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BeiGene, Ltd.
百濟神州有限公司
(incorporated in the Cayman Islands with limited liability)
(Stock Code: 06160)

OVERSEAS REGULATORY ANNOUNCEMENT – FORM 10-K

This announcement is issued pursuant to Rule 13.10B of the Rules Governing the Listing of Securities on The Stock Exchange of Hong Kong Limited.

Please refer to the attached for the document which has been published by BeiGene, Ltd. on the website of the U.S. Securities and Exchange Commission on February 27, 2023.

By order of the Board
BeiGene, Ltd.
Mr. John V. Oyler
Chairman

Hong Kong, February 27, 2023

As of the date of this announcement, the Board of Directors of the Company consists of Mr. John V. Oyler as Chairman and Executive Director, Dr. Xiaodong Wang and Mr. Anthony C. Hooper as Non-executive Directors, and Dr. Margaret Han Dugan, Mr. Donald W. Glazer, Mr. Michael Goller, Mr. Ranjeev Krishana, Mr. Thomas Malley, Dr. Alessandro Riva, Dr. Corazon (Corsee) D. Sanders and Mr. Qingqing Yi as Independent Non-executive Directors.

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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2022

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 KY1-1108

(Address of principal executive offices, including 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	Trading Symbol(s)	Name of each exchange on which registered
American Depositary Shares, each representing 13 Ordinary Shares, par value $0.0001 per share	**BGNE**	**The NASDAQ Global Select Market**
Ordinary Shares, par value $0.0001 per share*	**06160**	**The Stock Exchange of Hong Kong Limited**

*Included in connection with the registration of the American Depositary Shares ("ADSs") with the U.S. Securities and Exchange Commission. The ordinary shares are not listed for trading in the United States but are listed for trading on The Stock Exchange of Hong Kong Limited ("HKEx").

Securities registered pursuant to Section 12(g) of the Act: The RMB shares are ordinary shares of the registrant issued to permitted investors in the People's Republic of China and listed and traded on the STAR Market in Renminbi. The RMB shares are not listed for trading in the United States or on the HKEx and are not fungible with the ordinary shares listed on the HKEx or the ADSs representing the ordinary shares listed on NASDAQ, and in no event will any RMB shares be able to be converted into the ordinary shares listed on the HKEx or the ADSs listed on NASDAQ, or vice versa.

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

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

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

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

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

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

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

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☒

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

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

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

As of June 30, 2022, 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 ADSs, each representing 13 ordinary shares, held by non-affiliates of the registrant was approximately $16.8 billion, based upon the closing price of the registrant's ADSs on the NASDAQ Global Select Market on June 30, 2022.

As of February 14, 2023, 1,356,140,180 ordinary shares, par value $0.0001 per share, were outstanding, of which 863,876,312 ordinary shares were held in the form of 66,452,024 ADSs, and 115,055,260 were RMB shares.

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, 2022. Portions of such definitive proxy statement are incorporated by reference into Part III of this Annual Report on Form 10-K.

BeiGene, Ltd.
Annual Report on Form 10-K
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Forward-Looking Statements and Market Data

This Annual Report on Form 10-K (the "Annual Report") contains forward-looking statements that involve substantial risks and uncertainties. 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. 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. Forward looking statements often include words such as, but not limited to, "aim," "anticipate," "believe," "can," "continue," "could," "estimate," "expect," "goal," "intend," "may," "ongoing," "plan," "potential," "predict," "project," "seek," "should," "target," "will," "would" or the negative of these terms or similar expressions. These forward-looking statements include, among other things, statements about:

- our ability to successfully commercialize our approved medicines and to obtain approvals in additional indications and territories for our medicines;
- our ability to successfully develop and commercialize our in-licensed medicines and drug candidates and any other medicines and drug candidates we may in-license;
- our ability to further develop sales and marketing capabilities and launch and commercialize new medicines, if approved;
- our ability to maintain and expand regulatory approvals for our medicines and drug candidates, if approved;
- the pricing and reimbursement of our medicines and drug candidates, if approved;
- 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 and obtain regulatory approvals;
- 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 implementation of our business model, strategic plans for our business, medicines, drug candidates and technology;
- the scope of protection we (or our licensors) are able to establish and maintain for intellectual property rights covering our medicines, 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;
- the regulatory environment and regulatory developments in the United States, China, the United Kingdom, Switzerland, the European Union ("EU") and other jurisdictions in which we operate;
- 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 and maintain strategic arrangements;
- our plans and expectations to build significant technical operations and independent production capabilities for small molecule medicines and large molecule biologics to support the global demand for both commercial and clinical supply;
- 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 medicines for commercial sale;
- the rate and degree of market access and acceptance of our medicines and drug candidates, if approved;

- developments relating to our competitors and our industry, including competing therapies;
- the size of the potential markets for our medicines 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, key milestones, expenses, capital expenditures, capital requirements and share performance;
- the future trading price of our American Depositary Shares ("ADS") listed on NASDAQ, our ordinary shares listed on HKEx, and our ordinary shares issued to permitted investors in China and listed and traded on the STAR in Renminbi ("RMB Shares"), as well as the impact of securities analysts' reports on these prices; and
- the impact of the COVID-19 pandemic on our clinical development, regulatory, commercial, manufacturing, and other operations.

These statements involve risks and uncertainties, including those that are described in "Part I-Item 1A-Risk Factors" of this Annual Report, that may cause actual future events or results to differ materially from those expected. Given these uncertainties, you should not place undue reliance on these forward-looking statements.

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.

Summary of Risk Factors

Below is a summary of the material factors that make an investment in our ADSs, ordinary shares or RMB Shares speculative or risky. This summary does not address all of the risks that we face. Additional discussion of the risks summarized in this risk factor summary, and other risks that we face, are summarized in "Part I-Item 1A-Risk Factors" and should be carefully considered, together with other information in this Annual Report and our other filings with the SEC, before making an investment decision regarding our ADSs, ordinary shares or RMB shares.

- Our medicines may fail to achieve and maintain the degree of market acceptance by physicians, patients, third-party payors, and others in the medical community necessary for commercial success.
- We have limited experience in launching and marketing our internally developed and in-licensed medicines. If we are unable to further develop marketing and sales capabilities or enter into agreements with third parties to market and sell our medicines, we may not be able to generate substantial product sales revenue.
- We face substantial competition, which may result in others discovering, developing, or commercializing competing medicines before or more successfully than we do.
- The market opportunities for our medicines may be limited to those patients who are ineligible for or have failed prior treatments and may be small.
- If we or any third parties with which we may collaborate to market and sell our medicines are unable to achieve and maintain coverage and adequate levels of reimbursement, our commercial success and business operations could be adversely affected.
- We depend substantially on the success of the clinical development of our medicines and drug candidates. If we are unable to successfully complete clinical development, obtain regulatory approvals and commercialize our medicines and drug candidates, or experience significant delays in doing so, our business will be materially harmed.
- Clinical 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.
- 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.
- If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.
- All material aspects of the research, development, manufacturing and commercialization of pharmaceutical products are heavily regulated, and we may face difficulties in complying with or be unable to comply with such regulations, which could have a material adverse effect on our business.
- The approval processes of regulatory authorities in the United States, China, Europe and other comparable regulatory authorities are lengthy, time consuming, costly and inherently unpredictable. If we experience delays or are ultimately unable to obtain regulatory approval for our drug candidates, our business will be substantially harmed.
- Our medicines 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 medicines and drug candidates.
- Even if we are able to commercialize our medicines and any approved drug candidates, the medicines may become subject to unfavorable pricing regulations or third-party reimbursement practices or healthcare reform initiatives, which could harm our business.
- 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 not become profitable.
- We may 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 of our drug candidates or achieve profitability.

- If we are unable to obtain and maintain patent protection for our medicines and drug candidates through intellectual property rights, or if the scope of such intellectual property rights is not sufficiently broad, third parties may compete against us.
- We rely on third parties to manufacture some of our commercial and clinical 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.
- We have entered into licensing and collaboration arrangements and may enter into additional collaborations, licensing arrangements, or strategic alliances in the future, and we may not realize the benefits of such arrangements.
- If we fail to maintain an effective distribution channel for our medicines, our business and sales could be adversely affected.
- If third-party manufacturers fail to comply with manufacturing regulations, our financial results and financial condition could be adversely affected.
- If we are not able to successfully develop and/or commercialize Amgen's oncology products, the expected benefits of the collaboration will not materialize.
- We have significantly increased and expect to continue to increase our research, development, manufacturing, and commercial capabilities, and we may experience difficulties in managing our growth.
- Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.
- Our business is subject to complex and evolving industry-specific laws and regulations regarding the collection and transfer of personal data. These laws and regulations can be complex and stringent, and many are subject to change and uncertain interpretation, which could result in claims, changes to our data and other business practices, significant penalties, increased cost of operations, or otherwise adversely impact our business.
- We manufacture some of our medicines and intend to manufacture some of our drug candidates, if approved. Failure to comply with regulatory requirements could result in sanctions being imposed against us and delays in completing and receiving regulatory approvals for our manufacturing facilities, or damage to, destruction of or interruption of production at such facilities, could delay our development plans or commercialization efforts.
- Changes in the political and economic policies of the PRC government or in relations between China and the United States or other governments and the significant oversight and discretion the PRC government has over the conduct of the business operations of our PRC subsidiaries may materially and adversely affect our business, financial condition, and results of operations and may result in our inability to sustain our growth and expansion strategies.
- The audit reports included in our previous annual reports on Form 10-K filed with the SEC have historically been prepared by auditors who are not inspected fully by the Public Company Accounting Oversight Board, and as such, investors have previously been deprived of the benefits of such inspection.
- The trading prices of our ordinary shares, ADSs and/or RMB Shares can be volatile, which could result in substantial losses to you.

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 global biotechnology company that is developing and commercializing innovative and affordable oncology medicines to improve treatment outcomes and access for patients worldwide.

We currently have three approved medicines that were discovered and developed in our own labs, including BRUKINSA®, a small molecule inhibitor of Bruton's Tyrosine Kinase ("BTK") for the treatment of various blood cancers; tislelizumab, an anti-PD-1 antibody immunotherapy for the treatment of various solid tumor and blood cancers; and pamiparib, a selective small molecule inhibitor of PARP1 and PARP2. We have obtained approvals to market BRUKINSA in the United States, the People's Republic of China ("China" or the "PRC"), the European Union ("EU"), the United Kingdom ("UK"), Canada, Australia and additional international markets, and tislelizumab and pamiparib in China. By leveraging our China commercial capabilities, we have in-licensed the rights to distribute 13 approved medicines for the China market. Supported by our global clinical development and commercial capabilities, we have entered into collaborations with world-leading biopharmaceutical companies such as Amgen Inc. ("Amgen") and Novartis Pharma AG ("Novartis") to develop and commercialize innovative medicines.

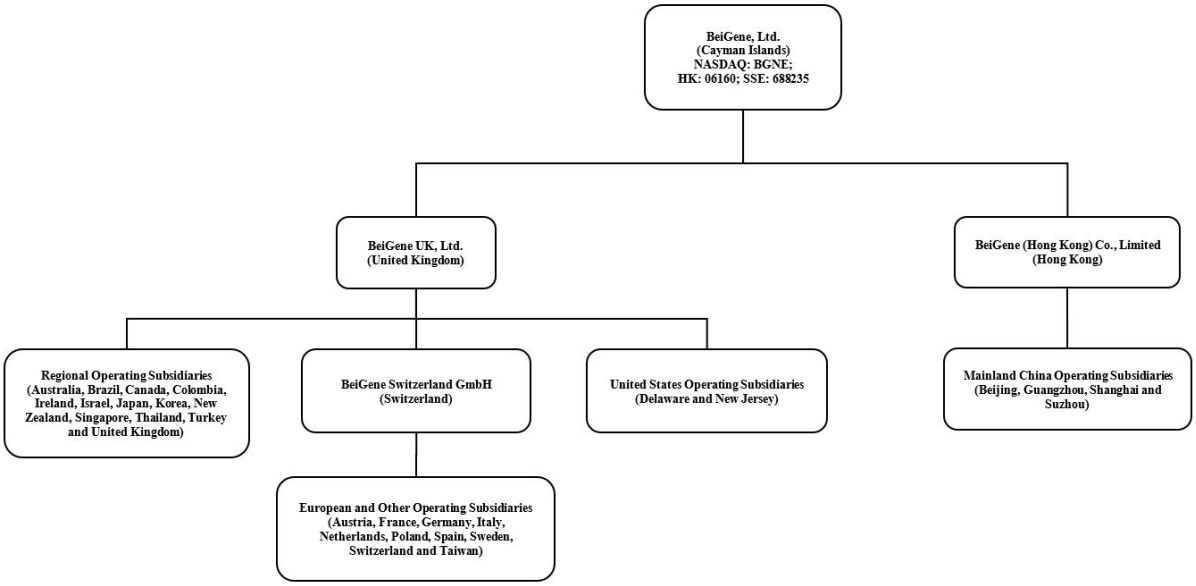
We are committed to advancing best and first-in-class clinical candidates internally or with like-minded partners to develop impactful and affordable medicines for patients across the globe. Our internal clinical development capabilities are deep, including a more than 2,700-person global clinical development and medical affairs team that is running more than 80 ongoing or planned clinical trials in over 50 medicines and drug candidates. This includes more than 30 pivotal or potentially registration-enabling trials across our portfolio, including our three internally discovered, approved medicines. We have enrolled in our clinical trials more than 18,000 subjects, of which approximately one-half have been outside of China.

We have built, and are expanding, our internal manufacturing capabilities through our state-of-the-art biologic and small molecule manufacturing facilities in China to support current and potential future demand of our medicines, and are building a commercial-stage biologics manufacturing and clinical R&D center in New Jersey. We also work with high quality contract manufacturing organizations ("CMOs") to manufacture our internally developed clinical and commercial products.

Since our inception in 2010, we have become a fully integrated global organization of over 9,000 employees in 29 countries and regions, including the United States, China, Europe, and Australia.

Our Holding Company Structure

We are a holding company incorporated in the Cayman Islands with operations primarily conducted through our subsidiaries in the United States, China, United Kingdom, Switzerland and Australia. The following diagram depicts a summary of our corporate structure. Currently, our corporate structure contains no variable interest entities.



Our Strategy

We were founded with the vision to create an integrated biopharmaceutical company to transform the biotech industry, creating impactful medicines that will be affordable and accessible to far more patients around the world. We have made significant progress towards accomplishing this vision over our first 12 years and have five strategic competitive advantages positioning us for success both near- and long-term:

1. **We have built one of the world's largest, most productive and cost-effective oncology research teams** with more than 950 scientists. Their efforts have been validated by commercial approvals, clinical data, and collaborations that have secured $1.4 billion in collaboration payments to the company. We have successfully developed three commercially approved medicines from our internal discovery engine, including BRUKINSA and tislelizumab. We design each research program with a differentiated biological hypothesis or a first-in-class mechanism of action. Our lead medicine, BRUKINSA, has demonstrated superiority for both progression-free survival and overall response rate versus ibrutinib in relapsed or refractory CLL. Our broad pipeline also includes internally developed products with the potential to be best-in-class or first-in-class, including our BCL-2 inhibitor, BGB-11417, our HPK1 inhibitor, BGB-15025, and BGB-16673, a BTK-targeted CDAC program that has demonstrated its potential with early data. Our pipeline also includes many early-stage assets for targets like OX40, LAG-3, and TIM-3. We have invested in technology platforms, including CDAC protein degraders, bispecific antibodies, tri-specific antibodies, ADC, CAR-NK, and mRNA. Our research and innovation capabilities will ensure we discover high-quality and impactful medicines for patients.

2. **We have built a substantial global clinical development team** of 2,300 people on five continents, allowing us to run clinical trials predominantly without reliance on third party contract research organizations ("CROs"). Clinical development accounts for over 75% of the cost and most of the time to develop a medicine. We believe that by fully integrating these capabilities, we can create a strategic competitive advantage. By retaining clinical development activities internally, we can decrease the costs of our trials, increase enrollment speed, and leverage technology to ensure quality and consistency across trials and clinical sites. It also allows us to become more inclusive in the location and number of clinical sites to help improve the diversity of patients in our trials. Our demonstrated ability to complete large-scale, multi-regional clinical trials is one of our most important strategic competitive advantages and addresses an immense challenge in the pharmaceutical industry.

3. **We have built a strong commercial portfolio, centered around two cornerstone medicines, BRUKINSA and tislelizumab,** that are becoming primary revenue sources and will support the development of our future pipeline and

additional combination therapies. Our hematological franchise is led by BRUKINSA, which is supported by a broad clinical program with over 4,800 patients in 35 trials in 29 markets. We ran two extensive head-to-head studies versus ibrutinib with over 800 patients enrolled. We are the first and only BTK inhibitor to demonstrate superior efficacy versus ibrutinib, and the data from the head-to-head ALPINE trial were selected for the prestigious late-breaker session at the American Society of Hematology ("ASH") meeting in late 2022, with simultaneous publication in *The New England Journal of Medicine*. Based on the pooled safety data generated from our trials, we have shown a very favorable safety profile, especially when compared to ibrutinib in cardiovascular safety, including atrial fibrillation, ventricle arrhythmia, and hypertension. We believe BRUKINSA allows us to build a strong position in heme-oncology with our pipeline medicines, including our BCL-2 inhibitor, in both monotherapy and combination settings. Our solid tumor franchise is led by our anti-PD-1 monoclonal antibody, tislelizumab, which is currently approved in China in ten indications. Tislelizumab has achieved the commercial market leader position in China in the PD-1/PDL-1 class. Outside of China, in conjunction with our partner Novartis, we have filed applications for approval in the U.S. and EU. With tislelizumab and the potentially best-in-class or first-in-class pipeline assets targeting OX40, TIGIT, LAG-3, and TIM-3, we are well-positioned to build our immuno-oncology business and deliver innovative therapies and combinations to patients.

4. **We have a differentiated international commercial organization** of over 3,500 people to deliver medicines to patients around the globe. In China, the commercial team is actively driving the uptake of our internally developed and partnered medicines across solid tumors and hematology. BRUKINSA and tislelizumab have achieved market leadership positions in China in the BTKi and PD-1/PDL-1 classes, respectively, and we have launched and sell more than 13 products from our business partners around the globe. In North America, our U.S. team has continued to grow BRUKINSA sales as we launch new indications and expand to Canada. In Europe, we have built a targeted commercial team focused on medical thought leaders in blood cancer treatments. Altogether, BRUKINSA has been approved in over 65 markets, with additional filings pending or planned. Our strategy is to commercialize our medicines broadly throughout the world. Our commercial capabilities have expanded into the Asia Pacific region through our affiliates, the Latin America region, and other emerging markets through distribution partners. We have built a global commercial organization that will drive the delivery of highly effective and differentiated medicines to patients around the globe, and will collaborate with business partners to bridge health inequities.

5. **We have financial strength**. In a time when the cost of capital has risen, we are well positioned financially. We already have substantial revenue from our cornerstone assets, which we expect to continue to grow significantly in 2023 and beyond. We expect product revenue growth to outpace our operating expense growth in the near-term, which will allow us to continue to improve our operating leverage. We will continue to be thoughtful and strategic in how we deploy our capital, and we are committed to generating long-term value.

Our Commercial and Registration Stage Products

The following table summarizes the status of our commercial products and new products that are pending approval as of February 27, 2023:

PRODUCT	LEAD INDICATIONS	MECHANISM OF ACTION	REGULATORY STATUS	BEIGENE COMMERCIAL RIGHTS	PARTNER
Brukinsa™ 80mg zanubrutinib capsules	U.S.: CLL/SLL, R/R MCL[1], WM & R/R MZL[1]; China: R/R MCL[2], R/R CLL/SLL[2] & R/R WM[2]; EU[3]: WM, R/R MZL, R/R CLL/SLL	BTK inhibitor	Approved in more than 65 markets, incl. U.S., China, EU and other markets	Global	N/A
Tislelizumab	1L Squamous and Non-Squamous NSCLC/ 2/3 L NSCLC/ R/R classical Hodgkin's lymphoma[2] / 2/3 L HCC[2]/ R/R PD-L1+ UC[2], MSI-H or dMMR solid tumors, 2L ESCC, 1L NPC, 1L GC/GEJC	Anti-PD-1 antibody	Approved in China; BLA accepted in U.S.[4]; MAA accepted in EU[4]	Outside North America, Japan, EU and six other European countries	NOVARTIS
Partruvix pamiparib	3L BRCA-mutated ovarian cancer[2]	PARP inhibitor	Approved in China	Global	N/A
XGEVA® (denosumab) injection	Giant cell tumor of bone[8] / Skeletal Related Events (SREs)[8]	Anti-RANK ligand antibody	Approved in China	Mainland China	AMGEN
BLINCYTO® (blinatumomab) for injection 35 mcg single-dose vial	R/R Acute lymphocytic leukemia[8]	Anti-CD19 x anti-CD3 bispecific T-cell engager (BiTE)	Approved in China	Mainland China	AMGEN
Kyprolis® (carfilzomib) for Injection	R/R Multiple myeloma[8]	Proteasome inhibitor	Approved in China	Mainland China	AMGEN
Revlimid® (lenalidomide) capsules 2.5 · 5 · 10 · 15 · 20 · 25 mg	R/R adult multiple myeloma, newly diagnosed multiple myeloma, previously treated follicular lymphoma	Anti-angiogenesis, immuno-modulation	Approved in China	Mainland China	Bristol Myers Squibb™
Vidaza® azacitidine for injection	Myelodysplastic syndromes, acute myeloid leukemia, chronic myelomonocytic leukemia	DNA hypomethylation	Approved in China	Mainland China	Bristol Myers Squibb™
sylvant® siltuximab	Idiopathic multicentric Castleman disease	IL-6 antagonist	Approved in China	Greater China	EUSAPharma
Qarziba®▼ Dinutuximab beta	High-risk neuroblastoma[2]	Anti-GD2 antibody	Approved in China	Mainland China	EUSAPharma
POBEVCY® (Avastin biosimilar)	Colorectal and lung cancers	Anti-VEGF antibody	Approved in China	Greater China	百奥泰 BIO-THERA
TAFINLAR® (dabrafenib)	Melanoma[5]	BRAF inhibitor	Approved in China	China Broad Markets[7]	NOVARTIS
MEKINIST® (trametinib)	Melanoma[5]	MEK inhibitor	Approved in China	China Broad Markets[7]	NOVARTIS
VOTRIENT® (pazopanib)	Advance renal cell carcinoma	VEGFR inhibitor	Approved in China	China Broad Markets[7]	NOVARTIS
AFINITOR® (everolimus)	Advanced renal cell carcinoma[6]	mTOR inhibitor	Approved in China	China Broad Markets[7]	NOVARTIS
ZYKADIA® (ceritinib)	ALK + NSCLC	ALK inhibitor	Approved in China	China Broad Markets[7]	NOVARTIS

1. Approved under accelerated approval. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial. 2. Conditionally approved. Full approval for these indications is contingent upon results from ongoing randomized, controlled confirmatory clinical trials. 3. The approval is applicable to all 27 EU member states, plus Iceland, Lichtenstein and Norway. 4. U.S.: For patients with unresectable recurrent locally advanced or metastatic ESCC after prior systemic therapy. EU: For patients with advanced or metastatic ESCC after prior systemic chemotherapy and for patients with NSCLC including: locally advanced or metastatic NSCLC after prior chemo, in combination with chemotherapy for 1L advanced or metastatic squamous NSCLC, and in combination with chemotherapy for 1L locally advanced or metastatic non-squamous NSCLC with no EGFR or ALK positive mutations. 5. TAFINLAR and MEKINIST are being investigated in combination by Novartis for NSCLC indications. 6. Following progression on or after vascular endothelial growth factor (VEGF)-targeted therapy. 7. Rights to promote and market in China's broad markets pursuant to a Market Development Agreement with an affiliate of Novartis Pharma AG. 8. Conditionally approved. Full approval of any particular indication will depend on the results of required post-marketing study(ies) in China.

