codes of conduct. Several states also impose other marketing restrictions or require pharmaceutical companies to make marketing or price disclosures to the state. There are ambiguities as to what is required to comply with these state requirements, and if we fail to comply with an applicable state law requirement, we could be subject to penalties.

Violations of fraud and abuse laws may be punishable by criminal and/or civil sanctions, including penalties, fines and/or exclusion or suspension from federal and state healthcare programs such as Medicare and Medicaid and debarment from contracting with the U.S. government. In addition, private individuals have the ability to bring actions on behalf of the U.S. government under the federal False Claims Act as well as under the false claims laws of several states.

Neither the U.S. government nor the U.S. courts have provided definitive guidance on the applicability of fraud and abuse laws to our business. Law enforcement authorities are increasingly focused on enforcing these laws, and it is possible that some of our practices may be challenged under these laws. Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. 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 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, disgorgement, 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. In addition, the approval and commercialization of any of our drug candidates outside the United States will also likely subject us to non-U.S. equivalents of the healthcare laws mentioned above, among other non-U.S. laws.

If any of the physicians or other providers or entities with whom we expect to do business are 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.

We may explore the licensing of commercialization rights or other forms of collaboration worldwide, which will expose us to additional risks of conducting business in additional international markets.

Non-U.S. markets are an important component of our growth strategy. For example, in connection with the Celgene transactions, we retained exclusive rights for the development and commercialization of tislelizumab for hematological cancers globally and for solid tumors in China and the rest of Asia, other than Japan. We initially intend to focus on opportunities in China, in particular. If we fail to obtain licenses or enter into collaboration arrangements with third parties in other markets, or if these parties are not successful, our revenue-generating growth potential will be adversely affected. Moreover, international business relationships subject us to additional risks that may materially adversely affect our ability to attain or sustain profitable operations, including:

- efforts to enter into collaboration or licensing arrangements with third parties in connection with our international sales, marketing and distribution efforts may increase our expenses or divert our management's attention from the acquisition or development of drug candidates;
- difficulty of effective enforcement of contractual provisions in local jurisdictions;
- potential third-party patent rights or potentially reduced protection for intellectual property rights;
- unexpected changes in tariffs, trade barriers and regulatory requirements, including the loss of normal trade status between China and the United States;
- economic weakness, including inflation;
- compliance with tax, employment, immigration and labor laws for employees traveling abroad;
- the effects of applicable non-U.S. tax structures and potentially adverse tax consequences;

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- currency fluctuations, which could result in increased operating expenses and reduced revenue;
- workforce uncertainty and labor unrest;
- failure of our employees and contracted third parties to comply with Office of Foreign Asset Control rules and regulations and the Foreign Corrupt Practices Act and other anti-bribery and corruption laws; and
- business interruptions resulting from geo-political actions, including trade disputes, war and terrorism, or natural disasters, including earthquakes, volcanoes, typhoons, floods, hurricanes and fires.

These and other risks may materially adversely affect our ability to attain or sustain revenue from international markets.

The illegal distribution and sale by third parties of counterfeit versions of our drugs or stolen products could have a negative impact on our reputation and business.

Third parties might illegally distribute and sell counterfeit or unfit versions of our drugs, which do not meet our or our collaborators' rigorous manufacturing and testing standards. A patient who receives a counterfeit or unfit drug may be at risk for a number of dangerous health consequences. Our reputation and business could suffer harm as a result of counterfeit or unfit drugs sold under our or our collaborators' brand name(s). In addition, thefts of inventory at warehouses, plants or while in-transit, which are not properly stored and which are sold through unauthorized channels, could adversely impact patient safety, our reputation and our business.

Risks Related to Our Financial Position and Need for Additional Capital

We have a limited operating history, which may make it difficult to evaluate our current business and predict our future performance.

We are a commercial-stage biotechnology company formed in October 2010. Our operations to date have focused on organizing and staffing our company, business planning, raising capital, establishing our intellectual property portfolio, conducting preclinical studies and clinical trials of our drug candidates, developing and operating internal manufacturing capabilities, and the commercialization of our drugs. We have not yet completed large-scale, pivotal or registrational clinical trials, obtained regulatory approvals, or manufactured or had manufactured a commercial scale drug. We have no internally-developed products approved for commercial sale and have not generated any revenue from internally-developed product sales. Since September 2017, we have generated revenues from the sale of drugs in China licensed from Celgene. Our limited operating history, particularly in light of the rapidly evolving cancer treatment field, may make it difficult to evaluate our current business and reliably predict our future performance. We may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. If we do not address these risks and difficulties successfully, our business will suffer.