Abbreviations: ALK = anaplastic lymphoma kinase; BLA = Biologics License Application; BRAF = B-rapidly accelerated fibrosarcoma; CLL = chronic lymphocytic leukemia; EGFR = epidermal growth factor receptor; ESCC = esophageal squamous cell carcinoma; GC = gastric cancer; GEJC = gastroesophageal junction cancer; HCC = hepatocellular carcinoma; MAA = marketing aothorization application; MCL = mantle cell lymphoma; MEK = mitogen-activated protein kinase (MAPK) / Extracellular-signal regulated kinase (ERK); mTOR = Mammalian target of rapamycin; MZL = marginal zone lymphoma; NPC = nasopharyngeal cancer; NSCLC = non-small cell lung cancer; R/R = relapsed / refractory; SLL = small lymphocytic lymphoma; UC = urothelial carcinoma; VEGFR = vascular endothelial growth factor receptor; WM = Waldenström's macroglobulinemia

We commercialize the following internally developed cancer medicines:

BRUKINSA

BRUKINSA is a next-generation small molecule inhibitor of BTK designed to maximize BTK occupancy and minimize off-target binding effects. Zanubrutinib is an orally active inhibitor that covalently binds to BTK, resulting in irreversible inactivation of the enzyme.

We are marketing BRUKINSA in the United States, China, Europe, the United Kingdom, Canada, Australia and other markets.

In the United States, BRUKINSA received accelerated approval as a treatment for mantle cell lymphoma (MCL) in adult patients who have received at least one prior therapy (November 2019), and has since also been approved for patients with Waldenström's macroglobulinemia (WM) and relapsed or refractory (R/R) marginal zone lymphoma (MZL) who have received at least one anti-CD20-based regimen. The MCL and MZL indications were approved under accelerated approval based on overall response rate. Continued approval for these indications may be contingent upon verification and description of clinical benefit in a confirmatory trial. In January 2023, BRUKINSA was approved by the U.S. Food and Drug Administration (FDA) for the treatment of adult patients with CLL or small lymphocytic lymphoma (SLL).

In Europe, BRUKINSA has received approval from the European Commission ("EC") for the treatment of adult patients with WM who have received at least one prior therapy or for the first-line treatment of patients unsuitable for chemo-immunotherapy, as well as for the treatment of patients with MZL and for the treatment of patients with CLL.

In China, BRUKINSA has received conditional approval for adult patients with MCL who have received at least one prior therapy and adult patients with CLL or SLL who have received at least one prior therapy and for the treatment of patients with R/R WM. In addition, a supplemental new drug application ("sNDA") has been accepted for review by the China National Medical Products Administration ("NMPA") for the treatment of adult patients with treatment-naïve CLL or SLL and WM. In December 2021, we announced the inclusion of BRUKINSA for R/R WM in the updated National Reimbursement Drug List ("NRDL") by the China National Healthcare Security Administration ("NHSA"). Currently, all three approved indications for BRUKINSA are included in the NRDL.

BRUKINSA is approved across several indications in more than 65 markets as of February 2023.

Market Opportunity

Lymphomas are blood-borne cancers involving lymphatic cells of the immune system. They can be broadly categorized into non-Hodgkin's lymphoma and Hodgkin's lymphoma. In 2022, estimated global revenues for BTK inhibitors were approximately $8.5 billion according to published reports. Global revenues are projected to be more than $20 billion in 2026, according to published reports.

Tislelizumab

Tislelizumab is a humanized IgG4 monoclonal antibody against the immune checkpoint receptor programmed cell death protein 1 (PD-1) that we specifically designed to minimize binding to Fc receptor gamma (FcγR), which is believed to play an essential role in activating phagocytosis in macrophages, to minimize its negative impact on T effector cells.

Tislelizumab is approved in China in ten indications, including full approval for the first-line treatment of patients with locally advanced unresectable or metastatic gastric or gastroesophageal junction adenocarcinoma with high PD-L1 expression in combination with fluoropyrimidine and platinum chemotherapy, first-line treatment of patients with advanced squamous non-small cell lung cancer (NSCLC) in combination with chemotherapy, for first-line treatment of patients with advanced non-squamous NSCLC in combination with chemotherapy, for second- or third-line treatment of patients with locally advanced or metastatic NSCLC who progressed on prior platinum-based chemotherapy, for the treatment of patients with locally advanced or metastatic esophageal squamous cell carcinoma (ESCC) who have disease progression following or are intolerant to first-line standard chemotherapy, and for first-line treatment of patients with recurrent or metastatic nasopharyngeal cancer (NPC). The NMPA also granted conditional approval for the treatment of patients with classical Hodgkin's lymphoma (cHL) who received at least two prior therapies, for the treatment of patients with locally advanced or metastatic urothelial carcinoma (UC) with PD-L1 high expression whose disease progressed during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy, for the treatment of patients with hepatocellular carcinoma (HCC) who have received at least one systemic therapy, for patients with previously treated, locally advanced unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair-deficient (dMMR) solid tumors. Full approval for these indications is contingent upon results from ongoing randomized, controlled, confirmatory clinical trials. Tislelizumab was included in the NRDL in 2020 for cHL and UC, in 2021 for non-squamous NSCLC, squamous NSCLC and HCC, and in 2022 for locally advanced or metastatic NSCLC, for MSI-H solid tumors, for locally advanced or metastatic ESCC following progression or intolerance to prior first-line chemotherapy, and for first-line recurrent or metastatic NPC.

In addition, we have submitted two supplemental Biologics License Applications ("sBLAs") for tislelizumab that are under review by the Center for Drug Evaluation ("CDE") of the NMPA, including for patients with first-line unresectable or metastatic hepatocellular carcinoma (HCC), and in combination with chemotherapy as first-line treatment in patients with unresectable locally advanced, recurrent or metastatic esophageal squamous cell carcinoma.

We are evaluating tislelizumab in a broad pivotal clinical program for both solid tumor and hematological indications, both globally and in China. We have initiated or completed 17 potentially registration-enabling clinical trials in China and globally, including 13 Phase 3 trials and four pivotal Phase 2 trials.

In January 2021, we announced a collaboration and license agreement with Novartis to develop, manufacture and commercialize tislelizumab in the United States, Canada, Mexico, the EU, UK, Norway, Switzerland, Iceland, Liechtenstein, Russia and Japan (the "Novartis Territory"). We retained worldwide rights to commercialize outside of the Novartis Territory and with our proprietary products in combination with tislelizumab.

In the United States, we have filed a BLA with the FDA for tislelizumab as a treatment for patients with unresectable recurrent locally advanced or metastatic ESCC after prior systemic therapy. In addition, Novartis has disclosed plans to submit additional marketing applications in its territory.

Market Opportunity

Globally, the top four PD-1/PD-L1 antibody medicines had revenues of approximately $36 billion in 2022 based on public reports. The 2022 China PD-1/L1 market (net revenue) was approximately $2.2 billion.

Global revenues are projected to be more than $50 billion by 2025 according to published reports, driven by multiple factors including indication expansion, approvals and adoptions in earlier lines of therapies, further market penetration, and extension of duration of therapy.

Pamiparib

Pamiparib is a selective small molecule inhibitor of poly ADP-ribose polymerase 1 (PARP1) and PARP2 enzymes. Pamiparib has demonstrated pharmacological properties such as brain penetration and PARP-DNA complex trapping in preclinical models. Pamiparib is currently in global clinical development as a monotherapy or in combination with other agents for a variety of solid tumor malignancies. To date, more than 1,300 patients have been enrolled in clinical trials of pamiparib.

In China, pamiparib received conditional approval for treatment of patients with germline BRCA (gBRCA) mutation-associated recurrent advanced ovarian, fallopian tube, or primary peritoneal cancer who have been treated with two or more lines of chemotherapy in May 2021. Full approval for this indication is contingent upon results from ongoing corroborative trials confirming the clinical benefit of pamiparib in this population. Pamiparib was included in the 2021 NRDL in its approved indication.

We are currently commercializing, or plan to commercialize, the following cancer medicines in China under an exclusive license from Amgen:

XGEVA®

XGEVA (denosumab) is an antibody-based RANK ligand (RANKL) inhibitor that was approved globally for the prevention of skeletal-related events ("SREs") in patients with bone metastases from solid tumors and in patients with multiple myeloma, and for the treatment of adults and skeletally mature adolescents with giant cell tumor of bone (GCTB). XGEVA is approved in over 70 countries worldwide. In China, XGEVA received conditional approval in the GCTB indication in May 2019 and received conditional approval for the SRE indications in November 2020. We began marketing XGEVA in China in July 2020. In December 2020, we announced the inclusion of XGEVA in the NRDL for the treatment of GCTB, which was successfully renewed for inclusion in 2023.

BLINCYTO®

BLINCYTO (blinatumomab), a bispecific CD-19 directed CD3 T-cell engager, is the first and only approved bi-specific T-cell engager (BiTE) immunotherapy. It has been approved in 60 countries for use in patients with acute lymphoblastic leukemia (ALL). In China, BLINCYTO received conditional approval as a treatment for adult patients with R/R ALL in December 2020 and was conditionally approved in April 2022 for pediatric patients with R/R B-cell precursor ALL. We began commercializing BLINCYTO in August 2021.

KYPROLIS®

KYPROLIS (carfilzomib), a proteasome inhibitor, has been approved in over 60 countries for use in patients with R/R multiple myeloma (MM). It was approved in China as a treatment for patients with R/R MM in July 2021 and we began commercializing KYPROLIS in January 2022. KYPROLIS was included on the NRDL beginning in March 2023 for its approved indication in China.

We commercialize the following cancer medicines in China under an exclusive license from BMS:

REVLIMID®

REVLIMID (lenalidomide) is an oral immunomodulatory medicine that was approved in China in 2013 for the treatment of multiple myeloma (MM) in combination with dexamethasone in adult patients who have received at least one prior therapy. In February 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.

REVLIMID was listed on the NRDL in June 2017. In November 2019, we announced that REVLIMID received formal inclusion on the NRDL in China for R/R multiple myeloma. In November 2020 our sNDA for the use of REVLIMID in combination with rituximab in adult patients with previously treated follicular lymphoma was approved by the NMPA.

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 (MDS), chronic myelomonocyte leukemia (CMML) and acute myeloid leukemia (AML) with 20% to 30% blasts and multi-lineage dysplasia. In January 2018, VIDAZA became commercially available in China.

In addition to REVLIMID and VIDAZA, we previously commercialized ABRAXANE® (paclitaxel albumin-bound particles for injectable suspension), a solvent-free chemotherapy approved for use in certain patients with metastatic breast cancer, in China until March 2020. On March 25, 2020, the NMPA suspended the importation, sales and use of ABRAXANE in China supplied to us by BMS, and the drug was subsequently recalled by BMS and is not currently available for sale in China. This suspension was based on inspection findings at BMS's contract manufacturing facility in the United States. Additionally, in October 2021, BMS provided 180-days' notice to us, which we dispute, purporting to terminate our license to market ABRAXANE in China. We have not had any sales of ABRAXANE since the suspension and do not expect future revenue from ABRAXANE. We have initiated an arbitration proceeding against BMS asserting that it has breached and continues to breach the terms and conditions of the license and supply agreement. For additional information, please see the section of this Annual Report titled "Legal Proceedings".

We are commercializing or planning to commercialize the following medicines in China under an exclusive license from EUSA Pharma:

SYLVANT®

SYLVANT (siltuximab), an interleukin-6 (IL-6) antagonist, was approved as a treatment for patients with idiopathic multicentric Castleman disease (iMCD) who are human immunodeficiency virus (HIV) negative and human herpesvirus-8 (HHV-8) negative. SYLVANT was approved in China in December 2021 for the treatment of adult patients with multicentric Castleman disease (MCD) who are human immunodeficiency virus (HIV) negative and human herpes virus-8 (HHV-8) negative, also known as idiopathic MCD (iMCD).

QARZIBA®▼

QARZIBA (dinutuximab beta), a mouse-human chimeric monoclonal GD2 antibody, was granted conditional approval by the NMPA for the treatment of high-risk neuroblastoma in patients aged 12 months and above who have previously received induction chemotherapy and achieved at least a partial response, followed by myeloablative therapy and stem cell transplantation, as well as patients with a history of relapsed or refractory (R/R) neuroblastoma with or without residual disease. We began commercializing QARZIBA in December 2021.

We commercialize the following product in China under an exclusive license from Bio-Thera:

POBEVCY® (BAT1706)

POBEVCY is a biosimilar to Avastin (bevacizumab) developed by Bio-Thera Solutions, Ltd., a commercial-stage biopharmaceutical company located in Guangzhou, China. In China, Avastin is approved for the treatment of patients with metastatic colorectal cancer, liver cancer and NSCLC.

POBEVCY was approved by the NMPA in China in November 2021 and launched in late 2021 for the treatment of patients with advanced, metastatic or recurrent NSCLC and metastatic colorectal cancer.

We have acquired the right to develop, manufacture and commercialize POBEVCY in China, including Hong Kong, Macau, and Taiwan. Bio-Thera submitted a marketing application to the EMA and a BLA to the FDA in November 2020.

Reimbursement and Market Access

Our sales are largely dependent on the availability and extent of coverage and reimbursement by third party payors. In many markets these third parties are government health systems and in some markets such as the United States there are also private payors such as private health insurers and health systems. In 2022, we commercialized our products in 60 markets.

In China, there is one main payor, the government's national health care coverage system, which provides Basic Medical Insurance to the majority (greater than 95%) of China's approximately 1.4 billion people. There are three types of coverage plans in China at the national level that depend on if a resident lives in an urban or rural setting and if they are employed. The different plans have different characteristics in terms of how the plan is paid for and what it covers. Coverage and reimbursement of pharmaceuticals in China comes under the purview of the NHSA, which oversees the NRDL. The NRDL is composed of three lists. The 'A' and 'B' list are commonly referred to as the 'regular' lists. The A list generally includes older, off-patent medicines, while the B list generally includes newer medicines, some with remaining patent protection, which are reimbursed at a lower rate compared to the A list. In 2017, a third list was added to the system, often referred to as the 'C' list or the 'negotiation' list. This list generally includes newer innovative medicines which are accepted on the list after successful negotiation between the NHSA and the company. Typically, inclusion on the C list is accompanied by a discount to the prevailing list price in China for the medicine at the time of inclusion. The NRDL price for a medicine is its prevailing price in China, but the actual reimbursement rate that is used can be modified at the provincial level. Innovatively, in the 2022 NRDL, a price bidding process for non-exclusive drugs was undertaken on the C list to set the national reimbursement price benchmark.

Several of our medicines are listed on the NRDL. In the most recent NRDL list announced in January 2023, the following medicines were included in the NRDL, effective March 1, 2023:

- Tislelizumab in nine of its eligible approved indications:
  - For the treatment of adult patients with locally advanced or metastatic non-squamous non-small cell lung cancer (NSCLC) who are negative for epidermal growth factor receptor (EGFR) and anaplastic mesenchymal lymphoma kinase (ALK) mutations and have progressed after or are intolerant of prior chemotherapy with platinum-containing regimens; and adult patients with locally advanced or metastatic squamous NSCLC who are negative

or unknown for EGFR and ALK mutations and have progressed after or are intolerant of prior chemotherapy with platinum-containing regimens (approved in January 2022 and included in the NRDL in 2023);

- For the treatment of adult patients with advanced unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) solid tumors: patients with advanced colorectal cancer with disease progression after prior treatment with fluoropyrimidines, oxaliplatin and irinotecan; patients with other advanced solid tumors with disease progression after prior treatment and no satisfactory alternative treatment options (approved in March 2022 and included in the NRDL in 2023);
- For the treatment of patients with locally advanced or metastatic esophageal squamous cell carcinoma who have progressed after or are intolerant of prior first-line standard chemotherapy (approved in April 2022 and included in the NRDL in 2023);
- As a first-line treatment for patients with recurrent or metastatic nasopharyngeal cancer (approved in June 2022 and included in the NRDL in 2023);
- For use in combination with pemetrexed and platinum chemotherapy as a first-line treatment in patients with unresectable, locally advanced or metastatic non-squamous non-small cell lung cancer (NSCLC), with EGFR genomic tumor aberrations negative and ALK genomic tumor negative (approved in June 2021 and included in the NRDL in 2021);
- For the treatment of patients with hepatocellular carcinoma (HCC) who have been previously treated with at least one systemic therapy (conditionally approved in June 2021 and included in the NRDL in 2021);
- For use in combination with paclitaxel and carboplatin as a first-line treatment in patients with unresectable, locally advanced or metastatic squamous NSCLC (approved in January 2021 and included in the NRDL in 2021);
- For the treatment of patients with locally advanced or metastatic urothelial carcinoma (UC) with PD-L1 high expression whose disease progressed during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy (conditionally approved in April 2020 and included in NRDL in 2020); and
- For the treatment of patients with classical Hodgkin's lymphoma (cHL) who have received at least two prior therapies (conditionally approved in December 2019 and included in the NRDL in 2020).

- BRUKINSA in all three of its approved indications:
  - For the treatment of adult patients with Waldenström's macroglobulinemia (WM) who have received at least one prior therapy (conditionally approved in June 2021 and included in the NRDL in 2021);
  - For the treatment of adult patients with MCL who have received at least one prior therapy (conditionally approved in June 2020 and included in the NRDL in 2020); and
  - For the treatment of adult patients with chronic lymphocytic leukemia (CLL) /small lymphocytic lymphoma (SLL) who have received at least one prior therapy (conditionally approved in June 2020 and included in the NRDL in 2020).
- Pamiparib in its approved indication:
  - For the treatment of patients with germline BRCA (gBRCA) mutation-associated recurrent advanced ovarian, fallopian tube, or primary peritoneal cancer who have been treated with two or more lines of chemotherapy (conditionally approved in May 2021 and included in the NRDL in 2021).
- KYPROLIS in its approved indication as of March 1, 2023:
  - For the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least two prior therapies, including a proteasome inhibitor and an immunomodulatory agent.
- XGEVA was successfully renewed in NRDL as of March 2023 in its approved indication:
  - For the treatment of patients with giant cell tumor of the bone (GCTB) that is unresectable or where surgical resection is likely to result in severe morbidity (first included in NRDL in 2020).

Additionally, two of our medicines were listed in past NRDLs: REVLIMID was included in the 2017 NRDL negotiation list and later received formal inclusion in the 2019 B list, while VIDAZA was listed in the 2018 NRDL negotiation list and later received formal inclusion to the 2020 B list.

In 2018, China started a new program to centrally purchase non-exclusive medicines for the nation's health care system called "volume-based procurement", or "group purchasing organization" or "4+7" when the program was first piloted in 11 major cities. After the 2018 pilot program, it was implemented nationally in 2019. It is a tender-based system that provides guaranteed volume for lowered pricing. Participation in the program requires a product to have passed a generic quality consistency evaluation, which in turn requires passing a bioequivalence comparison to the reference listed drug (RLD). The system offers a major portion of a market's volume to winning bidders. More than one company can win a given tender, and more guaranteed volume is awarded as more bidders win. The system is still evolving and, as such, the exact terms of how many bidders win and what amount of volume are won and at what price is also evolving.

It is common in China for pharmaceutical companies to employ patient assistance programs to help patients afford their innovative medicines. Usually these programs have been offered to patients who are self-paying. A typical program provides a certain number of free doses to patients after a certain number of doses have been paid for. Usually these programs end when a medicine is included in the NRDL. We offer these types of patient assistance programs to our patients.

In the United States, most health insurance coverage is provided by private insurers, often accessed via employer-sponsored plans, and the two main public insurance programs, Medicare and Medicaid. All three types of programs usually have some type of coverage for pharmaceutical products. Often this is through a pharmacy benefit manager ("PBM"). The structure of the pharmacy benefit can be quite different for different beneficiaries depending on the negotiations between plan sponsors and plan purchasers. There is no central list of covered pharmaceuticals in the United States, as there is no single payer system. As such, the prices paid for pharmaceuticals in the United States can vary.

We offer patient assistance programs in the United States under our myBeiGene program. This program seeks to enhance access to BRUKINSA by assisting with obtaining reimbursement, co-pay assistance when allowed, temporary supply of free product for insurance delays, and free product assistance for some uninsured and underinsured patients. The programs also seek to support patients and caregivers by providing education and information about BRUKINSA and its approved indications, nurse advocates, and connecting patients to sources of support such as support groups and transportation/lodging assistance.

Our Pipeline Products

The following table summarizes the status of our internally-discovered drug candidates as of February 27, 2023:

ASSET	PROGRAM	PHASE 1	PHASE 2	PHASE 3
Zanubrutinib	monotherapy			R/R CLL/SLL
	+ rituximab			TN MCL and R/R MZL
	+/- venetoclax			TN CLL/SLL
	+ obinutuzumab		R/R FL	
Tislelizumab	monotherapy			2L advanced ESCC, 1L HCC, 2L/3L NSCLC
			Previously treated HCC, R/R cHL	
	+ chemotherapy			1L advanced ESCC, 1L GC/GEJC, 1L NPC
	+ zanidatamab + chemotherapy			1L GEA
	+ sitravatinib			2L NSCLC
		Solid tumors		
	+ fruquintinib		Solid tumors	
Ociperlimab	+ tislelizumab			1L PD-L1 high NSCLC
			2L PD-L1+ESCC, 2/3 L cervical cancer	
		Solid tumors		
	+ tislelizumab + chemotherapy		1L NSCLC	
	+ tislelzumab + concurrent chemoradiotherapy			LA NSCLC (PD-L!+)
			1L LS-SCLC	
Surzebiclimab	+ tislelizumab +/- LBL-007		Solid tumors	
BGB-A445	+ tislelizumab	Solid tumors		
BGB-10188	+ tislelizumab	Solid tumors		
	+/- zanubrutinib	B-cell lymphoid malignancies		
	+/- tislelizumab	B-cell malignancies		
BGB-15025	+ tislelizumab	Solid tumors		
Pamiparib	monotherapy		1L maintenance platinum-sensitive GC	
	+ temozolomide	Solid tumors		
BGB-3245	monotherapy	Solid tumors with BRAF mutations		
Lifirafenib	+ mirdametinib	Solid tumors		
BGB-11417	monotherapy		R/R MCL, R/R CLL/SLL	
	+/- zanubrutinib	Mature B-cell malignancies		
	+ azacitidine +/- posaconazole		Myeloid malignancies	
	+ dexamethasone +/- carfilzomib		R/R multiple myelome with t (11;14)	
BGB-16673	monotherapy	B-cell malignancies		
BGB-23339	monotherapy	Inflammation and immunology		
BGB-24714	+/- chemotherapy	Solid tumors		
BGB-B167	+/- tislelizumab	Solid tumors		

Abbreviations: cHL = classical Hodgkin lymphoma; CLL = chronic lymphocytic leukemia; ESCC = esophageal squamous-cell carcinoma; FL = follicular lymphoma; GC = gastric cancer; GEA = gastroesophageal adenocarcinoma; GEJC = gastroesophaegeal junction cancer; HCC = hepatocellular carcinoma; MCL = mantle cell lymphoma; MZL = marginal zone lymphoma; NPC = nasopharyngeal carcinoma; NSCLC = non-small cell lung cancer; R/R = relapsed/ refractory; SCLC = small cell lung cancer; SLL = small lymphocytic lymphoma; TN = treatment treatment-naïve

The following table summarizes the status of our in-licensed drug candidates as of February 27, 2023:

Partner	Molecule / Asset	Indications	Phase	Commercial Rights
AMGEN	Sotorasib	Solid tumors, CRC, NSCLC	Phase 3	China
	tarlatamab ^^	SCLC	Phase 2	China
	acapatamab ^^	Prostate cancer, NSCLC	Phase 1	China
	AMG 176	Hematologic malignancies	Phase 1	China
	AMG 427 ^^	AML	Phase 1	China
	AMG 509	Prostate cancer	Phase 1	China
	AMG 199 ^^	GC/GEJC	Phase 1	China
	AMG 650	Solid tumors	Phase 1	China
	AMG 256	Solid tumors	Phase 1	China
MIRATI THERAPEUTICS	Sitravatinib † + Tislelizumab	NSCLC	Phase 3	Asia, Australia, New Zealand
	Sitravatinib † + Tislelizumab	HCC, GC/GEJC	Phase 2	Asia, Australia, New Zealand
	Sitravatinib † + Tislelizumab	Solid tumors	Phase 1	Asia, Australia, New Zealand
zymeworks	Zanidatamab + chemo + Tislelizumab	GEA	Phase 3	Asia, Australia, New Zealand
	Zanidatamab (monotherapy)	BTC	Phase 2	Asia, Australia, New Zealand
	Zanidatamab	BC, GC, GEA	Phase 2	Asia, Australia, New Zealand
	ZW49	HER2 expressing cancers	Phase 1	Asia, Australia, New Zealand
SpringWorks THERAPEUTICS	BGB-3245[1]	Solid tumors	Phase 1	Asia
Seagen	SEA-CD70	MDS, AML	Phase 1	Asia, Australia, New Zealand
leaptherapeutics	DKN-01 + Tislelizumab + Chemo	GC/GEJC	Phase 2	Asia, Australia, New Zealand
Leads Biolabs	LBL-007 + Tislelizumab	Advanced solid tumors	Phase 2	Ex-China
assemblybio	ABI-H3733	Chronic hepatitis B virus	Phase 1	China

^ BiTE® molecule; ^^ Half-life extended BiTE®; † XmAb® is a registered trademark of Xencor, Inc. Mirati is also conducting its own clinical studies with sitravatinib, including the Phas3 SAPPHIRE trial in non Sq NSCLC; †† ZW25; 1 By MapKure, a JV with SpringWorks

Abbreviations: AML = acute myelogenous leukemia; BC = breast cancer; BTC = biliary tract cancers; CRC = colorectal cancer; GC = gastric cancer; GEA = gastroesophageal adenocarcinoma; GEJC = gastroesophaegeal junction cancer; HCC = hepatocellular carcinoma; MDS = myelodysplastic syndromes; NSCLC = non-small cell lung cancer; SCLC = small cell lung cancer

Our Commercial- and Clinical-Stage Drug Candidates

A description of our commercial- and clinical-stage drug candidates and clinical data from selected clinical trials is set forth below. Historically, we have made available, and we intend to continue to make available, clinical data and/or topline results from clinical trials of our drug candidates in our press releases and/or filings with the U.S. Securities and Exchange Commission ("SEC"), the Stock Exchange of Hong Kong Limited ("HKEx"), and the Shanghai Stock Exchange ("SSE"), copies of which are available on the Investors section of our website.

Commercial-Stage

BRUKINSA (zanubrutinib), a BTK Inhibitor

We are currently evaluating zanubrutinib in a broad pivotal clinical program globally to treat a number of B-cell malignancies. Zanubrutinib has demonstrated sustained 24-hour BTK occupancy in both the peripheral blood and lymph node compartments in patients. Zanubrutinib is the only BTK inhibitor to demonstrate superior progression-free survival versus IMBRUVICA® (ibrutinib), an approved BTK inhibitor.

Overview of Clinical Development Program and Regulatory Status

We have announced BRUKINSA approvals around the world, including in the United States, China, the EU, the U.K., Canada, Australia, South Korea and Switzerland. As of December 2022, 26 additional marketing authorization applications for BRUKINSA have been submitted and are under review, including by BeiGene and with support from our five distribution partners: Adium Pharma in Latin America and the Caribbean, NewBridge Pharmaceuticals in the Middle East and North Africa, Erkim in Turkey, Nanolek in Russia, and Medison in Israel.

Based on the clinical data to date, we believe that BRUKINSA has a best-in-class profile, and we are running a broad global pivotal program in multiple indications, including 10 registration or registration-enabling clinical trials. Five of the 10 trials are Phase 3 and five are designed to be registration-enabling Phase 2 trials.

We have reported results from the monotherapy head-to-head Phase 3 trial versus ibrutinib in WM (ASPEN, NCT03053440), which has been included in several filings globally. We have also reported results from the Phase 3 trial comparing BRUKINSA to bendamustine and rituximab in patients with treatment-naïve (TN) CLL/SLL (SEQUOIA, NCT03336333) and the head-to-head Phase 3 trial in R/R CLL/SLL versus ibrutinib (ALPINE, NCT03734016). Both trials are the basis for our approvals in CLL in the U.S. and EU. Our fourth Phase 3 trial is an ongoing Phase 3 confirmatory trial in patients with TN MCL (NCT04002297). Our fifth Phase 3 trial is an ongoing Phase 3 confirmatory trial in patients with R/R follicular lymphoma (FL) or R/R MZL (NCT05100862). Additionally, we have five filed or ongoing Phase 2 trials that are designed to be registration-enabling, including four monotherapy studies in R/R MCL, R/R WM, R/R CLL/SLL (NCT03206970, NCT03332173, NCT03206918), and R/R MZL (MAGNOLIA, NCT03846427) and an ongoing pivotal Phase 2 trial in combination with GAZYVA® (obinutuzumab) in patients with R/R FL (ROSEWOOD, NCT03332017). Data from the ROSEWOOD trial were presented at the European Hematology Association (EHA) 2022, meeting its primary endpoint. Finally, we are also investigating zanubrutinib in several combination studies in MCL, MZL and CLL/SLL, including a Phase 3 trial in combination with venetoclax in front-line CLL/SLL.

We continue to pursue regulatory approvals for BRUKINSA globally. Besides our recent approvals in CLL/SLL in the United States (January 2023) and EU (November 2022) we expect continued regulatory decisions for some of our global filings this year, including potential additional approvals in more than 10 markets.

Tislelizumab, an anti-PD-1 Antibody

Tislelizumab is a humanized monoclonal antibody against the immune checkpoint receptor PD-1 that is currently being evaluated in pivotal clinical trials globally 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.

Overview of Clinical Development Program and Regulatory Status

BeiGene has initiated or completed 21 potentially registration-enabling clinical trials in China and globally, including 13 Phase 3 trials and four pivotal Phase 2 trials intended to support regulatory submissions globally and in China.

Our trials in lung cancer include:

- A global Phase 3 trial evaluating tislelizumab as a second- or third-line treatment compared to docetaxel in patients with locally advanced or metastatic NSCLC (NCT03358875);
- Two Phase 3 trials in China evaluating tislelizumab plus chemotherapy versus chemotherapy in squamous and non-squamous NSCLC (NCT03594747 and NCT03663205, respectively);
- A Phase 3 trial in China in 1L SCLC evaluating tislelizumab plus chemotherapy versus chemotherapy (NCT04005716); and
- A Phase 3 trial in China of tislelizumab in combination with platinum-based doublet chemotherapy as neoadjuvant treatment for patients with NSCLC (NCT04379635).

Our trials in liver cancer include:

- A global Phase 3 trial comparing tislelizumab with sorafenib as first-line treatment for patients with HCC (NCT03412773); and
- A global single-arm pivotal Phase 2 trial in second or third line unresectable HCC (NCT03419897).

Our trials in gastric cancer include:

- A global Phase 3 trial of tislelizumab combined with chemotherapy versus placebo combined with chemotherapy as first-line treatment for patients with gastric cancer (NCT03777657).

Our trials in lymphoma include:

- A Phase 3 trial in China comparing tislelizumab to salvage chemotherapy in patients with relapsed or refractory classical Hodgkin Lymphoma (cHL; NCT04486391); and
- A Phase 2 trial in China in patients with relapsed or refractory cHL (NCT03209973).

Our trials in urothelial carcinoma include:

- A Phase 3 trial in China in patients with locally advanced or metastatic urothelial carcinoma (NCT03967977); and
- Phase 2 trial in China in patients with locally advanced or metastatic urothelial bladder cancer (NCT04004221).

Our trials in ESCC include:

- A global Phase 3 trial comparing tislelizumab with chemotherapy as second-line treatment for patients with advanced ESCC (NCT03430843);
- A global Phase 3 trial of tislelizumab in combination with chemotherapy as first-line treatment for patients with ESCC (NCT03783442); and
- A Phase 3 trial in China of tislelizumab versus placebo in combination with chemoradiotherapy in patients with localized ESCC (NCT03957590).

Finally, our trials in solid tumors and nasopharyngeal cancer include:

- A Phase 2 trial in China in patients with MSI-H/dMMR solid tumors (NCT03736889); and
- A Phase 3 trial in China and Thailand of tislelizumab combined with chemotherapy versus placebo combined with chemotherapy as first-line treatment in patients with nasopharyngeal cancer (NCT03924986).

As of December 2022, we had enrolled over 11,000 subjects in clinical trials of tislelizumab in 31 geographies, including more than 4,000 subjects outside of China. These studies include 11 multi-regional registrational trials that are designed for global regulatory approvals. Data from our trials thus far suggested that tislelizumab was generally well-tolerated and exhibited anti-tumor activity in a variety of tumor types.

Pamiparib, a PARP1 and PARP2 Inhibitor

Pamiparib is a selective small molecule inhibitor of poly ADP-ribose polymerase 1 (PARP1) and PARP2 enzymes 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.

Overview of Clinical Development Program and Regulatory Status

In China, pamiparib received conditional approval in May 2021 for treatment of patients with germline BRCA (gBRCA) mutation-associated recurrent advanced ovarian, fallopian tube, or primary peritoneal cancer who have been treated with two or more lines of chemotherapy. Full approval for this indication is contingent upon results from ongoing corroborative trials confirming the clinical benefit of pamiparib in this population.

In addition, our clinical development program includes a Phase 3 trial as a maintenance therapy in patients with platinum-sensitive recurrent OC (NCT03519230), a Phase 2 trial in first-line platinum-sensitive GC maintenance (NCT03427814), and a Phase 1b trial in combination with temozolomide in solid tumors (NCT03150810).

Clinical-Stage

Ociperlimab (BGB-A1217), a TIGIT Inhibitor

Ociperlimab (BGB-A1217) is an investigational humanized IgG1-variant monoclonal antibody directed against TIGIT. An immune checkpoint molecule, ociperlimab is currently being investigated in two global Phase 3 clinical trials, the AdvanTIG-301 (NCT04866017) and AdvanTIG-302 (NCT04746924) trials, in combination with tislelizumab in NSCLC. As of December 2022, more than 1,600 subjects have been enrolled across the ociperlimab development program, which includes eight global trials in patients with lung cancers, esophageal squamous cell carcinoma, and cervical cancer.

In December 2021 we announced an option, collaboration and license agreement with Novartis to develop, manufacture and commercialize ociperlimab in North America, Europe, and Japan, as discussed further below under "Novartis Collaboration — *Option Collaboration and License Agreement for Ociperlimab"*.

We have completed patient enrollment in the AdvanTIG-202 trial (NCT04693234) in patients with previously treated recurrent or metastatic cervical cancer. We expect to initiate additional pivotal clinical trials and announce data from Phase 2 trial expansion cohorts in 2023 to inform our subsequent development for ociperlimab.

Lifirafenib (BGB-283) and BGB-3245, Inhibitors of RAF

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 (MAPK), pathway, including BRAF gene mutations and KRAS/NRAS gene mutations where first generation BRAF inhibitors are not effective. 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.

BeiGene is working together with SpringWorks Therapeutics, Inc. (SpringWorks) in a global clinical collaboration and has initiated a Phase 1b clinical trial (NCT03905148) to evaluate the safety, tolerability, and preliminary efficacy of lifirafenib in combination with SpringWorks' investigational MEK inhibitor, mirdametinib (PD-0325901), in patients with advanced solid tumors.

In addition to the collaboration, BeiGene and SpringWorks formed a separate company, MapKure, LLC, to develop BGB-3245, an investigational, selective next-generation RAF kinase inhibitor discovered by BeiGene scientists. MapKure has an ongoing Phase 1 clinical trial of BGB-3245 (NCT04249843) in patients with advanced or refractory tumors harboring specific v-RAF murine sarcoma viral oncogene homolog B (B-RAF) genetic mutations.

Sitravatinib, a Multi-Kinase Inhibitor

In January 2018, we entered into an exclusive license agreement with Mirati Therapeutics, Inc. (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 Phase 3 SAPPHIRE trial of sitravatinib in NSCLC initiated in 2019. In 2022, as part of our collaboration with Mirati, we initiated patient enrollment for a Phase 2 clinical trial of sitravatinib in combination with tislelizumab in locally advanced unresectable or metastatic ESCC that progressed on or after anti-PD-L1 antibody therapy (NCT05461794).

We are evaluating sitravatinib in multiple clinical trials including a Phase 3 trial combined with tislelizumab in NSCLC (NCT04921358).

BGB-11417, a Small Molecule Bcl-2 Inhibitor

BGB-11417 is an investigational small molecule Bcl-2 inhibitor. We have completed preclinical and investigational new drug (IND) -enabling studies of BGB-11417, which demonstrated potent activity and high selectivity against the pro-apoptotic protein Bcl-2. The molecule appears to be more potent than venetoclax and shows the potential to overcome resistance to venetoclax. Further, it is more selective than venetoclax for Bcl-2 relative to Bcl-xL. Finally, we believe that it is well-positioned to be combined with BRUKINSA. Phase 1 clinical data for non-Hodgkin's lymphoma, CLL, acute myeloid leukemia (AML) and multiple myeloma (MM) (NCT04883957, NCT04277637, NCT04771130, and NCT04973605) were presented at ASH 2022. We initiated patient dosing in a Phase 2 study to evaluate BCL-2 inhibitor BGB-11417 in patients with relapsed or

refractory mantle cell lymphoma (NCT05471843) and relapsed or refractory chronic lymphocytic leukemia or small lymphocytic lymphoma (NCT05479994) in 2022 and expect data readouts from ongoing studies in 2023.

BGB-A445, an OX40 Agonist Antibody

BGB-A445 is an investigational agonistic antibody directed to the OX40 antigen. BGB-A445 is a non-ligand competing antibody that does not disrupt OX40 to OX40 ligand engagement. Preclinical experiments showed that BGB-A445 has increasing effectiveness at higher doses versus an antibody that was ligand-competing, which showed falling effectiveness at higher doses. BGB-A445 has also showed in preclinical tests the potential to be combined with several agents, such as tislelizumab, as well as a TLR9 agonist, a PI3Kδ inhibitor, sitravatinib, and chemotherapy. We have an ongoing Phase 1 trial (NCT04215978) of BGB-A445 in combination with tislelizumab in patients with advanced solid tumors and initiated tumor-specific dose expansion cohorts in a Phase 1 monotherapy trial (NCT04215978) in patients with solid tumors in 2022. We initiated patient dosing in a Phase 2 basket trial in melanoma, renal cell cancer and bladder cancer (NCT05661955).

ZW25 (Zanidatamab), a bispecific HER2-targeted antibody

Zanidatamab, a novel investigational Azymetric™ bispecific antibody targeting HER2, is currently in late-stage clinical development with Zymeworks Inc. BeiGene has development and commercial rights to zanidatamab in Asia (excluding Japan), Australia, and New Zealand. We are participating in three ongoing clinical studies with zanidatamab. The first is a Phase 1/2 study (NCT04215978) in HER2-positive breast and gastric cancer. The breast cancer arm combines zanidatamab with docetaxel, and the gastric cancer arm combines zanidatamab with our PD-1 inhibitor tislelizumab and chemotherapy. The second study HERIZON-BTC-01 (NCT04466891) is a Phase 2b study in patients with advanced or metastatic HER2-amplified biliary tract cancers (BTC) in which zanidatamab is being used as monotherapy. Positive topline results from this trial were announced in 2022. We initiated a global Phase 3 clinical trial (NCT05152147) examining zanidatamab in combination with chemotherapy with and without tislelizumab in HER2-positive gastroesophageal cancer in late 2021. We completed enrollment in 2L biliary tract cancer in 2022.

Surzebiclimab (BGB-A425), a TIM-3 Inhibitor

Surzebiclimab (BGB-A425) is an investigational humanized IgG1-variant monoclonal antibody against T-cell immunoglobulin and mucin-domain containing-3 (TIM-3). We have an ongoing Phase 1/2 trial (NCT03744468) of surzebiclimab in combination with tislelizumab in various solid tumors.

BGB-15025, a Small Molecule HPK1 Inhibitor

BGB-15025 is an investigational small molecule inhibitor of HPK1, which is a key negative feedback regulator of TCR signaling. Inhibition of HPK1 leads to enhanced T-cell activation pre-clinically. In addition, preclinical studies showed that BGB-15025 exhibits combination activity with tislelizumab and has a wide therapeutic window. We initiated a Phase 1 trial (NCT04649385) of BGB-15025 alone and in combination with tislelizumab in patients with advanced solid tumors in 2021. This trial is being conducted in multiple countries globally. We expect to initiate dose-expansion for BGB-15025 in 2023.

BGB-16673, a BTK-targeted CDAC

BGB-16733 is an investigational BTK-targeting chimeric degradation activation compound (CDAC) active against both wild-type and mutant BTK. BGB-16673 has demonstrated preclinical antitumor activity in models with wild-type BTK and models with BTK inhibitor–resistant mutations commonly observed in patients who have progressed on prior BTK inhibitor treatment. A Phase 1 open-label, dose-escalation, and dose-expansion trial (NCT05006716) in adult patients with relapsed/refractory (R/R) B-cell malignancies is currently enrolling.

BGB-23339, a TYK2 inhibitor

BGB-23339 is a potent, highly selective, allosteric, investigational tyrosine kinase 2 (TYK2) inhibitor discovered and being developed by BeiGene. TYK2 is a member of the JAK family and functions as a critical mediator in cytokine signaling pathways implicated in multiple immune-mediated disorders. Designed to target the regulatory pseudokinase (JH2) domain on TYK2, BGB-23339 has demonstrated strong selectivity in preclinical studies with potent inhibition of interleukin (IL)-12, IL-23, and Type 1 interferons (IFNs)—pro-inflammatory cytokines that play a determinant role in the induction of inflammation. BGB-23339 is currently being evaluated in a Phase 1 clinical study (NCT05093270).

BGB-24714, a SMAC mimetic

BGB-24714 is an investigational Second Mitochondrial-derived Activator of Caspase (SMAC) mimetic currently enrolling in a Phase 1 clinical trial (NCT05381909) as monotherapy or in combination with paclitaxel in advanced solid tumors.

BGB-B167, a CEA x 4-1BB bispecific

BGB-B167 is an investigational first-in-class CEA x 4-1BB bispecific antibody. It is currently enrolling in a Phase 1 clinical trial (NCT05494762) as a monotherapy and in combination with tislelizumab in patients with selected CEA-expressing advanced or metastatic solid tumors, including colorectal cancer (CRC).

BGB-10188 (PI3K inhibitor)

BGB-10188 is an investigational PI3Kδ inhibitor being evaluated in a Phase 1 clinical trial (NCT04282018) as monotherapy or in combination with BRUKINSA in hematology malignancies, or in combination with tislelizumab in solid tumors.

Our Preclinical Programs

We have a proprietary biology research platform that has allowed us to research and develop both small molecules and biologic molecules. In the last decade, this platform has generated more than 10 clinical stage assets, including three internally-developed molecules that have been approved by regulatory bodies in the United States, China, EU and other markets, with other filings pending globally and planned to be submitted. The platform is a full-process technology system spanning from early discovery to commercialization of oncology medicines based on multiple drug technology platforms that can be applied to oncology and other fields. We have core technology platforms for the development of small molecule and antibody medicines and the manufacturing of our own and potentially other medicines. Currently, we have over 60 pre-clinical programs and we believe the majority have best-in-class or first-in-class potential.

We anticipate advancing multiple our preclinical drug candidates into the clinic in the next 12 months. We believe that 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 medicines and drug candidates.

Manufacturing and Supply

We manufacture our medicines and drug candidates internally and in some cases with the help of third-party CMOs. The manufacturing of our medicines and drug candidates 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 facilities of the CMOs we use to manufacture our medicines and drug candidates operate under current good manufacturing practice regulations ("cGMP") conditions. cGMP regulations are requirements for the production of pharmaceuticals that will be used in humans.

Our Manufacturing Facilities

We have manufacturing facilities for small molecule drugs and large molecule biologics in Suzhou and Guangzhou, China, respectively, to support the commercialization and potential future demand of our internally developed or in-licensed products.

Our manufacturing facility in Suzhou is over 13,000 square meters and consists of a manufacturing base for small molecule drug products with an annual production capacity of about 100 million tablets and capsules and a biologics clinical development production facility with 2 x 500 liters capacity to produce biologics candidates for clinical supply. The facility meets or exceeds design criteria of the United States, EU, and China regulatory requirements. The facility has received a manufacturing license to produce commercial volumes of BRUKINSA and pamiparib for the China market. As a result of our growing commercial and clinical demands, we have broken ground on a new small molecule manufacturing facility nearby in Suzhou that will have the capability to produce up to 600 million solid oral dosages annually. This approximately 50,000 square meter facility is expected to replace our current Suzhou site and support our growing pipeline of small molecule medicines and drug candidates.