We have incurred significant net losses since our inception and anticipate that we will continue to incur net losses for the foreseeable future and may never become profitable.

Investment in pharmaceutical drug development is highly speculative. It entails substantial upfront capital expenditures and significant risk that a drug candidate will fail to gain regulatory approval or become commercially viable. We continue to incur significant expenses related to our ongoing operations. As a result, we have incurred losses in each period since our inception, except in the third quarter of 2017, when we were profitable due to revenue recognized from an up-front license fee from Celgene. As of December 31, 2018 and 2017, we had an accumulated deficit of $1.0 billion and $330.5 million, respectively. Substantially all of our operating losses have resulted from costs incurred in connection with our research and development programs and from selling, general and administrative expenses associated with our operations.

We expect to continue to incur losses for the foreseeable future, and we expect these losses to increase in the near term as we continue and expand our development of, and seek regulatory approvals for, our drug candidates, and our manufacturing facilities, and continue to commercialize the drugs that we have licensed from Celgene in China and any other drugs that we may successfully develop or license. Typically, it takes many years to develop one new drug from the time it is discovered to when it is available for treating patients. In addition, we will continue to incur costs associated with operating as a public company in the United States and Hong Kong. We will also incur costs in support of our growth as a commercial-stage global biotechnology company. The size of our future net losses will depend, in part, on the number and scope of our drug development programs and the associated costs of those programs, the cost of our manufacturing activities, the cost of commercializing any approved products, our ability to

generate revenues and the timing and amount of milestones and other

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payments we make or receive with arrangements with third parties. If any of our drug candidates fail in clinical trials or do not gain regulatory approval, or if approved, fail to achieve market acceptance, we may never become profitable. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations.

We will need to obtain additional financing to fund our operations, and if we are unable to obtain such financing, we may be unable to complete the development and commercialization of our primary drug candidates.

Our drug candidates will require the completion of clinical development, regulatory review, scale up and availability of manufacturing resources, significant marketing efforts and substantial investment before they can provide us with product sales revenue. Our operations have consumed substantial amounts of cash since inception. Our operating activities used $547.7 million and provided $12.8 million of net cash during the years ended December 31, 2018 and 2017, respectively. We recorded negative net cash flows from operating activities in 2018 primarily due to our net loss of $674.0 million. Although we recorded positive net cash flows from operating activities in 2017, primarily due to the upfront fees received from the Celgene collaboration, we cannot assure you that we will be able to generate positive cash flows from operating activities in the future. Our liquidity and financial condition may be materially and adversely affected by the negative net cash flows, and we cannot assure you that we will have sufficient cash from other sources to fund our operations. If we resort to other financing activities to generate additional cash, we will incur financing costs and we cannot guarantee that we will be able to obtain the financing on terms acceptable to us, or at all, and if we raise finance by issuing further equity securities your interest in our company may be diluted. If we have negative operating cash flows in the future, our liquidity and financial condition may be materially and adversely affected.

We expect to continue to spend substantial amounts on drug discovery, advancing the clinical development of our drug candidates, developing our manufacturing capabilities and securing drug supply, commercializing our drugs and launching and commercializing any drug candidates for which we receive regulatory approval, including building our own commercial organization to address markets in China, the United States and other markets.

While we have generated product revenue in China since September 2017 from sales of our drugs licensed from Celgene, these revenues are not sufficient to support our operations. Although it is difficult to predict our liquidity requirements, based upon our current operating plan, we believe that we have sufficient cash, cash equivalents and short-term investments to meet our projected operating requirements for at least the next 12 months. However, we believe that our existing cash, cash equivalents and short-term investments will not be sufficient to enable us to complete all global development or commercially launch all of our current drug candidates for the currently anticipated indications and to invest in additional programs. Accordingly, we will require further funding through public or private offerings, debt financing, collaboration and licensing arrangements or other sources. Our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement and involves risks and uncertainties, and actual results could vary as a result of a number of factors, including the factors discussed elsewhere in this “Risk Factors” section. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we currently expect. Our future funding requirements will depend on many factors, including:

- the progress, timing, scope and costs of our clinical trials, including the ability to timely enroll patients in our planned and potential future clinical trials;
- the outcome, timing and cost of regulatory approvals of our drug candidates;
- the number and characteristics of drug candidates that we may in-license and develop;
- the amount and timing of the milestone and royalty payments we receive from our collaborators;
- the cost of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights;
- selling and marketing costs associated with our drugs in China and any future drug candidates that may be approved, including the cost and timing of expanding our marketing and sales capabilities;
- the terms and timing of any potential future collaborations, licensing or other arrangements that we may establish;
- cash requirements of any future acquisitions, licensing and/or the development of other drug candidates;

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- the cost and timing of development and completion of commercial-scale internal or outsourced manufacturing activities; and
- our headcount growth and associated costs.