We continue to invest in our state-of-the-art commercial-scale manufacturing facility in Guangzhou of approximately 100,000 square meters for the manufacturing of large molecule biologics. Phases 1 and 2 of the facility were completed in September 2019 and December 2020, respectively, with 24,000 liters of single use disposable capacity. Additionally, total capacity has been increased to 54,000 liters, with an additional expansion of 10,000 liters expected in the second quarter of 2023, which will bring the final capacity to 64,000. Phase 1 is currently approved for the end-to-end commercial production of tislelizumab for the China market. We have purchased an adjacent tract of land to the south of the current site and initiated the next phase of expansion to support our growing pipeline of large molecule medicines and drug candidates.

We have also commenced construction on our commercial-stage manufacturing and clinical R&D campus at the 42-acre site at the Princeton West Innovation Park in Hopewell, New Jersey. The property, located strategically in the Interstate 95

corridor of New Jersey, with a deep and rich talent pool, has more than one million square feet of developable real estate for potential future expansion to cover our existing medicines and pipeline.

Contract Manufacturing Organizations

We currently rely on, and expect to continue to rely on, a limited number of third-party CMOs and CROs for the production of some drug products and drug substances and the supply of raw materials to meet the commercial, clinical, and preclinical needs of our medicines and drug candidates. We have adopted procedures to ensure that the production qualifications, facilities, and processes of the third-party suppliers engaged by us comply with relevant regulatory requirements and our internal quality and operational 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 business terms.

We have commercial supply and related agreements with most of our manufacturing service providers. For example, we entered into a commercial supply agreement with Catalent Pharma Solutions, LLC ("Catalent") to produce BRUKINSA at Catalent's Kansas City, Missouri site for clinical and commercial use in the United States and other countries outside of China. We currently source the active pharmaceutical ingredient for BRUKINSA from a supplier in China and are in the process of bringing online an additional source of supply outside of China. In addition, we entered into a commercial supply agreement with Boehringer Ingelheim Biopharmaceuticals (China) Ltd. ("Boehringer Ingelheim") for tislelizumab, which is being manufactured at Boehringer Ingelheim's facility in Shanghai, China. Additionally, our collaboration agreements with Novartis include the right for Novartis to manufacture tislelizumab and ociperlimab for its territory, to be managed by Novartis following tech transfer, and our right to conduct a specified percentage of production at our planned U.S. manufacturing site, subject to the terms of the agreements. For our commercial and clinical stage products in-licensed from Amgen, BMS and others, we rely on the licensors and their manufacturing facilities or their CMOs for the supply of those medicines and drug candidates.

Our agreements with the outsourced suppliers engaged by us 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 specified 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.

We generally obtain raw materials for our manufacturing activities from various 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 third-party CROs and excipients, which are commercially available from well-known vendors that meet the requirements of the relevant regulatory agencies. The core raw materials used in manufacturing at our Guangzhou facility are genetically modified cell lines that we have co-developed and licensed from Boehringer Ingelheim and other third parties.

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 any defects in our finished products.

Amgen Collaboration

Collaboration Agreement

On October 31, 2019, our wholly-owned subsidiary, BeiGene Switzerland GmbH ("BeiGene Switzerland"), entered into a Collaboration Agreement with Amgen, which became effective on January 2, 2020 (as amended, the "Amgen Collaboration Agreement"). Pursuant to the terms of the Amgen Collaboration Agreement, we are responsible for commercializing Amgen's oncology products XGEVA, BLINCYTO and KYPROLIS in China (excluding Hong Kong, Macao and Taiwan) for a period of five or seven years following each product's regulatory approval in China, as specified in the Amgen Collaboration Agreement, with the commercialization period for XGEVA commencing following the transition of operational responsibilities for the product. In addition, as specified in the agreement, we have the option to retain one of the three products to commercialize for as long as the product is sold in China. The parties have agreed to equally share profits and losses for the products in China during each product's commercialization period. After expiration of the commercialization period for each product, the products not retained will be transitioned back to Amgen and we will be eligible to receive tiered mid-single to low-double digit royalties on net sales in China of each product for an additional five years.

Additionally, pursuant to the terms of the Amgen Collaboration Agreement, we and Amgen have agreed to collaborate on the global clinical development and commercialization of a portfolio of Amgen clinical- and late-preclinical-stage oncology

pipeline products. Starting from the commencement of the Amgen Collaboration Agreement, we and Amgen will co-fund global development costs, with BeiGene contributing up to $1.25 billion worth of development services and cash over the term of the collaboration. We will be eligible to receive tiered mid-single digit royalties on net sales of each product globally outside of China, other than LUMAKRAS™ (sotorasib) ("AMG 510"), on a 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 the earlier of eight years after the first commercial sale of such product in the country of sale and 20 years from the date of first commercial sale of such product anywhere in the world.

For each pipeline product that is approved in China, we will have the right to commercialize the product for seven years, with the parties sharing profits and losses for the product in China equally. In addition, we will have the right to retain approximately one of every three approved products, up to a total of six, other than AMG 510, to commercialize for as long as each such product is sold in China. After the expiration of the seven-year commercialization period, each product will be transitioned back to Amgen and we will be eligible to received tiered mid-single to low-double digit royalties on net sales in China for an additional five years. The parties are subject to specified exclusivity requirements in China and the rest of the world.

Recently, in connection with our ongoing assessment of the Collaboration Agreement cost-share contributions, we determined that our further investment in the development of AMG 510 was no longer commercially viable for BeiGene. As a result, in February 2023, we entered into an amendment to the Collaboration Agreement to (i) stop sharing costs with Amgen for the further development of AMG 510 during the period starting January 1, 2023 and ending August 31, 2023; and (ii) cooperate in good faith to prepare a transition plan with the anticipated termination of AMG 510 from the Collaboration Agreement.

BeiGene, Ltd. has guaranteed certain obligations of BeiGene Switzerland under the Amgen Collaboration Agreement pursuant to the terms of a separate Guarantee Agreement.

The Amgen Collaboration Agreement contains customary representations, warranties and covenants by the parties. The agreement will continue in effect on a product-by-product basis unless terminated by either party pursuant to its terms. The agreement may be terminated by mutual written consent of the parties, or by either party upon the other party's uncured material breach, insolvency, failure to comply with specified compliance provisions, or subject to a specified negotiation mechanism, certain adverse economic impacts or the failure to meet commercial objectives. In addition, Amgen may terminate the agreement with respect to a pipeline product in the event it suspends development of such pipeline product on specified terms, subject to the parties determining whether to continue development of the pipeline product in China.

Share Purchase Agreement

In connection with the Amgen Collaboration Agreement, pursuant to a share purchase agreement dated October 31, 2019, as amended, by and between BeiGene, Ltd. and Amgen (as amended, the "Share Purchase Agreement"), we issued to Amgen 206,635,013 ordinary shares in the form of 15,895,001 American Depositary Shares ("ADSs") of BeiGene, Ltd. on January 2, 2020, representing approximately 20.5% of our then outstanding shares, for an aggregate purchase price of $2.78 billion, or $13.45 per ordinary share, or $174.85 per ADS.

Pursuant to the Share Purchase Agreement, Amgen has agreed to (i) a lock-up on sales of its shares until the earliest of (a) the fourth anniversary of the closing, (b) the expiration or termination of the Collaboration Agreement and (c) a change of control of BeiGene, Ltd., (ii) a standstill until the date on which it holds less than 5% of our then outstanding shares, and (iii) a voting agreement to vote its shares on certain matters presented for shareholder approval until the later of (a) the fifth anniversary of the closing and (b) the expiration of the standstill period, all under specified circumstances and as set forth in the agreement. Following the later of (i) the expiration of the lock-up period and (ii) the expiration of the standstill period, Amgen has agreed not to sell shares representing more than 5% of our then outstanding shares in any rolling 12-month period. Under the terms of the Share Purchase Agreement, Amgen will also have specified registration rights upon expiration of the lock-up. Additionally, we have agreed to use reasonable best efforts to provide Amgen with an opportunity to participate in subsequent new securities offerings upon the same terms and conditions as other purchasers in the offering in an amount needed to allow Amgen to hold up to 20.6% of our shares, subject to applicable law and HKEx rules and other specified conditions.

On March 17, 2020, BeiGene, Ltd. and Amgen entered into an Amendment No. 2 (the "Second Amendment") to the Share Purchase Agreement in order to account for periodic dilution from the issuance of shares by us, which agreement was restated in its entirety on September 24, 2020 (the "Restated Second Amendment"). Pursuant to the Restated Second Amendment, Amgen has an option (the "Direct Purchase Option") to subscribe for additional ADSs in an amount necessary to enable it to increase (and subsequently maintain) its ownership at approximately 20.6% of our outstanding shares. The Direct Purchase Option is exercisable on a monthly basis, but only if Amgen's interest in our outstanding shares at the monthly reference date is less than 20.4%. The Direct Purchase Option (i) is exercisable by Amgen solely as a result of dilution arising from issuance of

new shares by us under our equity incentive plans from time to time, and (ii) is subject to annual approval by our independent shareholders each year during the term of the Restated Second Amendment. The exercise period of the Direct Purchase Option commenced on December 1, 2020 and will terminate on the earliest of: (a) the date on which Amgen and its affiliates collectively own less than 20% of the outstanding share capital of the Company as a result of Amgen's sale of shares; (b) at least 60-day advance written notice from either Amgen or the Company that such party wishes to terminate the Direct Purchase Option; or (c) December 1, 2023. The Direct Purchase Option has no vesting period.

Novartis Collaboration

Collaboration and License Agreement for Tislelizumab

On January 11, 2021, our wholly-owned subsidiary, BeiGene Switzerland GmbH, entered into a Collaboration and License Agreement, which became effective on February 26, 2021 (the "Novartis Collaboration and License Agreement") with Novartis, pursuant to which Novartis will have the right to develop, manufacture and commercialize tislelizumab in the United States, Canada, Mexico, member countries of the European Union, United Kingdom, Norway, Switzerland, Iceland, Liechtenstein, Russia, and Japan (the "Licensed Territory").

Under the Novartis Collaboration and License Agreement, we received an upfront cash payment of $650 million from Novartis. Additionally, we are eligible to receive up to $1.3 billion upon the achievement of regulatory milestones, $250 million upon the achievement of sales milestones, and tiered royalties based on percentages of annual net sales of tislelizumab in the Licensed Territory ranging from the high-teens to high-twenties, with customary reductions in specified circumstances. Royalties are payable on a country-by-country basis from the time of the first commercial sale until the latest of the expiration of the last valid patent claim, the expiration of regulatory exclusivity, or 10 years after the first commercial sale of tislelizumab in the country of sale.

Under the Novartis Collaboration and License Agreement, we and Novartis have agreed to jointly develop tislelizumab in the Licensed Territory, with Novartis responsible for regulatory submissions after a transition period and for commercialization upon regulatory approvals. In addition, both companies may conduct clinical trials to explore potential combinations of tislelizumab with other cancer treatments. We will be responsible for funding the ongoing clinical trials of tislelizumab, and Novartis has agreed to fund any new registrational, bridging, or post-marketing studies in the Licensed Territory. Subject to specified conditions, both parties have agreed to jointly fund other new clinical trials in the Licensed Territory agreed by the parties, provided that each party will be responsible for funding clinical trials evaluating tislelizumab in combination with its own- or third-party cancer treatments. We will initially be responsible for supplying tislelizumab to Novartis, with Novartis having the right to conduct manufacturing for its use in the Licensed Territory after successful transfer of the manufacturing process. In addition, we have an option to co-detail the product in the United States, Canada and Mexico, on an indication-by-indication basis, funded in part by Novartis. Each party retains the worldwide right to commercialize its propriety products in combination with tislelizumab. We retain the rights to manufacture and supply a specified percentage of commercial supply of tislelizumab from our planned U.S. manufacturing facility to be built in Hopewell, New Jersey, subject to the terms of the agreement.

The Novartis Collaboration and License Agreement contains customary representations, warranties and covenants by the parties. Unless earlier terminated, the agreement will expire on a country-by-country basis upon expiration of the royalty term in such country and in its entirety upon the expiration of all applicable royalty terms in all countries in the Licensed Territory. We may terminate the agreement in its entirety upon written notice (i) if Novartis challenges the licensed BeiGene patents, or (ii) if Novartis files a biologics license application for its anti-PD-1 antibody, spartalizumab, in the Licensed Territory, and we do not elect to include spartalizumab as a licensed product under the agreement or Novartis does not divest the product candidate, in which case Novartis would pay us a specified termination fee. The agreement may be terminated by Novartis upon 120 days' prior written notice if delivered before first commercial sale or 180 days' prior written notice if delivered following first commercial sale of tislelizumab in the Licensed Territory, or by either party upon the other party's bankruptcy or uncured material breach.

Option, Collaboration and License Agreement for Ociperlimab

On December 19, 2021, BeiGene Switzerland GmbH entered into an Option, Collaboration and License Agreement (the "Novartis Option, Collaboration and License Agreement") with Novartis, pursuant to which we have granted Novartis an exclusive time-based option to receive an exclusive license to develop, manufacture and commercialize our investigational TIGIT inhibitor ociperlimab in the Licensed Territory.

Under the Novartis Option, Collaboration and License Agreement, we received an upfront cash payment of $300 million from Novartis and are eligible to receive an additional payment of $600 million or $700 million upon exercise by Novartis of an exclusive time-based option prior to mid-2023 or late-2023, respectively, subject to receipt of required antitrust approval.

Additionally, following option exercise, we are eligible to receive up to $745 million upon the achievement of regulatory approval milestones, $1.15 billion upon the achievement of sales milestones, and tiered royalties based on percentages of annual net sales of ociperlimab in the Licensed Territory ranging from the high-teens to mid-twenties, with customary reductions in specified circumstances. Royalties are payable on a country-by-country basis from the time of the first commercial sale until the latest of the expiration of the last valid patent claim, the expiration of regulatory exclusivity, or 10 years after the first commercial sale of ociperlimab in the country of sale.

Under the Novartis Option, Collaboration and License Agreement, during the option period, Novartis has agreed to initiate, conduct and fund additional global clinical trials of ociperlimab in combination with tislelizumab in selected tumor types and we have agreed to expand enrollment in two ongoing trials. Additionally, following the option exercise, the companies have agreed to jointly develop ociperlimab in the Licensed Territory, with Novartis sharing development costs of global trials and responsible for regulatory submissions after a transition period and for commercialization upon regulatory approvals in the Licensed Territory. In addition, both companies may conduct clinical trials globally to explore potential combinations of ociperlimab with other cancer treatments. We will initially be responsible for supplying ociperlimab to Novartis, with Novartis having the right to conduct manufacturing for its use in the Licensed Territory after successful transfer of the manufacturing process. Following approval, we have agreed to provide 50% of the co-detailing and co-field medical efforts in the United States and have an option to co-detail up to 25% in Canada and Mexico, in each case funded in part by Novartis. Each party retains the worldwide right to commercialize its proprietary products in combination with ociperlimab, as is the case with tislelizumab under the parties' existing collaboration agreement. We retain the rights to manufacture and supply a specified percentage of commercial supply of ociperlimab from our planned U.S. manufacturing facility to be built in Hopewell, New Jersey, subject to the terms of the agreement.

The Novartis Option, Collaboration and License Agreement contains customary representations, warranties and covenants by BeiGene and Novartis. Unless earlier terminated, the agreement will expire on a country-by-country basis upon the expiration of the royalty term in such country. The Novartis Option, Collaboration and License Agreement will expire in its entirety upon the expiration of all applicable royalty terms under the agreement in all countries in the Licensed Territory. The agreement may be terminated by Novartis upon 120 days’ prior written notice if delivered before first commercial sale or 180 days’ prior written notice if delivered following first commercial sale of ociperlimab in the Licensed Territory, or by either party upon the other party’s bankruptcy or uncured material breach. BeiGene may terminate the agreement in its entirety upon written notice if Novartis challenges the licensed BeiGene patents. Either party may terminate the agreement in its entirety effective immediately upon written notice to the other party (i) if the option terminates or expires, or (ii) in the event that the license effective date has not occurred within six months after the date of the Hart-Scott-Rodino Antitrust Improvements Act filing, subject to extension.

Celgene License and Supply Agreement

On July 5, 2017, we and Celgene Logistics Sàrl, now a wholly-owned subsidiary of BMS, 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 BMS’s approved cancer therapies, REVLIMID, VIDAZA and ABRAXANE 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 subsequently assigned the agreement to our wholly-owned subsidiary, BeiGene Switzerland.

On March 25, 2020, the NMPA suspended the importation, sales and use of ABRAXANE in China supplied to us by BMS, and the drug was subsequently recalled by BMS and is not currently available for sale in China. This suspension was based on inspection findings at BMS’s contract manufacturing facility in the United States. Additionally, in October 2021, BMS provided 180-days' notice to us, which we dispute, purporting to terminate our license to market ABRAXANE in China. We have not had any sales of ABRAXANE since the suspension and do not expect future revenue from ABRAXANE. We have initiated an arbitration proceeding against BMS asserting that it has breached and continues to breach the terms and conditions of the license and supply agreement. For additional information, please see the section of this Annual Report titled “Legal Proceedings”.

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. BMS also has the right to terminate the agreement with respect to REVLIMID at any time upon written notice to us under certain circumstances.

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

Intellectual Property

The proprietary nature of, and protection for, our medicines, 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 filed patent applications and obtained patents in the United States and other countries and regions, such as China and Europe, relating to our medicines and 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 January 30, 2023, we owned 48 issued U.S. patents, 32 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 ("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. In China, the Amended PRC Patent Law provides a patent term extension of up to five years, similar to the United States.

The key patents for our medicines and late-stage clinical drug candidates as of January 30, 2023, are summarized below:

Molecule	Territory	General Subject Matter	Expiration[1]
BRUKINSA® (Zanubrutinib)	U.S.	Compound and composition	2034
	U.S.	Use for the treatment of autoimmune diseases	2034
	U.S.	Use for the treatment of B-cell proliferative disorder	2034
	U.S.	Crystalline forms	2037
	China	Compound and composition	2034
Tislelizumab	U.S.	Antibodies	2033
	U.S.	Use for the treatment of cancer	2033
	U.S.	Antibodies and use for the treatment of cancer	2033
	U.S.	Antibodies	2033
	U.S.	Antibodies	2033
	China	Antibodies	2033
	China	Antibodies	2033
	China	Antibodies	2033
	China	Antibodies	2033
	China	Antibodies	2033
Pamiparib	U.S.	Compound and composition	2031
	U.S.	Compound and composition	2031
	U.S.	Use for the treatment of cancer	2031
	U.S.	Compositions	2031
	U.S.	Crystalline forms	2036
	U.S.	Crystalline forms	2038
	China	Compound and composition	2031
	China	Use for the treatment of cancer	2031
	China	Crystalline forms	2036
Ociperlimab	U.S.	Antibodies	2038

(1) The expected expiration does not include any additional term for patent term extensions.

We currently have two in-licensed medicines in China from BMS. The key patents for them in China as of January 30, 2023 are summarized below:

Product	Territory	General Subject Matter	Expiration
REVLIMID® (lenalidomide)	China	Use for the treatment of multiple myeloma	2023
	China	Use for the treatment of multiple myeloma	2023
	China	Use for the treatment of multiple myeloma	2023
	China	Use for the treatment of multiple myeloma	2023
VIDAZA® (azacitidine)	China	No patent	N/A

Under our collaboration with Amgen, we have the right to commercialize three medicines in China. The key patents for them in China as of January 30, 2023 are summarized below:

Product	Territory	General Subject Matter	Expiration
XGEVA® (denosumab)	China	Antibodies	2022
BLINCYTO® (blinatumomab)	China	Use for the treatment of pediatric acute lymphoblastic leukemia	2029
KYPROLIS® (carfilzomib)	China	Compound and Composition	2025

Although various extensions may be available, the life of a patent and the protection it affords, is limited. REVLIMID and VIDAZA face competition from generic medications, and we may face similar competition for our medicines and any approved drug candidates even if we successfully obtain patent protection. The scope, validity or enforceability of our or our collaborators' patents may be challenged in court or other authorities, and we or they 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. Additionally, in China, the NMPA may approve a generic version of a brand-name medicine that still has patent protection, such as has occurred with REVLIMID. Under our license agreements with BMS and Amgen, they retain the responsibility for, but are 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 or biosimilar competition for these medicines.

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 ("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 in obtaining FDA regulatory approval. 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 China, the Amended PRC Patent Law provides both patent term adjustment and patent term extension, similar to the United States.

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, our corporate logo and product names and logos in the United States, China, the EU and other jurisdictions, and we are seeking further trademark protection for BeiGene, our corporate logo, product names and logos, and other marks in jurisdictions where available and appropriate.

Competition

We operate in a highly competitive environment and our marketed products face intense competition in regulated markets around the world. Our main competitors include other global research-based biopharmaceutical companies as well as smaller regional and local companies. These companies participate in one or more activities including the development, production, and promotion of products that are intended to treat diseases or indications that are like products we currently market or are in the process of developing to market. For example:

BRUKINSA – 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 BTK inhibitor IMBRUVICA (ibrutinib), marketed by AbbVie and Janssen, 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 been approved in over 90 countries and regions and has expanded its indications. Another BTK inhibitor, AstraZeneca's 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, and in November 2019 for use in adults with CLL/SLL as a single agent or in combination with obinutuzumab. On January 27, 2023, the FDA approved Lilly's JAYPIRCA™ (pirtobrutinib, a reversible BTK inhibitor) for the treatment of adult patients with R/R MCL after at least two lines of systemic therapy, including a BTK inhibitor. In China, BRUKINSA competes with IMBRUVICA (ibrutinib), which received approval in 2017, and YINUOKAI® (orelabrutinib) from Innocare, which was approved in 2020.

Tislelizumab – A number of PD-1 or PD-L1 antibody medicines have been approved by the FDA. These include Merck's KEYTRUDA® (pembrolizumab), BMS's OPDIVO® (nivolumab), Roche's TECENTRIQ® (atezolizumab), AstraZeneca's IMFINZI® (durvalumab), Pfizer and Merck Sereno's BAVENCIO® (avelumab), Regeneron and Sanofi's LIBTAYO® (cemiplimab), and GSK's JEMPERLI® (dostarlimab). In the global setting, several PD-1 or PD-L1 antibody agents are in late-stage clinical development in addition to tislelizumab. In China, as of February 1, 2023, there are nine other approved PD-1 antibodies: OPDIVO® (nivolumab) and KEYTRUDA® (pembrolizumab), Junshi's TUOYI® (toripalimab), Innovent's TYVYT® (sintilimab), Hengrui's AIRUIKA® (camrelizumab), Akeso's ANNIKE® (penpulimab), Gloria's YUTUO® (zimberelimab), Henlius's HANSIZHUANG® (serplulimab) and Lepu's PUYOUHENG® (pucotenlimab). There are four approved PD-L1 antibody agents: AstraZeneca's IMFINZI® (durvalumab), Roche's TECENTRIQ® (atezolizomab), CStone's ZEJIEMEI® (sugemalimab), and Alphamab's ENWEIDA® (envafolimab). Akeso's PD-1xCTLA-4 bispecific antibody, KAITANNI® (cadonilimab) was approved in China. There are approximately 40 more PD-1 and PD-L1 agents in clinical development in China.