Adequate additional funding may not be available to us on acceptable terms, or at all. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate our research and development programs or future commercialization efforts. Our inability to obtain additional funding when we need it could seriously harm our business.

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

We may seek additional funding through a combination of equity offerings, debt financings, collaborations and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect your rights as a holder of our ordinary shares and/or ADSs. The incurrence of additional indebtedness or the issuance of certain equity securities could result in increased fixed payment obligations and could also result in certain additional restrictive covenants, such as limitations on our ability to incur additional debt or issue additional equity, limitations on our ability to acquire or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. In addition, issuance of additional equity securities, or the possibility of such issuance, may cause the market price of our ADSs and/or ordinary shares to decline. In the event that we enter into collaborations or licensing arrangements in order to raise capital, we may be required to accept unfavorable terms, including relinquishing or licensing to a third party on unfavorable terms our rights to technologies or drug candidates that we otherwise would seek to develop or commercialize ourselves or potentially reserve for future potential arrangements when we might be able to achieve more favorable terms.

Fluctuations in exchange rates could result in foreign currency exchange losses and could materially reduce the value of your investment.

We incur portions of our expenses, and derive revenues, in currencies other than the U.S. dollar or Hong Kong dollar, in particular, the RMB, the Euro, and Australian dollar. As a result, we are exposed to foreign currency exchange risk as our results of operations and cash flows are subject to fluctuations in foreign currency exchange rates. We do not regularly engage in hedging transactions to protect against uncertainty in future exchange rates between particular foreign currencies and the U.S. dollar. A decline in the value of the U.S. dollar against currencies in countries in which we conduct clinical trials could have a negative impact on our research and development costs. We cannot predict the impact of foreign currency fluctuations, and foreign currency fluctuations in the future may adversely affect our financial condition, results of operations and cash flows.

The value of the RMB against the U.S. dollar and other currencies may fluctuate and is affected by, among other things, changes in political and economic conditions and the foreign exchange policy proposed or adopted by the People’s Republic of China, or PRC, Australia and other non-U.S. governments. It is difficult to predict how market forces or PRC, Australia, other non-U.S. governments and U.S. government policies may impact the exchange rate of RMB and the U.S. dollar or any other currencies in the future. There remains significant international pressure on the PRC government to adopt a more flexible currency policy, including from the U.S. government, which has threatened to label China as a “currency manipulator,” which could result in greater fluctuation of the RMB against the U.S. dollar. Substantially all of our revenues are denominated in U.S. dollars and RMB, and our costs are denominated in U.S. dollars, Australian dollars and RMB, and a large portion of our financial assets and a significant portion of our debt is denominated in U.S. dollars and RMB. Any significant revaluation of the RMB may materially reduce any dividends payable on our ordinary shares and/or ADSs in U.S. dollars. To the extent that we need to convert U.S. dollars into RMB for our operations, appreciation of the RMB against the U.S. dollar would have an adverse effect on the RMB amount we would receive. Conversely, if we decide to convert RMB into U.S. dollars for the purpose of making payments for dividends on our ADSs or for other business purposes, appreciation of the U.S. dollar against the RMB would have a negative effect on the U.S. dollar amount we would receive.

In addition, there are limited instruments available for us to reduce our foreign currency risk exposure at reasonable costs. Furthermore, we are also currently required to obtain the State Administration of Foreign Exchange's approval

before converting significant sums of foreign currencies into RMB. All of these factors could materially and adversely affect our business, financial condition, results of operations and prospects, and could reduce the value of, and dividends payable on, our ordinary shares and/or ADSs in foreign currency terms.

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Our business, profitability and liquidity may be adversely affected by deterioration in the credit quality of, or defaults by, our distributors and customers, and an impairment in the carrying value of our short-term investments could negatively affect our consolidated results of operations.

We are exposed to the risk that our distributors and customers may default on their obligations to us as a result of bankruptcy, lack of liquidity, operational failure or other reasons. As we continue to expand our business, the amount and duration of our credit exposure will be expected to increase over the next few years, as will the breadth of the entities to which we have credit exposure. Although we regularly review our credit exposure to specific distributors and customers that we believe may present credit concerns, default risks may arise from events or circumstances that are difficult to detect or foresee.

Also, the carrying amounts of cash and cash equivalents, restricted cash and short-term investments represent the maximum amount of loss due to credit risk. We had cash and cash equivalents of $712.9 million and $239.6 million, restricted cash of $27.8 million and nil and short-term investments of $1.1 billion and $597.9 million at December 31, 2018 and 2017, respectively, most of which are deposited in financial institutions outside of China. Although our cash and cash equivalents in China are deposited with various major reputable financial institutions, the deposits placed with these financial institutions are not protected by statutory or commercial insurance. In the event of bankruptcy of one of these financial institutions, we may be unlikely to claim our deposits back in full. As of December 31, 2018 and December 31, 2017, our short-term investments consisted primarily of U.S. Treasury securities, U.S. agency securities and time deposits. Although we believe that the U.S. Treasury securities, U.S. agency securities and time deposits are of high credit quality and continually monitor the credit worthiness of these institutions, concerns about, or a default by, one institution in the U.S. market, could lead to significant liquidity problems, losses or defaults by other institutions, which in turn could adversely affect us.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain patent protection for our drug candidates and drugs through intellectual property rights, or if the scope of such intellectual property rights obtained is not sufficiently broad, third parties may compete directly against us.

Our success depends in large part on our ability to protect our proprietary technology and drug candidates and drugs from competition by obtaining, maintaining and enforcing our intellectual property rights, including patent rights. We seek to protect the drugs, drug candidates and technology that we consider commercially important by filing patent applications in the United States, the PRC and other countries, relying on trade secrets or pharmaceutical regulatory protection or employing a combination of these methods. This 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. 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.

The patent prosecution process is expensive, time-consuming and complex, and we may not be able to file, prosecute, maintain, enforce or license all necessary or desirable patent applications at a reasonable cost or in a timely manner. As a result, we may not be able to prevent competitors from developing and commercializing competitive drugs in all such fields and territories.

Patents may be invalidated and patent applications may not be granted for a number of reasons, including known or unknown prior art, deficiencies in the patent applications or the lack of novelty of the underlying invention or technology. It is also possible that we will fail to identify patentable aspects of our research and development output in time to obtain patent protection. Although we enter into non-disclosure and confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and any other third parties, any of these parties may breach such agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection. In addition, publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases, not at all. Therefore, we cannot be certain that we were the first to make the inventions claimed in our patents or pending patent applications or that we were the first to file for patent protection of such inventions. Furthermore, the PRC and, recently, the United States have

adopted the “first-to-file” system under which whoever first files a patent application will be awarded the patent if all other patentability requirements are met. Under the first-to-file system, third parties may be granted a patent relating to a technology which we invented.

In addition, under PRC patent law, any organization or individual that applies for a patent in a foreign country for an invention or utility model accomplished in China is required to report to the National Intellectual Property Administration, or NIPA, for security examination. Otherwise, if an application is later filed in China, the patent right will not be granted.

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The coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Even if patent applications we license or own currently or in the future issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us, or otherwise provide us with any competitive advantage. In addition, the patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions, and has been the subject of much litigation in recent years. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents may be challenged in the courts or patent offices in the United States, PRC and other countries. We may be subject to a third-party preissuance submission of prior art to the USPTO or become involved in opposition, derivation, revocation, re-examination, post-grant and inter partes review, or interference proceedings or similar proceedings in foreign jurisdictions challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or drug candidates and compete directly with us without payment to us, or result in our inability to manufacture or commercialize drug candidates without infringing, misappropriating or otherwise violating third-party patent rights. Moreover, we may have to participate in interference proceedings declared by the USPTO to determine priority of invention or in post-grant challenge proceedings, such as oppositions in a foreign patent office, that challenge the priority of our invention or other features of patentability of our patents and patent applications. Such challenges may result in loss of patent rights, loss of exclusivity, or in patent claims being narrowed, invalidated, or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and drug candidates. Such proceedings also may result in substantial costs and require significant time from our scientists and management, even if the eventual outcome is favorable to us. Consequently, we do not know whether any of our technology or drug candidates will be protectable or remain protected by valid and enforceable patents. Our competitors or other third parties may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner.

Furthermore, although various extensions may be available, the life of a patent and the protection it affords, is limited. For example, the approved cancer therapies we have licensed from Celgene in China, ABRAXANE®, REVLIMID®, and VIDAZA®, face or are expected to face competition from generic medications, and we may face similar competition for any approved drug candidates even if we successfully obtain patent protection once the patent life has expired for the drug or if the patents are not enforced. Manufacturers of generic drugs may challenge the scope, validity or enforceability of our patents in court, and we may not be successful in enforcing or defending those intellectual property rights and, as a result, may not be able to develop or market the relevant product exclusively, which would have a material adverse effect on any potential sales of that product. The issued patents and pending patent applications, if issued, for our drug candidates are expected to expire on various dates as described in “Part I-Item 1-Business-Intellectual Property” of our Annual Report on Form 10-K for the year ended December 31, 2018. Upon the expiration of our issued patents or patents that may issue from our pending patent applications, we will not be able to assert such patent rights against potential competitors and our business and results of operations may be adversely affected.