Pamiparib – We are competing with multiple PARP inhibitors in China. AstraZeneca received approval for olaparib in August 2018. Zai Labs obtained development and commercial rights for niraparib in China, and its NDA was approved by the NMPA in December 2019. Fluzoparib from Hengrui/Hansoh was approved in December 2020.

Ociperlimab – We are aware of several pharmaceutical companies developing TIGIT antibodies, including Agenus, Arcus, BMS, Compugen, Roche/Genentech, Innovent, iTeos Therapeutics, Merck KGaA, Mereo BioPharma, Seagen, Junshi, Bio-Thera and Akeso. To our knowledge, there are currently no approved anti-TIGIT antibodies and the most advanced agent is in Phase 3 development.

Many of the larger companies we compete with are well-capitalized and dedicate a significant number of financial resources to support their research and development, while using business development to supplement their internal pipelines. As a result, we must continuously invest and gain experience in the development, acquisition, and marketing of innovative and branded medicines and drug candidates to compete effectively in both current and future markets. This requires us to devote substantial funds and resources to R&D to prevent or slow the erosion of the sales of our existing products and potential sales of products in development.

The main forms of competition include efficacy, safety, and cost. The long-term success of our products depends on our ability to effectively demonstrate the value that each one of them offers to physicians, patients, and third-party payers. This requires a much greater use of a direct sales force to realize significant revenues. We also have and will continue to enter into co-promotion, contract sales force or other such arrangements with third parties, for example, where our own direct sales force is not large enough or sufficiently well-aligned to achieve maximum market penetration.

Government Regulation

Government authorities in the United States, China, Europe and other jurisdictions extensively regulate the research and clinical development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing, and export and import of drugs like those we are

developing and commercializing. Some jurisdictions also regulate drug pricing. Generally, for a new drug to 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 ("FDCA"), and its implementing regulations, and biologics under the FDCA, its implementing regulations, and the Public Health Service Act ("PHSA"), and its implementing regulations.

Cancer therapies are sometimes characterized according to line of therapy, and the FDA often approves new therapies initially only for second or third-line use. When cancer is detected early enough, first line therapy may be adequate to cure the cancer or prolong life without a cure. Whenever first line therapy, usually chemotherapy, hormone therapy, radiation, 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, and more invasive forms of surgery. In some cases, new technologies and investigational medicines, as part of a clinical trial, may be used as any line of therapy.

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 and animal studies according to Good Laboratory Practices ("GLP") guidance;
- completion of extensive chemistry, manufacturing, and control ("CMC") studies;
- submission to the FDA of an IND application, which must become effective before human clinical trials may begin;
- performance of adequate and well-controlled human clinical trials according to Good Clinical Practice ("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 small molecule 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;
- review of the product candidate by an FDA advisory committee, where appropriate and if applicable;
- payment of user fees for FDA review of the NDA or BLA (unless a fee waiver applies);
- 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.

Preclinical Studies and Clinical Trials

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 *in vitro* and animal studies. The conduct of the preclinical tests must comply with federal regulations and requirements, including GLP. 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 concerns before the clinical trial can begin. The FDA may also impose clinical holds 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 require that all research subjects provide informed consent in writing before their participation in any clinical trial. Further, an institutional review board ("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. Some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data safety monitoring board or committee. This group provides authorization as to whether or not a trial may move forward at designated check points based on access that only the group maintains to available data from the trial and may recommend halting the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy.

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.

A sponsor who wishes to conduct a clinical trial outside of the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, the sponsor may submit data from the clinical trial to the FDA in support of an NDA or BLA. The FDA will accept a well-designed and well-conducted foreign clinical study not conducted under an IND if the study was conducted in accordance with GCP requirements, and the FDA is able to validate the data through an onsite inspection if deemed necessary.

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 with the target disease or condition.

- **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.

In March 2022, the FDA released a final guidance entitled "Expansion Cohorts: Use in First-In-Human Clinical Trials to Expedite Development of Oncology Drugs and Biologics," which outlines how drug developers can utilize an adaptive trial design commonly referred to as a seamless trial design in early stages of oncology drug development (i.e., the first-in-human clinical trial) to compress the traditional three phases of trials into one continuous trial called an expansion cohort trial. Information to support the design of individual expansion cohorts are included in IND applications and assessed by the FDA. Expansion cohort trials can potentially bring efficiency to drug development and reduce developmental costs and time.

Post-approval trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication and are commonly intended to generate additional safety data regarding use of the product in a clinical setting. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA or BLA. Failure to exhibit due diligence with regard to conducting required Phase 4 clinical trials could result in withdrawal of approval for products.

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 may 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. The sponsor must submit an IND safety report within 15 calendar days after the sponsor determines that the information qualifies for reporting. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information. 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, or a data safety monitoring board may recommend the suspension or termination of, 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. Expanded Access

Expanded access, sometimes called "compassionate use," is the use of investigational products outside of clinical trials to treat patients with serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory alternative treatment options. There is no requirement for a company to provide expanded access to its investigational products. However, if a company decides to make one of its investigational products available for expanded access, the FDA reviews each request for expanded access and determines if treatment may proceed. A sponsor of an investigational drug for a serious disease or condition is required to make available, such as by posting on its website, its policy on evaluating and responding to requests for individual patient access to such investigational drug. This requirement applies on the earlier of the first initiation of a Phase 2 or Phase 3 trial of the investigational drug or, as applicable, 15 days after the drug receives a designation as a breakthrough therapy, fast track product, or regenerative advanced therapy. We make available on our website the BeiGene contact information for requesting access to our investigational drugs and expected timeline for us to acknowledge receiving such requests.

U.S. Review and Approval Processes

The results of product development, preclinical studies and clinical trials, along with descriptions of the CMC, 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 small molecule drug or a BLA for a biologic, requesting approval to market the product. The submission of an 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. Additionally, before approving an NDA or BLA, the FDA may inspect one or more clinical trial sites to assure compliance with GCP and other requirements and the integrity of the clinical data submitted to the FDA.

The approval process can be 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 program 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.

Regulation of Companion Diagnostics in the United States

If safe and effective use of a therapeutic depends on an *in vitro* diagnostic, then the FDA generally will require approval or clearance of that diagnostic, known as a companion diagnostic, at the same time that the FDA approves the therapeutic product. In August 2014, the FDA issued final guidance clarifying the requirements that will apply to approval of therapeutic products and *in vitro* companion diagnostics. According to the guidance, for novel drugs, a companion diagnostic device and its corresponding therapeutic should be approved or cleared contemporaneously by the FDA for the use indicated in the therapeutic product's labeling. Once cleared or approved, the companion diagnostic must adhere to post-marketing requirements including the requirements of FDA's quality system regulation, medical device reporting, recalls and corrections along with product marketing requirements and limitations. Companion diagnostic manufacturers are subject to unannounced FDA inspections at any time during which the FDA will conduct an audit of the product(s) and the company's facilities for compliance with its authorities.

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 disease or 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 or biologic product candidate may request the FDA to designate the product candidate as a fast track product concurrently with, or at any time after, submission of an IND, and the FDA must determine if the product 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 product's NDA or BLA before the application is complete. This rolling review is available 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.

Zanubrutinib was granted fast track designation by the FDA for the treatment of WM and MZL. Tislelizumab was granted fast track designation by the FDA for the treatment of 1L HCC.

Accelerated Approval

Under FDA's accelerated approval regulations, the FDA may approve a drug, including a biologic, intended to treat a serious or life-threatening disease or condition that generally provides meaningful therapeutic benefit to patients over available treatments and demonstrates an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, 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 product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of post-approval clinical trials to confirm the effect on irreversible morbidity or mortality or other clinical benefit. Under the Food and Drug Omnibus Reform Act of 2022 ("FDORA"), the FDA is now permitted to require, as appropriate, that post-approval confirmatory trials be underway prior to approval or within a specific time period after accelerated approval is granted. Failure to conduct required post-approval studies with due diligence, or to confirm a clinical benefit during post-marketing studies, will allow the FDA to withdraw the drug from the market and, under FDORA, the FDA has increased authority for expedited procedures to withdraw approval of a product granted accelerated approval. In general, all promotional materials for drug candidates approved under accelerated regulations are subject to prior review by the FDA unless otherwise informed by the agency.

Zanubrutinib was granted accelerated approval by FDA for the treatment of adult patients with MCL who have received at least one prior therapy and for the treatment of adult patients with relapsed or refractory MZL who have received at least one anti-CD20-based regimen.

Breakthrough Designation

Breakthrough therapy designation is intended to expedite the development and review of a breakthrough therapy. A drug or biologic product candidate 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 the drug or biologic, alone or in combination with one or more other drugs or biologics, may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. A sponsor may request that a product candidate 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 candidate's marketing application, including by meeting with the sponsor throughout the product candidate'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 product candidate does not continue to meet the criteria for breakthrough therapy designation.

Zanubrutinib was granted breakthrough therapy designation by the FDA for the treatment of adult patients with MCL who have received at least one prior therapy.

Priority Review

The FDA may grant an NDA 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.

The NDA for zanubrutinib was granted priority review by the FDA for the treatment of adult patients with MCL who have received at least one prior therapy.

Designated Platform Technology

Under FDORA, a platform technology incorporated within or utilized by a drug or biologic is eligible for designation as a designated platform technology if (1) the platform technology is incorporated in, or utilized by, a product approved under an NDA or BLA; (2) preliminary evidence submitted by the sponsor of the approved or licensed product, or a sponsor that has been granted a right of reference to data submitted in the application for such product, demonstrates that the platform

technology has the potential to be incorporated in, or utilized by, more than one product without an adverse effect on quality, manufacturing, or safety; and (3) data or information submitted by the applicable person indicates that incorporation or utilization of the platform technology has a reasonable likelihood to bring significant efficiencies to the drug development or manufacturing process and to the review process. A sponsor may request the FDA to designate a platform technology as a designated platform technology concurrently with, or at any time after, submission of an IND application for a product that incorporates or utilizes the platform technology that is the subject of the request. If so designated, the FDA may expedite the development and review of any subsequent original NDA or BLA for a product that uses or incorporates the platform technology. Designated platform technology status does not ensure that a product will be developed more quickly or receive FDA approval. In addition, the FDA may revoke a designation if the FDA determines that a designated platform technology no longer meets the criteria for such designation.

Pediatric Information

Under the Pediatric Research Equity Act, as amended ("PREA"), certain NDAs and BLAs and certain NDA and BLA supplements must contain data that can be used to assess the safety and efficacy of the product candidate for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of pediatric data or full or partial waivers. The FDCA requires that a sponsor who is planning to submit a marketing application for a product candidate that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration submit an initial Pediatric Study Plan, or PSP, within 60 days of an end-of-Phase 2 meeting or, if there is no such meeting, as early as practicable before the initiation of the Phase 3 or Phase 2/3 study. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. The FDA and the sponsor must reach an agreement on the PSP. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from preclinical studies, early phase clinical trials and/or other clinical development programs. Unless otherwise required by regulation, PREA does not apply to a drug or biologic for an indication for which orphan designation has been granted except that PREA will apply to an original NDA or BLA for a new active ingredient that is orphan-designated if the drug or biologic is a molecularly targeted cancer product intended for the treatment of an adult cancer and is directed at a molecular target that FDA determines to be substantially relevant to the growth or progression of a pediatric cancer.

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.

The Drug Supply Chain Security Act ("DSCSA") was enacted in 2013 with the aim of building an electronic system to identify and trace certain prescription drugs distributed in the United States. The DSCSA mandates phased-in and resource-intensive obligations for pharmaceutical manufacturers, wholesale distributors, and dispensers over a 10-year period that is expected to culminate in November 2023. The law’s requirements include the quarantine and prompt investigation of a suspect product to determine if it is illegitimate, and notifying trading partners and FDA of any illegitimate product. Drug manufacturers and other parties involved in the supply chain must also meet chain of distribution requirements for product tracking and tracing, including a requirement to place a unique product identifier on prescription drug packages. This identifier consists of the National Drug Code, serial number, lot number and expiration date, in the form of a 2 dimensional data matrix barcode that can be read by humans and machines.

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 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 Regulatory 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 Act. The Hatch-Waxman Act permits 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.

Data 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 data 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 data 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.

Regulatory exclusivity in the United States can also include pediatric exclusivity and orphan drug exclusivity. Pediatric exclusivity, if granted, provides an additional six months of exclusivity, which runs from the end of other regulatory exclusivity or patent periods. This six-month exclusivity may be granted based on the voluntary completion of a pediatric trial in accordance with an FDA-issued ‘‘Written Request’’ for such a trial. Orphan drug exclusivity is described below under "Orphan Drugs."

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.

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 is eligible for a period of exclusivity against other biologics submitted under the abbreviated approval pathway during which time the FDA may not determine that another product is interchangeable with the same reference product for any condition of use. The FDA may approve multiple "first" interchangeable products so long as they are all approved on the same first day of marketing. This exclusivity period, which may be shared amongst multiple first interchangeable products, lasts 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 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 United States 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 orphan drug designation status by the FDA for the treatment of WM, CLL, MCL and MZL (3 subtypes). Tislelizumab was granted orphan drug designation status by the FDA for the treatment of ESCC, HCC and GC.

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 and in other countries, sales of any products for which we 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. Patients generally rely on third-party payors to reimburse all or part of the associated healthcare costs and no uniform policy of coverage and reimbursement for drug products exists among third-party payors. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor.

Additionally, 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, 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.

In some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost effectiveness of a particular product candidate to currently available therapies. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our product candidates. Historically, products launched in the European Union do not follow price structures of the United States and generally prices tend to be significantly lower.

Healthcare Reform

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. Such adoption of government controls and tightening of restrictive policies could limit payments for pharmaceuticals. For example, the Affordable Care Act (the "ACA") contains provisions that may reduce the profitability of drug products, including 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. Since its enactment, some of the provisions of the ACA have yet to be fully implemented, while certain provisions have been subject to judicial, Congressional, and Executive challenges. As a result, it is unclear how such efforts to challenge, repeal or replace the ACA, will impact our business.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, the Bipartisan Budget Act of 2018 amended the ACA by increasing the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D from 50% to 70% and closing the coverage gap in most Medicare drug plans. In addition, the Budget Control Act of 2011 and the Bipartisan Budget Act of 2015 led to aggregate reductions of Medicare payments to providers of up to 2% per fiscal year that will remain in effect through 2030 unless additional Congressional action is taken. In relation to the COVID-19 pandemic and pursuant to subsequent legislation, this 2% reduction was periodically suspended, but resumed on July 1, 2022. Further, the American Taxpayer Relief Act reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

The Centers for Medicare and Medicaid Services ("CMS") published a final rule that gives states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. CMS also published a final rule to allow Medicare Advantage Plans the option of using step therapy for Part B drugs.

There has also been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed bills designed to bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for pharmaceutical products. At the federal level, President Biden directed the FDA to work with states and Indian Tribes that propose to develop section 804 Importation Programs in accordance with the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, and the FDA's implementing regulations.

The FDA released a final rule, which went into effect in November 2020, providing guidance for states to build and submit importation plans for drugs from Canada. Further, authorities in Canada have passed rules designed to safeguard the Canadian drug supply from shortages. If implemented, importation of drugs from Canada may adversely affect the price we receive for our medicines.

In November 2020, the U.S. Department of Health and Human Services ("HHS") finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through PBMs, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between PBMs and manufacturers. Pursuant to court order, the removal and addition of the aforementioned safe harbors were delayed and recent legislation imposed a moratorium on implementation of the rule until January 1, 2032. Further, implementation of this change and new safe harbors for point-of-sale reductions in price for prescription pharmaceutical products and PBM service fees are currently under review by the Biden administration and may be amended or repealed.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical 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. While much of the focus of state pricing policies is limited to Medicaid, we cannot assess the impact that these and other measures such as state transparency policies will have on our business.

Other U.S. Healthcare Laws and Compliance Requirements

We are subject to various federal and state laws targeting fraud and abuse in the healthcare industry. These laws may impact, among other things, our 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 healthcare Anti-Kickback Statute ("AKS"), which prohibits, among other things, knowingly and willfully soliciting, receiving, providing, 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 reward, or in return for, either the referral of an individual, or the purchase, lease, order or recommendation or arrangement 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. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other. Although there are several statutory exceptions and regulatory safe harbors protecting certain common activities from prosecution, they are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exception or safe harbor. A person or entity can be found guilty of violating the AKS without actual knowledge of the statute or specific intent to violate it. In addition, the government may assert that a claim including items or services resulting from a violation of the AKS constitutes a false or fraudulent claim for purposes of the federal False Claims Act ("FCA") or federal civil money penalties statute. Violations of the AKS carry potentially significant civil fines and criminal penalties, including imprisonment, fines, administrative federal civil monetary penalties, and exclusion from participation in federal healthcare programs. This law applies to our marketing practices, educational programs, pricing policies and relationships with healthcare providers, by prohibiting, among other things, soliciting, receiving, offering or providing remuneration intended to induce the purchase or recommendation of an item or service reimbursable under a federal healthcare program, such as the Medicare or Medicaid programs. There are safe harbor protections under the AKS for certain coordinated care and value-based arrangements among clinicians, providers, and others. We continue to evaluate what effect, if any, these rules will have on our business;

- the federal civil and criminal false claims and civil monetary penalty laws, such as the FCA, 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, fictitious or fraudulent; knowingly making or causing 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 may assert that a claim including items and services resulting from a violation of the federal AKS constitutes a false of fraudulent claim for purposes of the FCA. The government may deem manufacturers to have “caused” the submission of false or fraudulent claims by, for example, providing inaccurate billing or coding information to customers or promoting a product off-label. Companies that submit claims directly to payors may also be liable under the FCA for the direct submission of such claims. The FCA also permits a private individual acting as a “whistleblower” to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery. When an entity is determined to have violated the federal civil FCA, the government may impose civil fines and penalties for each false claim, plus treble damages, and exclude the entity from participation in Medicare, Medicaid and other federal healthcare programs. Our marketing and activities relating to the reporting of wholesaler or estimated retail prices for our products, the reporting of prices used to calculate Medicaid rebate

information and other information affecting federal, state and third-party reimbursement for our products, and the sale and marketing of our products and any future product candidates are subject to scrutiny under this law;

- the Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), which prohibits, among other things, 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. Similar to the federal Anti-Kickback Statute, a person or entity can be found guilty of violating HIPAA without actual knowledge of the statute or specific intent to violate it;

- HIPAA, as further amended by the Health Information Technology for Economic and Clinical Health Act of 2009 ("HITECH"), and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose certain 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 creation, maintenance, receipt, use, or disclosure of, individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs. In addition, there may be additional federal, state and non-U.S. laws which govern the privacy and security of health and other personal information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts;

- 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, with specific exceptions, to report annually to Centers for Medicare & Medicaid Services information related to payments or other transfers of value made to physicians, nurse practitioners, certified nurse anesthetists, anesthesiologist assistants, physician assistants, clinical nurse specialists, and certified nurse midwives as well as teaching hospitals. Manufacturers are also required to disclose ownership and investment interest held by physicians and their immediate family members;

- federal price reporting laws, which require manufacturers to calculate and report complex pricing metrics in an accurate and timely manner to government programs;

- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers; and

- the Foreign Corrupt Practices Act ("FCPA"), which prohibits companies and their intermediaries from making, or offering or promising to make, improper payments to non-U.S. officials for the purpose of obtaining or retaining business or otherwise seeking favorable treatment.

Similarly, state privacy laws may be broader and require greater protections than HIPAA. These data privacy and security laws may differ from each other in significant ways and often are not pre-empted by HIPAA, which may complicate compliance efforts. For example, in June 2018, the State of California enacted the California Consumer Privacy Act of 2018 ("CCPA"), which gives California residents expanded rights to access and delete their personal information, opt out of certain personal information sharing, and receive detailed information about how their personal information is used. CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. Further, the California Privacy Rights Act ("CPRA") will create additional obligations with respect to processing and storing personal information that are scheduled to take effect on January 1, 2023 (with certain provisions having retroactive effect to January 1, 2022). We will continue to monitor developments related to the CPRA and anticipate additional costs and expenses associated with CPRA compliance. Other U.S. states also are considering omnibus privacy legislation and industry organizations regularly adopt and advocate for new standards in these areas. While the legislation and proposed regulations including the CCPA and CPRA contain an exception for certain activities that involve PHI subject to HIPAA, we cannot yet determine the impact the CCPA, CPRA or other such future laws, regulations and standards may have on our business.

Additionally, we are subject to state 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 third-party payor, not just governmental payors, but also private insurers. These laws are enforced by various state agencies and through private actions. 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 that restrict the payments made to healthcare providers and other potential referral sources. Several states and local laws also impose other marketing restrictions or require pharmaceutical companies to make marketing or price disclosures to the state, require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers, and require the registration of pharmaceutical sales representatives. State and foreign laws, including for example the European Union General Data Protection Regulation, which became effective May 2018, also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. 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. Finally, there are state and foreign laws governing the privacy and security of health information, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

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

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

The scope and enforcement of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal and state enforcement has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry. Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations.

EU and UK Data Protection Laws

In the EU, the General Data Protection Regulation ("GDPR") governs the processing of personal data. The GDPR imposes a broad range of strict requirements on companies subject to the GDPR, such as including requirements relating to having legal bases for processing personal data relating to identifiable individuals and transferring such information outside the European Economic Area ("EEA"), including to the U.S., providing details to those individuals regarding the processing of their personal data, implementing safeguards to keep personal data secure, having data processing agreements with third parties who process personal data, providing information to individuals regarding data processing activities, responding to individuals’ requests to exercise their rights in respect of their personal data, obtaining consent of the individuals to whom the personal data relates, reporting security and privacy breaches involving personal data to the competent national data protection authority and affected individuals, appointing data protection officers, conducting data protection impact assessments, and record-keeping. The GDPR

substantially increases the penalties to which we could be subject in the event of any non-compliance, including fines of up to €20,000,000 or 4% of total annual global revenue, whichever is greater. The GDPR increases the responsibility and liability of pharmaceutical companies in relation to processing personal data, and companies may be required to put in place additional mechanisms to ensure compliance with the new EU data protection rules. In addition, further to the UK's exit from the EU on January 31, 2020, the GDPR ceased to apply in the UK at the end of the transition period on December 31, 2020. However, as of January 1, 2021, the UK's European Union (Withdrawal) Act 2018 incorporated the GDPR (as it existed on December 31, 2020 but subject to certain UK specific amendments) into UK law, referred to as the UK GDPR. The UK GDPR and the UK Data Protection Act 2018 set out the UK's data protection regime, which is independent from but aligned to the EU's data protection regime. Non-compliance with the UK GDPR may result in monetary penalties of up to £17.5 million or 4% of worldwide revenue, whichever is higher. Although the UK is regarded as a third country under the EU's GDPR, the EC has now issued a decision recognizing the UK as providing adequate protection under the EU GDPR and, therefore, transfers of personal data originating in the EU to the UK remain unrestricted. Like the EU GDPR, the UK GDPR restricts personal data transfers outside the UK to countries not regarded by the UK as providing adequate protection. The UK government has confirmed that personal data transfers from the UK to the EEA remain free flowing.

To enable the transfer of personal data outside of the EEA or the UK, adequate safeguards must be implemented in compliance with European and UK data protection laws. On June 4, 2021, the EC issued new forms of standard contractual clauses for data transfers from controllers or processors in the EU/EEA (or otherwise subject to the GDPR) to controllers or processors established outside the EU/EEA (and not subject to the GDPR). The new standard contractual clauses replace the standard contractual clauses that were adopted previously under the EU Data Protection Directive. The UK is not subject to the EC's new standard contractual clauses but has published a draft version of a UK-specific transfer mechanism, which, once finalized, will enable transfers from the UK. We will be required to implement these new safeguards when conducting restricted data transfers under the EU and UK GDPR and doing so will require significant effort and cost.

PRC Regulation

In the 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 legal framework for the administration of pharmaceutical products in China was established by the Drug Administration Law of the PRC (the "DAL"). The DAL applies to entities and individuals engaged in the development, production, trade, clinical use, as well as supervision and administration of pharmaceutical products by regulatory agencies. It provides for a framework for regulating pharmaceutical manufacturers, pharmaceutical trading companies, medical institutions, and the research, development, manufacturing, distribution, packaging, pricing, and advertisement activities related to pharmaceutical products. The Implementing Measures of the Drug Administration Law as amended in 2019 provides detailed implementation regulations for the DAL.

The Revised DAL

The DAL, revised in 2019 (the "rDAL"), embodies an expected regulatory trend to strengthen the life-cycle management of drugs, to balance the development of innovative drugs and generic drugs, and to enhance drug review and enforcement. It also reflects legislative efforts to address prominent problems of the pharmaceutical industry, such as counterfeit and substandard drugs and high drug prices.

The rDAL contains a dedicated chapter on the Marketing Authorization Holder ("MAH") system. Subject to approval by the NMPA, MAHs will be allowed to transfer their marketing authorizations. It is uncertain whether the transferability of MAH will offer more flexibility in structuring cross-border transactions. In addition, the implementation of the MAH system was accompanied by a range of new requirements for the MAHs. For example, a MAH must establish a quality assurance system and be responsible for the whole process and all aspects of preclinical research, clinical trials, manufacturing and distribution, post-marketing research, adverse drug reaction monitoring and reporting. A foreign MAH is required to engage a local agent to fulfill the MAH's obligations and the foreign MAH is subject to joint and several liability in the event of any wrongdoing. It is unclear how the scope of such joint liability will be defined.

The rDAL no longer requires the certification for GCP, good supply practice ("GSP"), and GMP. However, drug manufacturers and drug distributors must still comply with current GMP and GSP requirements. Pursuant to the rDAL, NMPA

and its local counterparts are directed to strengthen their surveillance of drug manufacturers and distributors, including through regular and continuous site inspections, to ensure their compliance. It remains to be seen how clinical trial institutions will ensure self-compliance with GCP requirements and whether there will be more inspections of clinical trial institutions.

The rDAL also requires MAHs, manufacturers, distributors, and medical institutions to establish and implement drug track and trace systems. The NMPA will issue related standards and regulations regarding drug track and trace system. A drug pharmacovigilance system will also be established to monitor, identify, evaluate and control adverse drug reactions and other possible drug-related problems.

The rDAL creates an expanded access pathway for investigational drugs under which a company sponsor of a clinical trial in China can apply to establish an expanded access treatment program for patients with life-threatening disease who otherwise do not satisfy the inclusion criteria of a clinical trial. To quality for expanded access: (1) the drug must be used for life-threatening diseases that lack effective treatment; (2) the drug must have demonstrated its potential efficacy based on medical observations; (3) such use is in line with ethical principles; (4) such expanded use has been reviewed and approved (although the approval pathway not clear), and has obtained patients' informed consent; and (5) the drug must be used within the clinical trial institution and used on patients with similar conditions.

The rDAL also significantly increases and expands penalties for violations. Depending on various types of violations, the rDAL imposes different penalties, including warnings, confiscation of illegal gains, fines of up to RMB5 million (about $725,000) or up to 30 times of illegal gains, revocation of required business and operating licenses, certificates or approval documents for drugs, suspension of business, temporary (10 years) or permanent debarment of companies, institutions and responsible persons, and criminal liabilities in the case of serious violations.

There are still uncertainties with respect to the interpretation and implementation of the rDAL. We plan to closely monitor the implementation of the rDAL and its impact on our operations in China.

Regulatory Authorities and Government Reorganization

In China, the NMPA is the primary regulator for pharmaceutical products and businesses. The agency was formed from the prior China Food and Drug Administration ("CFDA") in 2018 as part of a complete government reorganization. The NMPA is no longer an independent agency. Its parent agency is the State Administration for Market Regulation (the "SAMR"), into which agencies responsible for, among other areas, consumer protection, advertising, anticorruption, antitrust, 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 CDE, which remains under the NMPA, conducts the technical evaluation of each drug and biologic application for safety and efficacy.

The National Health Commission ("NHC") 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. The 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 programs for pharmaceutical products. This is the primary way that public hospitals and their internal pharmacies procure drugs.

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

Preclinical and Clinical Development

The NMPA requires preclinical data to support registration applications for new drugs. Preclinical work, including safety assessment studies, must meet the GLP standards, issued in 2003 and amended in 2017. The rDAL requires the NMPA to accredit GLP labs, and that nonclinical studies of chemical drug substances and preparations and biologics that are not yet marketed in China be conducted in GLP-certified labs. There are no approvals required from the NMPA to conduct preclinical studies.

A Certificate for Use of Laboratory Animals is required for performing experimentation on animals under the Regulations for the Administration of Affairs Concerning Experimental Animals issued in 1988 and last amended in 2017, the Administrative Measures on Good Practice of Experimental Animals issued in 1997, and the Administrative Measures on the Certificate for Experimental Animals (Trial) issued in 2001. Applicants for this certificate must satisfy a number of conditions,

including (1) the environment and facilities for lab animals' living and propagating must satisfy national requirements; (2) lab animals must be qualified and sourced from institutions with Certificates for Production of Lab Animals; and (3) the animals' feeding and experimentation must be conducted by professionals, specialized and skilled workers, or other trained personnel.

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., imported drugs).

Therapeutic biologics follow a similar categorization, with Category 1 being new to the world. Like with small molecule drugs, Category 1 is for innovative biologics that have not been approved inside or outside of China. Biosimilars are under Category 3. Each of zanubrutinib, tislelizumab, pamiparib and lifirafenib is classified as Category 1 based on the defined registration category by the NMPA. Zanubrutinib, pamiparib and tislelizumab have been approved by the NMPA as Category 1 drugs.

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. The NMPA's Drug Registration Rules effective from July 1, 2020 ("DRR") provides certain categories of drugs that may be eligible for priority status, among which, the following may be particularly relevant for us: (1) drugs that are clinically and urgently needed but insufficient in supply; (2) innovative drugs and improved new drugs for prevention and treatment of major contagious diseases and rare diseases; (3) new pediatric drugs, (4) drugs designated as breakthrough therapies, and (5) drugs that satisfy the conditional approval criteria.

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.

Amgen's sBLA for BLINCYTO has been accepted by the CDE and granted priority status. Our sNDA for tislelizumab for MSI-H/dMMR solid tumor has been accepted by the CDE and granted priority status.

Conditional Approval

NMPA also permits conditional approval of certain medicines based on early phase data. The agency has done this for medicines that meet unmet medical needs for life-threatening illnesses and also for medicines that treat orphan indications. Under the DRR, drugs that meet one of the three criteria might be eligible for conditional approval: (1) drugs that treat life threatening illnesses for which there are no effective treatment or preventive methods, but their clinical trials already have the data to prove efficacy and their clinical value is predictable, (2) drugs that are urgently needed for public health reasons, and their clinical trials already have the data to prove efficacy and their clinical value is predictable; or (3) vaccines that are urgently needed for major public health emergencies or otherwise deemed by the National Health Commission to be urgently needed, and it is concluded upon evaluation that their benefits outweigh their risks. Following approval, the MAH is required to take risk mitigation measures and complete a post-market study as required by the NMPA within a prescribed timeline.

BRUKINSA received conditional approval for the treatment of MCL in adult patients who have received at least one prior therapy, CLL or SLL in adult patients who have received at least one prior therapy, and for adult patients with WM who have received at least one prior therapy. Tislelizumab received conditional approval as a treatment for patients with cHL who have received at least two prior therapies and as a treatment for patients with locally advanced or metastatic UC, a form of bladder cancer, with PD-L1 high expression whose disease progressed during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy, and for the treatment of patients with hepatocellular carcinoma (HCC) who have been previously treated with at least one systemic therapy. Pamiparib received conditional approval for the treatment of patients with germline BRCA (gBRCA) mutation-associated recurrent advanced ovarian, fallopian tube, or primary peritoneal cancer who have been treated with two or more lines of chemotherapy. XGEVA received conditional approval for the treatment of adults and skeletally mature adolescents with giant cell tumor of the bone

(GCTB) that is unresectable or where surgical resection is likely to result in severe morbidity and for the prevention of SREs in patients with bone metastases from solid tumors and in patients with multiple myeloma. BLINCYTO received conditional approvals for the treatment of both adult and pediatric patients with R/R B-cell precursor acute lymphoblastic leukemia. KYPROLIS received conditional approval for the treatment of adult patients with R/R multiple myeloma. QARZIBA received conditional approval for high-risk neuroblastoma.

Breakthrough Therapy Designation

Breakthrough therapy designation ("BTD") is a process designed to expedite the development and review of clinical stage, innovative or improved new drugs that meet the following criteria: (1) they are intended to treat life threatening conditions or conditions that have serious negative impact on the quality of life, and (2) there are no effective treatment or preventive methods available, or there is preliminary clinical evidence indicating that they may demonstrate substantial improvement over available therapies. Applicants of drugs designated as breakthrough therapies will be entitled to direct communications with CDE at key states during the clinical trials, and may seek CDE's opinion on study progress.

Amgen's $KRAS^{G12C}$ inhibitor sotorasib was granted BTD in China for patients with *KRAS p.G12C*-mutated locally advanced or metastatic NSCLC who have received at least one prior systemic therapy. BRUKINSA as a treatment for adult patients with CLL/SLL was granted BTD in China. ZW25 (zanidatamab) as a treatment for R/R HER2-expressing biliary tract cancer was granted BTD.

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 and preliminary CMC 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.

Clinical Trial Approval

All clinical trials conducted in China for the purpose of seeking marketing approvals must be approved by the NMPA and conducted at hospitals satisfying GCP requirements. In addition to a standalone China trial to support development, imported drug applicants may include Chinese clinical sites as part of an international multicenter trial ("IMCT"). Domestically manufactured drugs are not subject to foreign approval requirements, and in contrast to prior practice, the NMPA has decided to permit those drugs to conduct development via an IMCT as well.

The rDAL has now also adopted an implied approval 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. The rDAL also expands the number of trial sites by abolishing the GCP accreditation system and requiring trial sites to follow a more simplified notification procedure.

New Policies on Clinical Value-Oriented R&D for Oncology Drugs

The NMPA finalized in November 2011 the Guideline on Clinical Value-Oriented Research and Development for Oncology Drugs, as part of its policies intended to encourage the research and development of innovative oncology drugs with significant clinical value, and discourage repeated research and development of "me-too" drugs with minimal or no clinical value to patients.

Clinical Trial Register

Clinical trials conducted in China must be registered and published through the Drug Clinical Trial Information Platform (http://www.chinadrugtrials.org.cn). Applicant are required to pre-register the trial information within one month after obtaining the clinical trial approval to obtain the trial's unique registration number and to complete registration of certain follow-up information before the first subject's enrollment in the trial. If the foregoing pre-registration and registration is not

obtained within one year after obtaining the clinical trial approval, the applicant shall submit an explanation, and if the procedure is not completed within three years, the clinical trial approval automatically expires.

Human Genetic Resources Regulation

The Regulation on the Administration of Human Genetic Resources ("HGR Regulation") became effective on July 1, 2019. The HGR Regulation applies to all human genetic resources ("HGR")-related activities for R&D purposes, including sampling, biobanking, use of HGR materials and associated data in China, and the provision or sharing of such materials or data with foreign parties.

The HGR Regulation applies to foreign parties, including foreign entities and entities established or actually controlled by foreign entities and individuals. As BeiGene, Ltd. is a Cayman Islands company, we and our activities in China are subject to the HGR Regulation. Such foreign parties seeking access to China's HGRs for scientific research, including clinical trials intended to support marketing approval of drugs and medical devices in China, must do so only through collaborations with Chinese parties, such as Chinese hospitals. The HGR Regulation prohibits foreign parties from independently sampling or biobanking any China HGR in China and requires approval for the sampling of certain HGR and biobanking of all HGR by Chinese parties. Any cross-border transfer of the HGR materials, either under an international collaboration or as a direct export, must be on an as-needed basis and requires approval. In addition, providing HGR data to foreign parties requires a record filing.

Another significant change is the HGR Regulation replaced the advance approval requirement with a record-filing procedure for international collaborations on clinical trials intended to support marketing approval of drugs in China that do not transfer HGR materials abroad, while the advance approval requirement still applies if such trials involve export of HGR materials or the collection, testing, analysis or disposals of HGR samples during the trials are not solely conducted at the clinical trial sites. Companies conducting global clinical trials may benefit little from this record filing procedure because those trials would often require cross-border transfer of HGR materials and the advance approval requirement would still apply.

The HGR Regulation retains the provision in the Interim Measures for the Administration of Human Genetic Resources issued in 1998 that parties should jointly apply for and own the patent rights arising from the results generated from international collaborations that utilize China HGR. Subject to approval, the parties may contractually agree on how to dispose of their patent rights and non-patent proprietary rights arising from the collaboration. As the joint ownership requirement is rather broad, it is unclear how this requirement will be implemented in practice.

The HGR Regulation also significantly increases and expands penalties for various violations, including warnings, disgorgement of illegal gains, confiscation of illegal HGR, fines up to RMB10 million ($1,450,000) or 5-10 times of illegal gains in the event such illegal gains exceed RMB1 million ($145,000), and temporary (1-5 years) or permanent debarment of companies, institutions and responsible persons from future HGR projects regulated by the HGR Regulation.

We expect that HGR-related activities will receive greater attention and focus from regulators going forward.

Trial Exemptions and Acceptance of Foreign Data

The NMPA may be flexible on the requirements of trials and data generated in China, 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. In 2018, the NMPA issued the Technical Guidance Principles on Accepting Foreign Drug Clinical Trial Data (the "Guidance Principles"), as one of the implementing rules for the Opinions on Deepening the Reform of the Evaluation and Approval Systems and Encouraging Innovation on Drugs and Medical Devices (the "Innovation Opinion"). According to the Guidance Principles, data from foreign clinical trials must meet authenticity, completeness and accuracy requirements and such data must be obtained in compliance with the relevant requirements under the GCP of the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use. Sponsors must be attentive to potentially meaningful ethnic differences in the subject population.

The NMPA now 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 in 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 to be approved in China without local clinical trials if they (1) prevent or treat orphan diseases, (2) 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 for such conditional approvals will be required to establish a risk mitigation plan and may be required to complete trials in China after the drug is approved. The CDE has developed a list of drugs that meet these criteria.

Clinical Trial Process and Good Clinical Practices

As in other parts of the world, clinical trials in China typically 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 and comply with GCP. The NMPA conducts inspections on clinical trials conducted in China to assess GCP compliance and may refuse to approve the drug if it finds substantial issues in the trials. In addition, upon granting the drug registration certificate, NMPA may, at its sole discretion, require a Phase 4 trial to be conducted by MAH within a specified period of time so as to further monitor and obtain safety and efficacy data of the drug.

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 first installment of a Marketed Drug List (China's "Orange Book") with information about drugs that may serve as reference products.

Pursuant to GCP, sponsors of clinical trials are responsible for proper packaging and labeling of drugs used for clinical trials, and in double-blinded clinical trials, the investigational drugs shall be consistent with the control drug or placebo in appearance, odor, packaging, labeling, and certain other features. Pharmaceutical packaging must comply with national and professional standards. If there is no national or professional standard available, companies may formulate and implement its own standards after obtaining the approval of the provincial administration for medical products or bureau of standards. Changes in such approved packaging standards need to be re-approved. Drugs of which the packaging standards are not approved shall not be released or marketed in China, except for those specifically supplied to the military.

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 domestically manufactured drugs, NDA sponsors must submit data derived from the submitted drugs in support of their approval. Under the rDAL, upon approval of the registration application, the NMPA will issue a drug registration certificate to the applicant which is in fact the marketing approval of the drug, and the applicant is no longer required to be equipped with relevant manufacturing capability.

Manufacturing and Distribution

All facilities that manufacture 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, and the manufacturing facility is also required to be in compliance with GMP.

Similarly, to conduct sales, importation, shipping and storage, a company must obtain a Drug Distribution License ("DDL") from the local drug regulatory authority, subject to renewal every five years. As with GMPs, companies are required to be in compliance with GSP. One exception is that the rDAL and relevant implementation rules allow the MAH to conduct wholesales of its drugs directly without holding a separate DDL for wholesale, however, a retail DDL would still be required if the MHA intends to conduct direct retail to patients.

China has developed 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 is 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.

Post-Marketing Surveillance

Under the rDAL, the MAH of a drug is ultimately 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 the MAH with any product recalls. An

MAH for 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 expressly 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

The amendments to the PRC Patent Law (the "Amended PRC Patent Law") became effective on June 1, 2021. The Amended PRC Patent Law contains both patent term extension and a mechanism for early resolution of patent disputes, which may be comparable to patent linkage in the United States. However, the provisions for patent term extension are unclear and/or remain subject to the approval of implementing regulations that are still in draft form or have not yet been proposed, leading to uncertainty about its scope and implementation.

Non-Patent Exclusivities

Regulatory Data Protection

The Innovation Opinion provided a foundation to improve and implement a system for regulatory data protection to protect innovative drugs. This protection will be available for 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. In the Trade Agreement, China has committed to providing for effective protection of undisclosed clinical trial or other data submitted as a condition of marketing approval.

The NMPA has published draft regulations 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.

The proposed regulations also call for a reduction in exclusivity 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 Amended PRC Patent Law provides a cause of action to allow a patent holder to initiate a declarative action during the regulatory review process of a drug to determine whether the drug falls within the patent scope, which may be comparable to the patent linkage system in the United States. The system requires 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.

Patent Term Extension

The Amended PRC Patent Law provides patent term extension, similar to the United States, for the patent term lost during the regulatory review process of a new drug upon the patent holder's request. The extended term shall not exceed five years, and the total patent term after market entry of the new drug shall not exceed 14 years. However, the provisions for patent term extension are unclear and/or remain subject to the approval of implementing regulations that are still in draft form, leading to uncertainty about the scope of implementation.

Reimbursement and Pricing

China's national medical insurance program currently consists of two fundamental sub-programs: (1) the basic medical insurance program for urban employees, under which urban employers are required to enroll their employees in the program and the insurance premium is jointly contributed by the employers and employees; and (2) the basic medical insurance program for urban and rural residents, which allows urban and rural residents who do not have employers to voluntarily participate in the basic medical insurance program and the insurance premium is jointly contributed by the participants and the government. 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 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 used 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 government has also been negotiating with manufacturers of exclusive 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 2023 covers approximately 3,000 drugs in total, including 147 drugs for which the prices were determined through negotiations between the drug companies and government. China has been pursuing a policy of expediting the addition of innovative oncology drugs to this list. REVLIMID has been included in the NRDL since 2017. VIDAZA has been included in the NRDL since 2018. BRUKINSA (zanubrutinib), tislelizumab, and XGEVA (120-mg denosumab) have been included in the NRDL since 2021. PARP inhibitor pamiparib has been included in the NRDL since 2022. KYPROLIS was included for the first time in the NRDL in January 2023, which will take effect on March 1, 2023.

Government Price Controls

China has abolished its previous 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 now 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 that are typically conducted once every year by provincial or municipal-level government agencies. 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 bid price, product quality, clinical effectiveness, product safety, level of technology, the manufacturer's qualifications and reputation, after-sale services and innovation.

Over the last decade, the government has employed various methods to improve the affordability of drugs. 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 governments have begun to allow medical institutions to collectively negotiate with manufacturers for a second price to further lower the already agreed bid price. The Two-Invoice System, described above, is also designed to reduce price mark-ups brought about by multi-tier distribution chains.

In 2019, the government approved a volume-based, centralized drug procurement program in an effort to deepen the reform of the medical and health sector and optimize the pricing of drugs. Drugs are selected from generic brands for volume-based, centralized drug procurement. The selected drugs must pass the equivalence evaluation on quality and efficacy. The program is aimed at further lowering drug costs for patients, reducing transaction costs for enterprises, regulating drug use by institutions, and improving the centralized drug procurement and pricing system. All approved enterprises that produce drugs on the procurement list in China may participate. Clinical effects, adverse reactions, and batch stability of the drugs will be considered, and their consistency will be the main criteria for evaluation, while production capacity and stability of the supplier will also be considered.

Other PRC National and Provincial Laws and Regulations

Pharmaceutical companies operating in China 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 patient medical information and the circumstances under which patient medical information may be released for inclusion in our information systems or released by us to third parties. The privacy of human subjects in clinical trials is also protected under regulations. For example, clinical trial case report forms must avoid disclosing names of 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

The Foreign Investment Law of the PRC (the "Foreign Investment Law") and its implementing rules (the "Implementing Rules") took effect in 2020 and replaced previous laws and regulations governing foreign investment in China. The Foreign Investment Law and Implementing Rules establish a basic framework for access to, and the promotion and administration of foreign investments in China. They reflected China's legislative efforts to rationalize China's foreign investment regulatory regime in line with prevailing international practice and to unify legal requirements for both foreign and domestic investments. The Implementing Rules further clarified that China would encourage and promote foreign investment, protect the lawful rights and interests of foreign investors, and continue to improve the foreign investment environment in China.