Given the amount of time required for the development, testing and regulatory review of new drug candidates, patents protecting such drug candidates might expire before or shortly after such drug candidates are commercialized. As a result, our patents and patent applications may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. Moreover, some of our patents and patent applications are, and may in the future be, co-owned with or licensed from third parties. If we are unable to obtain an exclusive license to any such third-party co-owners’ interest in such patents or patent applications, such co-owners may be able to license their rights to other third parties, including our competitors, and our competitors could market competing products and technology. In addition, we may need the cooperation of any such co-owners or the licensors of our patents in order to enforce such patents against third parties, and such cooperation may not be provided to us. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations and

prospects.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting, maintaining and defending patents on drug candidates in all countries throughout the world could be prohibitively expensive for us, and our intellectual property rights in some non-U.S. countries can have a different scope and strength than do those in the United States. In addition, the laws of certain non-U.S. countries do not protect intellectual property rights to the same extent as U.S. federal and state laws do. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing drugs made using our inventions in and into the United States or non-U.S. jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own drugs and further, may export otherwise infringing drugs to non-

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U.S. jurisdictions where we have patent protection, but where enforcement rights are not as strong as those in the United States. These drugs may compete with our drugs and drug candidates and our patent rights or other intellectual property rights may not be effective or adequate to prevent them from competing. In addition, we may not be able to enforce patents that we in-license from third parties, who may delay or decline to enforce patents in the licensed territory.

We currently hold issued trademark registrations and have trademark applications pending, any of which may be the subject of a governmental or third-party objection, which could prevent the maintenance or issuance of the same. If we are unsuccessful in obtaining trademark protection for our primary brands, we may be required to change our brand names, which could materially adversely affect our business. Moreover, as our products mature, our reliance on our trademarks to differentiate us from our competitors will increase, and as a result, if we are unable to prevent third parties from adopting, registering or using trademarks and trade dress that infringe, dilute or otherwise violate our trademark rights, our business could be materially adversely affected.

Many companies have encountered significant problems in protecting and defending intellectual property rights in certain jurisdictions, including China. The legal systems of some countries do not favor the enforcement of patents, trade secrets and other intellectual property, particularly those relating to biopharmaceutical products, which could make it difficult in those jurisdictions for us to stop the infringement or misappropriation of our patents or other intellectual property rights, or the marketing of competing drugs in violation of our proprietary rights.

We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop.

We may become involved in lawsuits to protect or enforce our intellectual property, which could be expensive, time consuming and unsuccessful. Our patent rights relating to our drug candidates could be found invalid or unenforceable if challenged in court or before the USPTO or comparable non-U.S. authority.

Competitors may infringe our patent rights or misappropriate or otherwise violate our intellectual property rights. To counter infringement or unauthorized use, litigation may be necessary in the future to enforce or defend our intellectual property rights, to protect our trade secrets or to determine the validity and scope of our own intellectual property rights or the proprietary rights of others. This can be expensive and time consuming. Any claims that we assert against perceived infringers could also provoke these parties to assert counterclaims against us alleging that we infringe their intellectual property rights. Many of our current and potential competitors have the ability to dedicate substantially greater resources to enforce and/or defend their intellectual property rights than we can. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing upon or misappropriating our intellectual property. An adverse result in any litigation proceeding could put our patent, as well as any patents that may issue in the future from our pending patent applications, at risk of being invalidated, held unenforceable or interpreted narrowly. 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 patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace, and there are numerous grounds upon which a third party can assert invalidity or unenforceability of a patent. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include ex parte re-examination, inter partes review, post-grant review, derivation and equivalent proceedings in non-U.S. jurisdictions, such as opposition proceedings. Such proceedings could result in revocation or amendment to our patents in such a way that they no longer cover and protect our drug candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity of our patents, for example, we cannot be certain that there is no invalidating prior art of which we, our patent counsel, and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our drug candidates. Such a loss of patent protection could have a material adverse impact on our business.

We may not be able to prevent misappropriation of our trade secrets or confidential information, particularly in countries where the laws may not protect those rights as fully as in the United States.

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If we are sued for infringing intellectual property rights of third parties, such litigation could be costly and time consuming and could prevent or delay us from developing or commercializing our drug candidates.