The Foreign Investment Law establishes a pre-entry national treatment and negative list system for the administration of foreign investments. "Pre-entry national treatment" means that the treatment afforded to foreign investors at the market access stage shall be no less favorable than that afforded to domestic investors. "Negative list" refers to the special administrative measures for foreign investors' access to specific fields or industries. Foreign investments outside of the negative list will be granted national treatment. Foreign investors shall not invest in the prohibited fields as specified in the negative list, and foreign investors who invest in the restricted fields shall comply with certain special requirements including the shareholding percentage and citizenship of senior executives. The current industry entry clearance requirements governing foreign investment activities in the PRC are set out in two categories, namely the Special Entry Management Measures for the Access of Foreign Investment (Negative List) (2022 version), and the Encouraged Industry Catalogue for Foreign Investment (2022 version) (the "2022 Encouraged Industry Catalogue"). Industries not listed in these two categories are generally deemed "permitted" for foreign investments unless specifically restricted by other applicable PRC laws or regulations. Pursuant to the 2022 Encouraged Industry Catalogue, the research, development and manufacture of innovative oncology drugs and certain other types of pharmaceutical products belongs to the encouraged industries for foreign investment.

Regulations Relating to Product Liability

Under a law which took effect in 2021, a defective product which causes property damage or physical injury to any person may subject the manufacturer or vendor of such product to civil liability for such damage or injury. Additionally, China's Product Quality Law, first adopted in 1993 and amended in 2018, governs the supervision and administration of product quality, aiming to protect the rights end-users and consumers. According to the Product Quality Law, manufacturers is liable for the quality of products produced by them, and sellers are required take measures to ensure the quality of the products sold by them. A manufacturer is liable for compensating for any bodily injury or property damage resulting from product defects unless the manufacturer is able to prove that: (1) the product was not distributed; (2) the defects causing injury or damage did not exist at the time that the product was distributed; or (3) science and technology at the time that the product was distributed was at a level incapable of detecting the defects. A seller is liable for compensating for any bodily injury or property damage of others caused by the defects in the product if such defects are attributable to the seller. A seller is required to pay compensation if it fails to indicate either the manufacturer or the supplier of the defective product. A person who is injured or whose property is damaged by the defects in the product may claim compensation from the manufacturer or the seller.

Regulations Relating to Commercial Bribery

Pharmaceutical companies involved in a criminal investigation or administrative proceeding related to bribery are listed in the Adverse Records of Commercial Briberies by the provincial health commissions. If a pharmaceutical company or its agent is listed, public medical institutions located in the local provincial level region are prohibited from making any purchase from the company for two years. Where a pharmaceutical company or its agent is listed in the adverse records on two or more occasions within five years, all public medical institutions in China are not permitted to purchase any products from that company for two years.

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 ("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 for payment beyond the business scope of the enterprises or the payment prohibited by relevant laws and regulations; directly or indirectly 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; or paying expenses related to the purchase of real estate that is not for self-use, except for real estate enterprises.

In 2017, new regulations were adopted which, among other things, relax the restrictions 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.

In 2019, SAFE issued the Circular of the State Administration of Foreign Exchange on Further Promoting the Facilitation of Cross-border Trade and Investment ("Circular 28"). Circular 28 allows non-investment foreign-invested enterprises to use their capital funds to make equity investments in China, provided that such investments do not violate the effective Special Entry Management Measures for the Access of Foreign Investment (Negative List) and the target investment projects are genuine and in compliance with laws. The interpretation and implementation of Circular 28 in practice are subject to substantial uncertainty.

Regulations Relating to Dividend Distributions

Foreign-invested companies 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 foreign invested PRC companies 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 companies. 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

Under Chinese law, employers must execute written labor contracts with their full-time employees and 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, and 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 these requirements may result in the imposition of fines and other administrative and criminal liability in the case of serious violations.

In addition, employers must provide employees with welfare schemes covering pension insurance, unemployment insurance, maternity insurance, work-related injury insurance, medical insurance and housing funds. These payments are made to local administrative authorities, and any employer who fails to contribute may be fined and ordered to pay the deficit amount within a stipulated time limit.

Regulations Relating to Overseas Listing

On February 17, 2023, the CSRC released the Trial Administrative Measures of Overseas Securities Offering and Listing by Domestic Companies, or the Overseas Listing Trial Measures, and five relevant guidelines, which will take effect from March 31, 2023, requiring Chinese domestic companies' overseas offerings and listings of equity securities be filed with the CSRC.

The Overseas Listing Trial Measures clarify the scope of overseas offerings and listings by Chinese domestic companies which are subject to the filing and reporting requirements thereunder, and provide, among others, that Chinese domestic companies that have already directly or indirectly offered and listed securities in overseas markets prior to the effectiveness of the Overseas Listing Trial Measures shall fulfil their filing obligations and report relevant information to the CSRC within three working days after conducting a follow-on offering of equity securities on the same overseas market, and follow the relevant reporting requirements within three working days upon the occurrence of any specified circumstances provided thereunder.

According to the Overseas Listing Trial Measures, if we were deemed as an indirect overseas listed Chinese domestic company but fail to complete the filing procedures with the CSRC for any of our follow-on offerings or follow any other reporting requirements required thereunder, we may be subject to penalties, sanctions and fines imposed by the CSRC and relevant departments of the State Council.

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, and other matters impacting our business vary from country to country. In all cases, clinical trials must be conducted in accordance with GCP requirements, applicable regulatory requirements, and the ethical principles having their origin in the Declaration of Helsinki.

Status under Holding Foreign Companies Accountable Act

In December 2021, the SEC adopted rules (the "Final Rules") to implement the Holding Foreign Companies Accountable Act (the "HFCAA"). The HFCAA includes requirements for the SEC to identify issuers who file annual reports with audit reports issued by independent registered public accounting firms located in foreign jurisdictions that the Public Company Accounting Oversight Board ("PCAOB") is unable to inspect or investigate completely because of a position taken by a non-U.S. authority in the accounting firm's jurisdiction ("Commission-Identified Issuers"). The HFCAA also requires that, to the extent that the PCAOB has been unable to inspect an issuer's independent registered public accounting firm for three consecutive years since 2021, the SEC shall prohibit the issuer's securities registered in the United States from being traded on any national securities exchange or over-the-counter markets in the United States. In December 2022, the Accelerating Holding Foreign Companies Accountable Act amended the HFCAA to shorten the three-year period to two years.

Under the Final Rules, the SEC adopted submission and disclosure requirements by amending Form 10-K and other annual reporting forms and established procedures to identify issuers and prohibit the trading of the securities of certain registrants as required by the HFCAA. Specifically, the Final Rules require each Commission-Identified Issuer to submit documentation to the SEC annually on or before its annual report due date that establishes that it is not owned or controlled by a government entity in its public accounting firm's foreign jurisdiction and require additional specified disclosures by "foreign issuers" as defined in Rule 3b-4 promulgated under the Securities Exchange Act of 1934, as amended (the "Exchange Act"). The SEC identifies an issuer as a Commission-Identified Issuer after the issuer files its annual report and on a rolling basis, and will impose an initial trading prohibition on an issuer as soon as practicable after it has been conclusively identified as a Commission-Identified Issuer for two consecutive years. To end an initial or subsequent trading prohibition, a Commission-Identified Issuer must certify that it has retained a registered public accounting firm that the PCAOB has determined it is able to inspect or investigate. To make that certification, the Commission-Identified Issuer must file financial statements that include an audit report signed by such a registered public accounting firm.

On March 30, 2022, as expected following its adoption of the Final Rules, the SEC added BeiGene, Ltd. to its conclusive list of issuers identified under the HFCAA, after being provisionally named as a Commission-Identified Issuer on March 8, 2022, following the filing of its annual report on Form 10-K with the SEC on February 28, 2022. Ernst & Young Hua Ming LLP, located in the PRC, served as our independent registered public accounting firm from 2014 to 2021, including for our annual report on Form 10-K for the year ended December 31, 2021. However, as our global business has expanded, we have built substantial organizational capabilities outside of the PRC and have evaluated, designed and implemented business processes and control changes. Therefore, on March 23, 2022, following a review process carried out by our audit committee, Ernst & Young Hua Ming LLP resigned as our independent registered public accounting firm for the audits of our financial statements and internal control over financial reporting to be filed with the SEC. On the same day, our audit committee approved the engagement of Ernst & Young LLP, located in Boston, Massachusetts, United States, as the Company's

independent registered public accounting firm for the audits of our financial statements and internal control over financial reporting for the fiscal year ending December 31, 2022. No changes were made to the accounting firms who audit our financial statements filed with the Shanghai Stock Exchange and the Hong Kong Stock Exchange, which will remain Ernst & Young Hua Ming LLP, located in Beijing, PRC, and Ernst & Young, located in Hong Kong, PRC, respectively.

In August 2022, the PCAOB signed a Statement of Protocol with the CSRC and the Ministry of Finance of the People's Republic of China, taking the first step toward opening access for the PCAOB to inspect and investigate registered public accounting firms headquartered in mainland China and Hong Kong. PCAOB staff members conducted on-site inspections and investigations from September to November 2022, and in December 2022, the PCAOB announced that it has secured complete access to inspect and investigate registered public accounting firms headquartered in mainland China and Hong Kong and confirmed that until such time as the PCAOB issues any new determination, there are no Commission-Identified Issuers at risk of having their securities subject to a trading prohibition under the HFCAA.

Given that Ernst and Young LLP (United States) now serves as the principal accountant to audit our consolidated financial statements to be filed with the SEC, we believe we are compliant with the HFCAA, which should preclude a further finding by the SEC that we are a Commission-Identified Issuer and therefore the delisting of our American Depositary Shares from the NASDAQ Global Select Market. For a detailed description of risks related to our doing business in China and status under the HFCAA, see "Item 1A. Risk Factors - Risks Related to Our Doing Business in the PRC.".

Doing Business in the PRC

As a result of our operations in the PRC, the PRC government may exert influence over our operations at any time, which could result in a material change in our operations and/or the value of our ADSs, ordinary shares, or RMB Shares. For example, the PRC government has recently published new policies that significantly affected certain industries such as the education and internet industries, and we cannot rule out the possibility that it will in the future release regulations or policies regarding any industry that could adversely affect the business, financial condition and results of operations of our company.

Furthermore, the PRC government has also recently indicated an intent to exert more oversight and control over securities offerings and other capital markets activities that are conducted outside of China and over foreign investment in China-based companies. Any such action, once taken by the PRC government, could significantly limit or completely hinder our ability to offer or continue to offer securities to investors and cause the value of such securities to significantly decline or in extreme cases, become worthless. Recently, the PRC government initiated a series of regulatory actions and statements to regulate business operations in China, including enforcement actions against illegal activities in the securities market, enhancing supervision over China-based companies listed outside of China using the variable interest entity structure, adopting new measures to extend the scope of cybersecurity reviews, and expanding the efforts in anti-monopoly enforcement. For example, in July 2021, the relevant PRC government authorities made public the Opinions on Intensifying Crack-Down on Illegal Securities Activities (the "Securities Opinions") which emphasized the need to strengthen the administration over illegal securities activities and the supervision on overseas listings by China-based companies and proposed to take measures, such as promoting the construction of relevant regulatory systems to deal with the risks and incidents faced by China-based overseas-listed companies. In November 2021, the Cyberspace Administration of China (the “CAC”) released the draft Administrative Regulations on Cyber Data Security for public comments, which requires, among others, that a prior cybersecurity review should be required for listing abroad of data processors which process over one million users’ personal information, and the listing of data processors in Hong Kong which affects or may affect national security. On February 17, 2023, the CSRC released the Overseas Listing Trial Measures, and five relevant guidelines, which will take effect from March 31, 2023, requiring the Chinese domestic companies’ overseas offerings and listings of equity securities be filed with the CSRC.

The Chinese government may further promulgate relevant laws, rules and regulations that may impose additional and significant obligations and liabilities on overseas listed PRC companies regarding data security, cross-border data flow, anti-monopoly and unfair competition, and compliance with China’s securities laws. It is uncertain whether or how these new laws, rules and regulations and the interpretation and implementation thereof may affect us, but among other things, our ability to obtain external financing through the issuance of equity securities in the United States, Hong Kong or other markets could be negatively affected, and as a result, the trading prices of our ADSs, ordinary shares and RMB Shares could significantly decline or become worthless. For a detailed description of risks related to our doing business in China, please see the section of this Annual Report titled “Item 1A. Risk Factors—Risks Related to Our Doing Business in the PRC.”

Flow of Funds with our PRC Operations

We are a holding company incorporated in the Cayman Islands with operations primarily conducted through subsidiaries in the United States, China, United Kingdom, Switzerland and Australia. The intercompany flow of funds within the organization is effected through capital contributions and intercompany loans. Since our formation in 2010, BeiGene, Ltd. has raised over $10.0 billion in various public and private stock offerings as of December 31, 2022. Of this amount, $1.9 billion and RMB 18.6

billion have been transferred as capital contributions to its operating subsidiaries; and $79 million and RMB 4.4 billion have been transferred as intercompany loans to its operating subsidiaries. BeiGene, Ltd., by itself or through its affiliates, is also the holder or licensee and developer of biopharmaceutical patents. Certain of these patents have been transferred to operating subsidiaries for further development and commercialization. BeiGene's wholly owned subsidiaries compensate each other for the intercompany provision of goods and services on an arm's length basis. As of December 31, 2022, BeiGene, Ltd. held $4.5 billion in cash, cash equivalents and short-term investments which are available for future investment in its programs and in our operating subsidiaries. To date, BeiGene, Ltd. has not received any dividends or distributions from its operating subsidiaries.

Further, our board of directors has adopted a dividend policy which provides that we currently intend to retain all available funds and earnings, if any, to fund the development and expansion of our business, and we do not anticipate paying any cash dividends in the foreseeable future. Subject to applicable law and our amended and restated articles of association, any future determination to pay dividends will be made at the discretion of our board of directors and may be based on a number of factors, including our future operations and earnings, capital requirements and surplus, general financial condition, contractual restrictions and other factors that our board of directors may deem relevant. This dividend policy reflects our board of directors' current views on our financial and cash flow position. We intend to continue to review our dividend policy from time to time, and there can be no assurance that dividends will be paid in any particular amount, if at all, for any given period.

We have never declared or paid any dividends on our ordinary shares or any other securities. If we pay dividends in the future, in order for us to distribute dividends to our shareholders and holders of ADSs, we may rely to some extent on dividends distributed by our PRC subsidiaries. PRC regulations may restrict the ability of our PRC subsidiaries to pay dividends to us, and such distributions will be subject to PRC withholding tax. In addition, PRC regulations currently permit payment of dividends of a PRC company only out of accumulated distributable after-tax profits, as determined in accordance with our articles of association and the accounting standards and regulations in the PRC.

We may rely on dividends and other distributions on equity paid by our PRC subsidiaries for our cash and financing requirements, including the funds necessary to pay dividends and other cash distributions to our shareholders or to service any debt we may incur. If any of our PRC subsidiaries incur debt on their own behalf in the future, the instruments governing the debt may restrict their ability to pay dividends or make other distributions to us. Under PRC laws and regulations, our PRC subsidiaries may pay dividends only out of their respective accumulated profits as determined in accordance with PRC accounting standards and regulations. In addition, a wholly foreign-owned enterprise is required to set aside at least 10% of its accumulated after-tax profits each year, if any, to fund a certain statutory reserve fund, until the aggregate amount of such fund reaches 50% of its registered capital. Such reserve funds cannot be distributed to us as dividends. At its discretion, a wholly foreign-owned enterprise may allocate a portion of its after-tax profits based on PRC accounting standards to an enterprise expansion fund, or a staff welfare and bonus fund. In addition, registered share capital and capital reserve accounts are also restricted from withdrawal in the PRC, up to the amount of net assets held in each operating subsidiary. As of December 31, 2022, these restricted assets totaled $3.5 billion.

Our PRC subsidiaries generate primarily all of their revenue in RMB, which is not freely convertible into other currencies. As a result, any restriction on currency exchange may limit the ability of our PRC subsidiaries to use their RMB revenues to pay dividends to us. However, conversion of RMB to other currencies are permitted for the purpose of dividends according to the PRC's regulations on Foreign Exchange Control.

Further, in response to the persistent capital outflow in the PRC and RMB's depreciation against the U.S. dollar in the fourth quarter of 2016, the People's Bank of China and the SAFE promulgated a series of capital control measures, including stricter vetting procedures for domestic companies to remit foreign currency for overseas investments, dividends payments and shareholder loan repayments. Such measures were relaxed in mid-2017 with the slowdown of the capital outflow and stabilizing of the RMB. However, the PRC government may revert to strengthen its capital controls, and more restrictions and substantial vetting process may be put forward by the SAFE for cross-border transactions falling under both the current account and the capital account. Any limitation on the ability of our PRC subsidiaries to pay dividends or make other kinds of payments to us could materially and adversely limit our ability to grow, make investments or acquisitions that could be beneficial to our business, pay dividends, or otherwise fund and conduct our business.

The PRC Enterprise Income Tax Law and its implementation rules provide that China-sourced income of foreign enterprises, such as dividends paid by a PRC subsidiary to its equity holders that are non-PRC resident enterprises, will normally be subject to PRC withholding tax at a rate of 10%, unless any such foreign investor's jurisdiction of incorporation has a tax treaty with China that provides for a reduced withholding rate arrangement and such non-PRC resident enterprises constitute the beneficiary of such income.

Pursuant to an arrangement between Mainland China and the Hong Kong Special Administrative Region and relevant tax regulations of the PRC, subject to certain conditions, a reduced withholding tax rate of 5% will be available for dividends from

PRC entities provided that the recipient can demonstrate it is a Hong Kong tax resident and it is the beneficial owner of the dividends. The government adopted regulations in 2018 which stipulate that in determining whether a non-resident enterprise has the status as a beneficial owner, comprehensive analysis shall be conducted based on the factors listed therein and the actual circumstances of the specific case shall be taken into consideration. Specifically, it expressly excludes an agent or a designated payee from being considered as a "beneficial owner." We own the PRC subsidiaries through BeiGene HK. BeiGene HK currently does not hold a Hong Kong tax resident certificate from the Inland Revenue Department of Hong Kong, and there is no assurance that the reduced withholding tax rate will be available.

Permissions Required from the PRC Authorities for Our Operations

We conduct our business in the PRC through our PRC subsidiaries. Our operations in the PRC are governed by PRC laws and regulations. As of the date of this annual report, our PRC subsidiaries have obtained all requisite licenses and permits from the PRC government authorities that are material for their business operations in the PRC, including, among others, business licenses issued by local counterparts of the SAMR, drug manufacturing licenses, drug trade license, CTAs, drug registration certificates, licenses for use of experimental animals, pollutant discharge licenses and permits for urban sewage discharge into drainage pipe network. No material permissions have been denied to us by relevant government authorities in China. As of the date of this annual report, we do not operate our businesses in China or elsewhere through variable interest entities, or VIEs, and therefore are not subject to risks associated with contractual arrangements with VIEs. As of the date of this annual report, we have not received any inquiry, notice, warning, or sanctions regarding our business operations and corporate structure from the CSRC, CAC or any other PRC governmental agency that would have a material impact on our business, results of operations or financial condition. However, given the uncertainties of interpretation and implementation of relevant laws and regulations and the enforcement practice by government authorities, we cannot assure you that we have obtained all the permits or licenses required for conducting our business in the PRC. If (i) we have inadvertently concluded that such permissions, approvals, licenses or permits have been acquired or are not required, or (ii) applicable laws, regulations, or interpretations change and we are required to obtain such permissions, approvals, licenses or permits in the future, then we may have to expend time and costs to procure them. If we are unable to do so on commercially reasonable terms or in a timely manner, it could cause significant disruption to our business operations and damage our reputation, which would in turn have a material adverse effect on our business, results of operations and financial condition.

In connection with our previous issuance of securities to foreign investors in stock markets outside the PRC, under current PRC laws, regulations and regulatory rules, as of the date of this annual report, we and our PRC subsidiaries, (i) are not required to obtain permissions from the CSRC, (ii) are not required to go through cybersecurity review by the Cyberspace Administration of China, or the CAC, and (iii) have not received or were denied such requisite permissions by any PRC authority. On February 17, 2023, the CSRC released the Overseas Listing Trial Measures and five relevant guidelines, which will take effect from March 31, 2023. The Overseas Listing Trial Measures require the Chinese domestic companies' overseas offerings and listings of equity shares, depositary receipts, convertible bonds, preferred shares or other equity securities be filed with the CSRC. See "Item 1. Business – Government Regulation – PRC Regulation – Regulations Relating to Overseas Listing". If we were deemed as an indirect overseas listed Chinese domestic company subject to the filing requirements under the Overseas Listing Trial Measures, our offering of equity securities on the NASDAQ Global Select Market or Hong Kong Stock Exchange in the future would be required to be filed with the CSRC within three working days after the offering is completed.

As of the date of this annual report, we have not received any inquiry, notice, warning or sanction regarding obtaining approval, completing filing or other procedures in connection with offering our equity securities in overseas stock markets from the CSRC or any other PRC governmental or regulatory authorities that have jurisdiction over our operations. However, there remains significant uncertainty as to the interpretation and implementation of regulatory requirements related to overseas securities offerings and other capital markets activities, including the Overseas Listing Trial Measures. If it is determined that filing or other procedure with the CSRC or any other regulatory authority is required for issuing our equity securities in overseas stock markets, it is uncertain whether we will be able to and how long it would take for us to complete the filing despite our efforts. If we, for any reason, are unable to complete, or experience significant delays in completing the requisite filing or other procedure(s), we may face sanctions by the CSRC or other Chinese regulatory authorities as applicable. These regulatory authorities may impose fines and penalties on our operations in the PRC, limit our ability to pay dividends outside of China, limit our operations in the PRC, delay or restrict the repatriation of funds into the PRC or take other actions that could have a material adverse effect on our business, financial condition, results of operations and prospects, as well as the trading price of our ADSs, ordinary shares and RMB Shares.

Cash Management Policies and Procedures

Under our Capitalization and Financing Policy, the frequency and amount of intercompany transfers of funds is determined based on the working capital needs of our subsidiaries and intercompany transactions, and is subject to internal approval

processes and funding arrangements. Our management reviews and monitors our cash flow forecast and working capital needs of our subsidiaries on a regular basis. In addition, capital contributions and intercompany loan arrangements are subject to local jurisdiction and banking regulations. In this regard, we have not faced difficulties or limitations in our ability to transfer cash between subsidiaries in any of our operating jurisdictions.

During the normal course of our business, cash is transferred between our subsidiaries via wire transfer to and from bank accounts to pay certain business expenses. Cash is maintained by BeiGene, Ltd. in its bank account and transferred to its subsidiaries when necessary to strengthen our business capabilities, such as paying for new office development, or marketing expenses. In addition, cash may be used by BeiGene, Ltd. to meet corporate expenses such as audit fees, attorneys' fees, stock exchange listing fees, IR/PR expenses, research and development costs and corporate administrative support expenses.