Our commercial success depends in part on our avoiding infringement of the patents and other intellectual property rights of third parties. We are aware of numerous issued patents and pending patent applications belonging to third parties that exist in fields in which we are developing our drug candidates. There may also be third-party patents or patent applications of which we are currently unaware, and given the dynamic area in which we operate, additional patents are likely to issue that relate to aspects of our business. There is a substantial amount of litigation and other claims and proceedings involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries generally. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our drug candidates may give rise to claims of infringement of the patent rights of others.

Third parties may assert that we are using technology in violation of their patent or other proprietary rights. Defense of these claims, regardless of their merit, could involve substantial litigation expense and divert our technical personnel, management personnel, or both from their normal responsibilities. Even in the absence of litigation, we may seek to obtain licenses from third parties to avoid the risks of litigation, and if a license is available, it could impose costly royalty and other fees and expenses on us.

If third parties bring successful claims against us for infringement of their intellectual property rights, we may be subject to injunctive or other equitable relief, which could prevent us from developing and commercializing one or more of our drug candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim against us of infringement or misappropriation, or a settlement by us of any such claims, we may have to pay substantial damages, including treble damages and attorneys' fees in the case of willful infringement, pay royalties or redesign our infringing drug candidates, which may be impossible or require substantial time and cost. In the event of an adverse result in any such litigation, or even in the absence of litigation, we may need to obtain licenses from third parties to advance our research or allow commercialization of our drug candidates. Any such license might not be available on reasonable terms or at all. In the event that we are unable to obtain such a license, we would be unable to further develop and commercialize one or more of our drug candidates, which could harm our business significantly. We may also elect to enter into license agreements in order to settle patent infringement claims or to resolve disputes prior to litigation, and any such license agreements may require us to pay royalties and other fees that could significantly harm our business.

We are aware of U.S. patents with claims covering certain antibodies that are relevant to tislelizumab for which patents are expected to expire in 2023 or 2024; complexes of irreversible BTK inhibitors that are relevant to zanubrutinib for which the patent is expected to expire in 2027; and the use of PARP inhibitors to treat certain cancers that are relevant to pamiparib for which patents are expected to expire between 2027 and 2031. We are also aware of issued patents in Europe and China relevant to pamiparib. Although we believe that the relevant claims of these patents would likely be held invalid, we can provide no assurance that a court or an administrative agency would agree with our assessment. If the validity of the relevant claims of one or more of these patents were to be upheld upon a validity challenge, and our related drug candidate was to be approved for sale in the United States before the expiration of the relevant patents, we would need a license to commercialize the drug candidate in the United States before the expiration of the relevant patents. In addition, depending upon the circumstances, we may need licenses for jurisdictions outside of the United States where we wish to commercialize a particular drug candidate before the expiration of corresponding patents covering that drug candidate. In such cases, we can provide no assurance that we would be able to obtain a license or licenses on commercially reasonable terms or at all, which could materially and adversely affect our business.

Even if litigation or other proceedings are resolved in our favor, 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 market price of the ordinary shares and/or ADSs. 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. 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.

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Obtaining and maintaining our 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 noncompliance with these requirements.

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and other patent agencies in several stages over the lifetime of the patent. The USPTO and various non-U.S. governmental patent agencies require compliance with a number of procedural, documentary, fee payment, and other similar provisions during the patent application process. Although an inadvertent 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. Noncompliance events that could result in abandonment or lapse of a patent or patent application include failure to respond to official actions within prescribed time limits, non-payment of fees, and failure to properly legalize and submit formal documents. In any such event, our competitors might be able to enter the market, which would have a material adverse effect on our business.

If we do not obtain patent term extension and data exclusivity for any drug candidates we may develop, our business may be materially harmed.

Depending upon the timing, duration and specifics of any FDA marketing approval of any drug candidates we may develop, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Action of 1984, or Hatch Waxman Amendments. The Hatch Waxman Amendments permit a patent extension term of up to five years as compensation for patent term lost during clinical trials and the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of drug approval, only one patent may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. However, we may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. In addition, no patent term extension system has been established in the PRC beyond the new pilot program, and implementation of the pilot program may not occur quickly. As a result, the patents we have in the PRC are not yet eligible to be extended for patent term lost during clinical trials and the regulatory review process. If we are unable to obtain patent term extension or term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our business, financial condition, results of operations, and prospects could be materially harmed.

Changes in patent law could diminish the value of patents in general, thereby impairing our ability to protect our drug candidates.

The United States has recently enacted and is currently implementing wide-ranging patent reform legislation. Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents once obtained, if any. Depending on decisions by the U.S. Congress, the federal courts and the USPTO, 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. There could be similar changes in the laws of foreign jurisdictions that may impact the value of our patent rights or our other intellectual property rights.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed. We may be subject to claims that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

In addition to our issued patent and pending patent applications, we rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position and to protect our drug candidates. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties that have access to them, such as our employees, corporate collaborators, outside scientific

collaborators, sponsored researchers, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. However, any of these parties may breach such agreements and disclose our proprietary information, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret can be difficult, expensive and time-consuming, and the outcome is unpredictable. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor,

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we would have no right to prevent them from using that technology or information to compete with us and our competitive position would be harmed.

Furthermore, many of our employees, including our senior management, were previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Some of these employees, including each member of our senior management, executed proprietary rights, non-disclosure and non-competition agreements in connection with such previous employment. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's former employer. We are not aware of any threatened or pending claims related to these matters or concerning the agreements with our senior management, but in the future litigation may be necessary to defend against such claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, while we typically require our employees, consultants and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own, which may result in claims by or against us related to the ownership of such intellectual property. If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our management and scientific personnel.

We may not be successful in obtaining or maintaining necessary rights for our development pipeline through acquisitions and in-licenses.

Because our programs may involve additional drug candidates that may require the use of proprietary rights held by third parties, the growth of our business may depend in part on our ability to acquire and maintain licenses or other rights to use these proprietary rights. We may be unable to acquire or in-license any compositions, methods of use, or other third-party intellectual property rights from third parties that we identify. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities. If we are unable to successfully obtain rights to required third-party intellectual property rights, our business, financial condition and prospects for growth could suffer.

If we fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could be required to pay monetary damages or could lose license rights that are important to our business.

We have entered into license agreements with third parties providing us with rights under various third-party patents and patent applications. These license agreements impose diligence, development or commercialization timelines and milestone payment, royalty, insurance and other obligations on us. If we fail to comply with our obligations under our current or future license agreements, our counterparties may have the right to terminate these agreements, in which event we might not be able to develop, manufacture or market any drug or drug candidate that is covered by the licenses provided for under these agreements or we may face claims for monetary damages or other penalties under these agreements. Such an occurrence could diminish the value of these products and our company. Termination of the licenses provided for under these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new or reinstated agreements with less favorable terms, or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology.

Risks Related to Our Reliance on Third Parties

We rely on third parties to conduct our preclinical studies and clinical trials and we must work effectively with collaborators to develop our drug candidates. If these third parties do not successfully carry out their contractual duties 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 have relied upon and plan to continue to rely upon third-party CROs to monitor and manage data for our ongoing preclinical and clinical programs. We rely on these parties for execution of our preclinical studies and clinical trials, and control

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only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards, and our reliance on the CROs does not relieve us of our regulatory responsibilities. We, our CROs for our clinical programs and our clinical investigators are required to comply with GCPs, which are regulations and guidelines enforced by the FDA, NMPA, EMA and other comparable regulatory authorities for all of our drugs in clinical development. If we or any of our CROs or clinical investigators fail to comply with applicable GCPs and other regulatory requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, NMPA, EMA or comparable regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. In addition, our pivotal clinical trials must be conducted with product produced under cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. We could also be subject to government investigation and enforcement actions.

If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs or to do so on commercially reasonable terms. In addition, our CROs are not our employees, and except for remedies available to us under our agreements with such CROs, we cannot control whether or not they devote sufficient time and resources to our ongoing clinical and nonclinical programs. 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 or our clinical investigators obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our drug candidates. As a result, our results of operations and the commercial prospects for our drug candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed.

Switching or adding additional CROs involves additional cost and delays, which can materially influence our ability to meet our desired clinical development timelines. There can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse effect on our business, financial condition and prospects.

Our future revenues are dependent on our ability to work effectively with collaborators to develop our drug candidates, including to obtain regulatory approval. Our arrangements with collaborators will be critical to successfully bringing products to market and commercializing them. We rely on collaborators in various respects, including to undertake research and development programs and conduct clinical trials, manage or assist with the regulatory filings and approval process and to assist with our commercialization efforts. We do not control our collaborators; therefore, we cannot ensure that these third parties will adequately and timely perform all of their obligations to us. If they fail to complete the remaining studies successfully, or at all, it could delay, adversely affect or prevent regulatory approval. We cannot guarantee the satisfactory performance of any of our collaborators and if any of our collaborators breach or terminate their agreements with us, we may not be able to successfully commercialize the licensed product which could materially and adversely affect our business, financial condition, cash flows and results of operations.

We expect to rely on third parties to manufacture at least a portion of our clinical and commercial drug supplies. Our business could be harmed if those third parties fail to provide us with sufficient quantities of product or fail to do so at acceptable quality levels or prices.

Although we currently have a facility that may be used as our clinical-scale manufacturing and processing facility and are building manufacturing facilities in China, we intend to at least partially rely on outside vendors to manufacture supplies and process our drugs and drug candidates. For example, we have entered into a commercial supply agreement for tislelizumab with Boehringer Ingelheim Biopharmaceuticals (China) Ltd. In addition, we rely on Celgene and its third-party manufacturers for supply of ABRAXANE®, REVLIMID®, and VIDAZA® in China. Our drug candidates have not yet been manufactured or processed on a commercial scale and we may not be able to do so for any of our drug candidates. We have limited experience in managing the manufacturing process, and our process may be more difficult or expensive than the approaches currently in use.

Although we intend to further develop our own manufacturing facilities, we also intend to use third parties as part of our manufacturing process and for the clinical and commercial supply of our drugs and drug candidates. Our anticipated reliance on a limited number of third-party manufacturers exposes us to the following risks:

- we may be unable to identify manufacturers on acceptable terms or at all because the number of potential manufacturers is limited and the FDA, NMPA, EMA or other comparable regulatory authorities must evaluate and/or approve any manufacturers as part of their regulatory oversight of our drug candidates. This evaluation would require new testing and cGMP-compliance inspections by FDA, NMPA, EMA or other comparable regulatory authorities;

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- our manufacturers may have little or no experience with manufacturing our drug candidates, and therefore may require a significant amount of support from us in order to implement and maintain the infrastructure and processes required to manufacture our drug candidates;
- our third-party manufacturers might be unable to timely manufacture our drugs and drug candidates or produce the quantity and quality required to meet our clinical and commercial needs, if any;
- manufacturers are subject to ongoing periodic unannounced inspection by the FDA and corresponding state agencies in the United States to ensure strict compliance with cGMPs and other government regulations and by other comparable regulatory authorities for corresponding non-U.S. requirements. We do not have control over third-party manufacturers' compliance with these regulations and requirements;
- we may not own, or may have to share, the intellectual property rights to any improvements made by our third-party manufacturers in the manufacturing process for our drug candidates and drugs;
- raw materials and components used in the manufacturing process, particularly those for which we have no other source or supplier, may not be available or may not be suitable or acceptable for use due to material or component defects; and
- our contract manufacturers and critical drug component suppliers may be subject to disruptions in their business, including inclement weather, as well as natural or man-made disasters.

Each of these risks could delay or prevent the completion of our clinical trials or the approval of any of our drug candidates, result in higher costs or adversely impact commercialization of our drugs. In addition, we will rely on third parties to perform certain specification tests on our drugs and drug candidates prior to delivery to patients. If these tests are not appropriately done and test data are not reliable, patients could be put at risk of serious harm and regulatory authorities could place significant restrictions on our company until deficiencies are remedied.

Currently, the raw materials for our manufacturing activities are supplied by multiple source suppliers, although portions of our supply chain may rely on sole source suppliers. We have agreements for the supply of drug materials with manufacturers or suppliers that we believe have sufficient capacity to meet our demands. In addition, we believe that adequate alternative sources for such supplies exist. However, there is a risk that, if supplies are interrupted, it would materially harm our business.

Manufacturers of drug and biological products often encounter difficulties in production, particularly in scaling up or out, validating the production process, and assuring high reliability of the manufacturing process (including the absence of contamination). These problems include logistics and shipping, difficulties with production costs and yields, quality control, including stability of the product, product testing, operator error, availability of qualified personnel, as well as compliance with strictly enforced federal, state and non-U.S. regulations. Furthermore, if contaminants are discovered in the supply of our drugs and drug candidates or in the manufacturing facilities, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination. We cannot assure you that any stability failures or other issues relating to the manufacture of our drug candidates will not occur in the future. Additionally, our manufacturers may experience manufacturing difficulties due to resource constraints or as a result of labor disputes or unstable political environments. If our manufacturers were to encounter any of these difficulties, or otherwise fail to comply with their contractual obligations, our ability to provide our drugs for commercial sale and our drug candidates to patients in clinical trials would be jeopardized. Any delay or interruption in the supply of clinical trial supplies could delay the completion of clinical trials, increase the costs associated with maintaining clinical trial programs and, depending upon the period of delay, require us to begin new clinical trials at additional expense or terminate clinical trials completely.

If third-party manufacturers fail to comply with manufacturing regulations, our financial results and financial condition will be adversely affected.

Before a third party can begin commercial manufacture of our drugs and drug candidates, contract manufacturers are subject to regulatory inspections of their manufacturing facilities, processes and quality systems. Due to the complexity of the processes used to manufacture drug and biological pro