Cash is transferred between subsidiaries in the form of capital contributions or through intercompany advances or loans, as follows:

- Cash may be transferred between BeiGene HK and its operating subsidiaries in mainland China through intercompany loans and capital contributions, and there are currently no restrictions on transferring funds between BeiGene HK and its subsidiaries in mainland China. Cash generated from BeiGene HK is used to fund operations of its subsidiaries, and no funds were transferred from BeiGene HK's subsidiaries in mainland China to fund operations of other BeiGene subsidiaries outside of mainland China for the year ended on December 31, 2021 and December 31, 2022. For the year ended December 31, 2021 and December 31, 2022, the amount of cash transferred between BeiGene HK and its subsidiaries in mainland China was $44 million and $351 million, respectively.

- Cash may be transferred between BeiGene UK and/or BeiGene Switzerland and their respective operating subsidiaries through intercompany fund advances and capital contributions. There are currently no restrictions on transferring funds between BeiGene UK or BeiGene Switzerland and their respective operating subsidiaries. Cash generated from BeiGene UK and BeiGene Switzerland are used to fund operations of their respective subsidiaries, and no funds were transferred from BeiGene UK's subsidiaries or from BeiGene Switzerland's subsidiaries to fund operations of other BeiGene subsidiaries (such as BeiGene HK and its subsidiaries in mainland China) for the year ended on December 31, 2021 and December 31, 2022. For the year ended December 31, 2021 and December 31, 2022, the amount of cash transferred between BeiGene UK to its respective subsidiaries was $2 million and $4 million, respectively. For the years ended December 31, 2021 and December 31, 2022, the amount of cash transferred between BeiGene Switzerland to its respective subsidiaries was $25 million and $65 million, respectively.

Human Capital Resources

We are committed to attracting and retaining exceptional, passionate people to work with a clear purpose: creating impactful, affordable and accessible medicines to help more patients around the world to live better. To this end, we support a team-oriented culture based on excellence that allows all colleagues to feel valued and challenged. We provide opportunities for employees to grow and develop in their careers, supported by competitive compensation, benefits and health and wellness programs, and by programs that build connections among our employees worldwide.

We believe that the success of our business is fundamentally connected to the well-being of our employees. Accordingly, we are committed to their health, safety and wellness. We offer our employees and their families innovative, flexible and convenient health and wellness programs, including benefits that confer peace of mind around events that may require time away from work or impact their financial well-being; that support their physical and mental health with tools and resources to help them improve or maintain their health status and encourage healthy behaviors; and that offer choice where possible so they can customize benefits to meet their needs and the needs of their families.

In order to support our employees during the COVID-19 pandemic, we implemented significant changes that we determined were in the best interest of our employees, as well as the communities in which we operate, and which comply with government regulations. This included initiating a number of mental-health programs and offering supplemental resources that are available to all of our employees, having our employees work from home and implementing additional safety measures for employees continuing critical work at our offices or in the field, as well as encouraging employees to adhere to preventative measures recommended by the World Health Organization, U.S. Centers for Disease Control and Prevention, and similar public health authorities.

Our worldwide teams are united by a common mission. We are committed to encouraging a culture of open communication where employees can ask questions, raise concerns and contribute creative solutions. Our management team routinely makes themselves available to all employees, including in regular town hall events that encourage open dialogue. Fostering a culture of accountability and compliance is also central to our human resource management. All of our employees complete trainings

on applicable corporate policies including our global Code of Conduct; Harassment, Discrimination, and Retaliation Policy; Conflicts of Interest Policy; Insider Trading Policy; and Anti-Corruption Policy.

We strive to provide competitive compensation and benefits programs to help meet the needs of our employees. In addition to base salaries, these programs include potential annual discretionary bonuses, equity awards, a 401(k) plan in the United States and pension plans in other jurisdictions, healthcare and insurance benefits, health savings and flexible spending accounts, paid time off, family leave, and flexible work schedules, among others. In addition to our broad-based equity award programs, we have used targeted equity-based grants with vesting conditions to facilitate retention of personnel. In addition to compensation and benefits, we provide our employees opportunities for growth through challenging job assignments, performance management and training opportunities. We seek to remain competitive in our compensation and benefits by routinely benchmarking against industry peers.

As part of our mission to create the innovative medicines to serve the patients, we continue to advance our environmental, social and governance ("ESG") efforts, including enhancing the diversity and inclusiveness of our workplace. We believe that diversity of backgrounds and ideas inspires creativity and helps us create the innovative medicines patients need. We appreciate one another’s differences and strengths, and are proud to be an equal opportunity employer. BeiGene does not discriminate on the basis of race, religion, color, sex, gender identity, sexual orientation, age, non-disqualifying physical or mental disability, national origin, veteran status or any other basis covered by applicable law. All employment is decided on the basis of qualifications, merit, and business need. Further, we have policies in place that prohibit harassment of all kinds. We maintain an inclusive culture where all voices are welcomed, heard, and respected.

As of January 31, 2023, we had approximately 9,200 full-time employees worldwide, with approximately 1,300 employees in the United States and approximately 7,900 employees outside of the United States. 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, except as required by local laws such as in some European countries. We have never experienced any employment-related work stoppages, we also track voluntary and involuntary turnover rates and we consider our relations with our employees to be good.

Environmental, Social and Governance Strategy

BeiGene’s mission is to expand access to high-quality, affordable medicines to billions more people globally. We are driven to deliver affordable medicines to all and create a more equitable and sustainable world for our patients, employees, and our communities. In 2022, we announced our global ESG strategy, *Change Is the Cure*, which guides our efforts across five focus areas: advancing global health, empowering people, innovating sustainably, supporting communities, and operating responsibly. Within each focus area, we have identified two strategic priorities against which we have set concrete targets. We will report our progress against these targets and announce new goals in our 2022 ESG Report which will be published in late April 2023.

While we are at the start of our ESG journey, we are proud of the progress we have made to date. We joined the United Nations Global Compact in 2022 and have aligned our efforts with UN Sustainable Development Goals. In 2022, we announced new measures to understand and further mitigate our climate impacts. We will share progress on those measures and announce new targets in our 2022 ESG Report.

We know that access to oncology treatments lags in many parts of the world, particularly in low-income countries. To help close this health equity gap, BeiGene became a founding member of the Union for International Cancer Control’s Access to Oncology Medicines Coalition which focuses on improving access to innovative medicines in lower-income countries and supporting them in developing the capacity to provide proper treatment for patients.

We believe that our people are critical to our success and, as a global company, we know that sharing diverse ideas and perspectives spurs greater innovation and enhances our ability to deliver results. Our culture celebrates and encourages the voices of all our employees and promotes a respectful, collaborative environment. In 2020, we formed the Inclusion, Diversity, Equity, and Awareness (“IDEA”) Council to provide a forum for U.S. employees to explore issues of diversity, equity, inclusion, and belonging. Introduced first in the U.S., the IDEA Council is now global, with members in geographies including Canada, Europe, China, and Australia. In 2022, we completed a three-year diversity, equity, inclusion and belonging strategy. Details will be shared in our 2022 ESG Report.

In addition to directly supporting patients through the delivery of cutting-edge therapies, we strive to support our communities through research, education, and sponsorships. We support patient advocacy organizations, charitable foundations, and hospitals through cash and in-kind donations.

More details about our ESG strategy, goals and progress to date will be available in our 2022 ESG Report, which will be developed with reference to the Global Reporting Initiative Standards and published in late April 2023. Our previous ESG Reports can be found online at: https://hkexir.beigene.com/governance/esg-report/.

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, please see the section of this Annual Report titled "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. 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 registered trademarks, trademark applications and unregistered trademarks and service marks, 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 SEC, in accordance with 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 securities filings with the HKEx and the Shanghai Stock Exchange. 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, the HKEx, and the SSE. We use our website as a means of disclosing material non-public information and for complying with our disclosure obligations under Regulation FD.

Item 1A. Risk Factors

The following section includes material 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, ordinary shares, or RMB 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, ordinary shares, and RMB 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. Please refer to the explanation of the qualifications and limitation on forward-looking statements set forth on page 1 hereof.

Risks Related to Clinical Development and Commercialization of Our Medicines and Drug Candidates

Our medicines may fail to achieve and maintain the degree of market acceptance by physicians, patients, third-party payors, and others in the medical community necessary for commercial success.

Our medicines may fail to achieve and maintain 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 medicines. If our medicines do not achieve and maintain an adequate level of market acceptance, the sales of our medicines may be limited and we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of our medicines will depend on a number of factors, including: the clinical indications for which our medicines are approved; physicians, hospitals, cancer treatment centers, and patients considering our medicines safe and effective; government agencies, professional societies, practice management groups, insurance carriers, physicians' groups, private health and science foundations, and organizations recommending our medicines and reimbursement; the perceived advantages and relative cost of alternative treatments; the prevalence and severity of any side effects; product labeling, including limitations or warnings, or product insert requirements of regulatory authorities; the timing of market introduction of our medicines as well as competitive medicines; the availability of adequate coverage, reimbursement and pricing by third-party payors and government authorities; and the effectiveness of our sales and marketing efforts.

Even if our medicines 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 medicines, are more cost effective or render our medicines obsolete.

We have limited experience in launching and marketing our internally developed and in-licensed medicines. If we are unable to further develop marketing and sales capabilities or enter into agreements with third parties to market and sell our medicines, we may not be able to generate substantial product sales revenue.

We became a commercial-stage company in 2017, when we entered into a license and supply agreement with Celgene Logistics Sàrl, now a Bristol Myers Squibb Company ("BMS"), to commercialize three of BMS's approved cancer therapies, in the People's Republic of China ("PRC" or "China"). In October 2019, we entered into a collaboration with Amgen for its commercial-stage oncology products and a portfolio of clinical- and late-preclinical-stage oncology pipeline products. We received the first approvals for our internally developed drug candidates in late 2019 in the United States, in 2020 in China, and in 2021 in Europe. Given this, we have limited experience in commercializing our internally developed and in-licensed medicines, including building and managing a commercial team, conducting a comprehensive market analysis, obtaining state licenses and reimbursement, and managing distributors and a sales force for our medicines. As a result, our ability to successfully commercialize our medicines may involve more inherent risk, take longer, and cost more than it would if we were a company with substantial experience in launching medicines.

If we are unable to, or decide not to, further develop internal sales, marketing, and commercial distribution capabilities for any or all of our medicines in any country or region, we will likely pursue collaborative arrangements regarding the sales and marketing of our medicines. 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. 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 medicines ourselves.

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

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

The development and commercialization of new medicines 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 medicines or are pursuing the development of medicines for the treatment of cancer for which we are commercializing our medicines or developing our drug candidates. For example, BRUKINSA, tislelizumab, and pamiparib face substantial competition, and some of our products face or are expected to face competition from generic therapies. 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 medicines that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than our medicines. Our competitors also may obtain approval from regulatory authorities for their medicines 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 medicines 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, management and marketing 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 medicines 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 have and 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 medicines 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 medicines and 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 diseases we are targeting, as well as the subset of people with these diseases in a position to receive later stage therapy and who have the potential to benefit from treatment with our medicines and drug candidates, 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 medicines and drug candidates may be limited or may not be amenable to treatment with our medicines and drug candidates. Even if we obtain significant market share for our medicines and 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.

If we or any third parties with which we may collaborate to market and sell our medicines are unable to achieve and maintain coverage and adequate levels of reimbursement, our commercial success and business operations could be adversely affected.

Our ability or the ability of any third parties with which we collaborate to commercialize our medicines successfully will depend in part on the extent to which reimbursement for these medicines is available on adequate terms, or at all, from government health administration authorities, private health insurers and other organizations. In the United States and markets in other countries, patients generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors is critical to new product acceptance. Sales of our medicines will depend substantially, both domestically and abroad, on the extent to which the costs of our medicines will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health administration authorities, private health coverage insurers and other third-party payors. Without third-party payor reimbursement, patients may not be able to obtain or afford prescribed medications. Third-party payors also are seeking to encourage the use of generic or biosimilar products or entering into sole source contracts with healthcare providers, which could effectively limit the coverage and level of reimbursement for our medicines and have an adverse impact on the market access or acceptance of our medicines. In addition, reimbursement guidelines and incentives provided to prescribing physicians by third party payors may have a

significant impact on the prescribing physicians' willingness and ability to prescribe our products. For additional information, please see the section of this Annual Report titled "Part I —Item 1 — Business — Government Regulation — Pharmaceutical Coverage, Pricing, and Reimbursement."

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 medicines on a payor-by-payor basis, with no assurance that coverage and adequate reimbursement will be obtained. The principal decisions about reimbursement for new medicines are typically made by the Centers for Medicare and Medicaid Services (the "CMS"). They decide whether and to what extent a new medicine will be covered and reimbursed under Medicare and private payors tend to follow CMS to a substantial degree. Factors payors consider in determining reimbursement are based on whether the product is: a covered benefit under its health plan; safe, effective and medically necessary; appropriate for the specific patient; cost-effective; and neither experimental nor investigational.

Coverage may be more limited than the purposes for which the medicine is approved by the FDA or comparable regulatory authorities in other countries. Even if we obtain coverage for a given medicine, 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 medicines. Patients are unlikely to use our medicines unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of the medicine. Because some of our medicines 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.

Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Furthermore, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives.

We cannot be sure that reimbursement will be available for any product candidate that we commercialize and, if reimbursement is available, the level of reimbursement. In addition, many pharmaceutical manufacturers must calculate and report certain price reporting metrics to the government, such as average sales price and best price. Penalties may apply in some cases when such metrics are not submitted accurately and timely.

In China, drug prices are typically lower than in the United States and Europe, and until recently, the market has been dominated by generic drugs. Government authorities regularly review the inclusion or removal of medicines from China's National Drug Catalog for Basic Medical Insurance, Work-related Injury Insurance and Maternity Insurance, or the National Reimbursement Drug List (the "NRDL"), or provincial or local medical insurance catalogues for the National Medical Insurance Program, and the tier under which a medicine will be classified, both of which affect the amounts reimbursable to program participants for their purchases of those medicines. There can be no assurance that our medicines and any approved drug candidates will be included in the NRDL or provincial reimbursements lists, or if they are, that they will be included at a price that allows us to be commercially successful. Products included in the NRDL have typically been generic and essential drugs. Innovative drugs similar to our medicines and 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. For example, BRUKINSA, tislelizumab, pamiparib and XGEVA have been included in the NRDL. While the demand for these medicines has generally increased after inclusion in the NRDL, there can be no assurance that demand will continue to increase and such increases will be sufficient to offset the reduction in the prices and our margins, which could have a material adverse effect on our business, financial condition and results of operations. We prepare for the NRDL negotiations in China for our eligible medicines/indications annually. If any of these medicines/indications are not included in the NRDL or included at a significantly lower price, the revenues for such medicines could be limited, which could have a material adverse effect on our business, financial condition and results of operations.

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 medicine 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 medicine which we commercialize. Obtaining or maintaining reimbursement for our medicines may be particularly difficult because of the higher prices often associated with medicines 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 medicine and drug candidate that we in-license or successfully develop.

There may be significant delays in obtaining reimbursement for approved medicines, and coverage may be more limited than the purposes for which the medicine is approved by regulatory authorities. Moreover, eligibility for reimbursement does not imply that any medicine 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 medicines, 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 medicine and the clinical setting in which it is used, may be based on payments allowed for lower cost medicines that are already reimbursed, and may be incorporated into existing payments for other services. Net prices for medicines 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 medicines 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 our medicines and any new medicines 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 medicines and drug candidates in the United States, China, Europe and in other jurisdictions. In some countries, such as those in Europe, 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 medicines will depend significantly on the availability of adequate coverage and reimbursement from third-party payors for our medicines and may be affected by existing and future health care reform measures.

We have operations in the United States, China, Europe, and other markets and plan to expand in these and new markets on our own or with collaborators, which exposes us to risks of conducting business in international markets.

We are currently developing and commercializing or plan to commercialize our medicines in international markets, including China, Europe and other markets outside of the United States, either on our own or with third party collaborators or distributors. Our 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 or actions taken by U.S. or China governmental authorities on companies with significant operations in the U.S. and China, such as us;
- 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;
- 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, disease or public health pandemics, such as COVID-19, or natural disasters, including earthquakes, volcanoes, typhoons, floods, hurricanes and fires.

These and other risks, including the risks described in "Risks Related to Our Doing Business in the PRC", may materially adversely affect our ability to attain or sustain revenue in international markets.

The illegal distribution and sale by third parties of counterfeit versions of our medicines 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 medicines, which do not meet our or our collaborators' rigorous manufacturing and testing standards. A patient who receives a counterfeit or unfit medicine 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 medicines 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.

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

Our business depends on the successful development, regulatory approval and commercialization of our medicines and other drug candidates we may develop. We have invested a significant portion of our efforts and financial resources in the development of our medicines and drug candidates. The success of our medicines and drug candidates depends 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;
- the performance by contract research organizations ("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 that we do not infringe, misappropriate or otherwise violate the valid patent, trade secret or other intellectual property rights of third parties;
- successfully launching our medicines and drug candidates, if and when approved;
- obtaining favorable reimbursement from third-party payors for our medicines and drug candidates, if and when approved;
- competition with other products;
- continued acceptable safety profile following regulatory approval; and
- manufacturing or obtaining sufficient supplies of our medicines, drug candidates and any competing drug products that may be necessary for use in clinical trials for evaluation of our drug candidates and commercialization of our medicines.

If we do not achieve and maintain 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 additional regulatory approvals for and/or to successfully commercialize our medicines 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.

Clinical 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 development 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 involved in such trials. A number of companies in our industry 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 durability of anti-tumor 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 ("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 CROs and trial sites, the terms of which can be subject to extensive negotiation and may vary significantly; manufacturing issues, including problems with manufacturing, supply quality, compliance with GMP, or obtaining 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 medicines and drug candidates, companion diagnostics or other materials necessary to conduct clinical trials of our drug candidates or commercialization of our medicines may be insufficient or inadequate.

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, or 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 or obtain reimbursement at a commercially viable level for use of the drug.

Significant clinical trial 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.

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 have and may continue to experience difficulties in patient 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, competition from competing companies, and natural disasters or public health epidemics, such as the COVID-19 pandemic.

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 delay or prevent completion of these trials and adversely affect our ability to advance the development of our drug candidates.

Risks Related to Regulatory Approval and Extensive Government Regulation

All material aspects of the research, development, manufacturing and commercialization of pharmaceutical products are heavily regulated, and we may face difficulties in complying with or be unable to comply with such regulations, which could have a material adverse effect on our business.

All jurisdictions in which we conduct or intend to conduct our pharmaceutical-industry activities regulate these activities in great depth and detail. We are currently focusing our activities in the major markets of the United States, China, Europe, and other select countries and regions. 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. Additionally, the NMPA's reform of the medicine and approval system may face implementation challenges. The timing and full impact of such reforms is uncertain and could prevent us from commercializing our medicines and drug candidates in a timely manner.

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 us 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, on March 25, 2020, the NMPA suspended the importation, sales and use of ABRAXANE® in China supplied to us by BMS, and the drug was subsequently recalled by BMS and is not currently available for sale in China. This suspension was based on inspection findings at BMS's contract manufacturing facility in the United States. We have not had any sales of ABRAXANE since the suspension and do not expect future revenue from ABRAXANE. For additional information, please see the section of this Annual Report titled "Legal Proceedings". Additionally, although we have obtained regulatory approvals of our medicines, regulatory authorities could suspend or withdraw these approvals. In any event, the receipt of regulatory approval does not assure the success of our commercialization efforts for our medicines.

We may be subject to 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 sales.

Healthcare providers, physicians and others play a primary role in the recommendation and prescription of any products for which we obtain regulatory approval. Our operations are subject to various federal and state fraud and abuse laws, including, without limitation, the federal Anti-Kickback Statute, the federal False Claims Act ("FCA"), and physician payment sunshine laws and regulations. These laws may impact, among other things, our proposed sales, marketing and education programs. In addition, we are subject to patient privacy regulation by both the federal government and the states in which we conduct our business.

Additionally, we are subject to state 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 third-party payor, not just governmental payors, but also private insurers. These laws are enforced by various state agencies and through private actions. 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 that restrict the payments made to healthcare providers and other potential referral sources. Several states and local laws also impose other marketing restrictions or require pharmaceutical companies to make marketing or price disclosures to the state, require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers, and require the registration of pharmaceutical sales representatives. In addition, the approval, commercialization, and other activities for our medicines and drug candidates outside the United States subjects us to non-U.S. equivalents of the healthcare laws such as those mentioned above, among other non-U.S. laws. As with the state equivalents mentioned above, some of these non-U.S. laws may be broader in scope. 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.

It is possible that we may make grants to independent charitable foundations that help financially needy patients with their premium, co-pay, and co-insurance obligations. If we choose to do so, and if we or our vendors or donation recipients are deemed to fail to comply with relevant laws or regulations in the operation of these programs, we could be subject to damages, fines, penalties, or other criminal, civil, or administrative sanctions or enforcement actions. We cannot ensure that our compliance controls and procedures will be sufficient to protect against acts of our employees, business partners, or vendors that may violate the laws or regulations of the jurisdictions in which we operate. Regardless of whether we have complied with the law, a government investigation could impact our business practices, harm our reputation, divert the attention of management, increase our expenses, and reduce the availability of foundation support for our patients who need assistance.

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 FCA 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, individual imprisonment, reputational harm, diminished profits and future earnings, and curtailment or restructuring of our operations, as well as additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws. Furthermore, if any of the physicians or other providers or entities with whom we 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 adversely affect our business.

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

We participate in the Medicaid Drug Rebate Program, the 340B program, the U.S. Department of Veterans Affairs, Federal Supply Schedule ("FSS") pricing program, and the Tricare Retail Pharmacy program, which require us to disclose average manufacturer pricing, and, in the future may require us to report the average sales price for certain of our drugs to the Medicare program. Pricing and rebate calculations vary across products and programs, are complex, and are often subject to interpretation by us, governmental or regulatory agencies and the courts. Furthermore, regulatory and legislative changes, and judicial rulings relating to these programs and policies (including coverage expansion), have increased and will continue to increase our costs and the complexity of compliance, have been and will continue to be time-consuming to implement, and could have a material adverse effect on our results of operations, particularly if CMS or another agency challenges the approach we take in our implementation. For example, in the case of our Medicaid pricing data, if we become aware that our reporting for a prior quarter was incorrect or has changed as a result of recalculation of the pricing data, we are generally obligated to resubmit the corrected data for up to three years after those data originally were due. Such restatements increase our costs and could result in an overage or underage in our rebate liability for past quarters. Price recalculations also may affect the ceiling price at which we are required to offer our products under the 340B program and give rise to an obligation to refund entities participating in the 340B program for overcharges during past quarters impacted by a price recalculation.

Civil monetary penalties can be applied if we are found to have knowingly submitted any false price or product information to the government, if we are found to have made a misrepresentation in the reporting of our average sales price, if we fail to submit the required price data on a timely basis, or if we are found to have charged 340B covered entities more than the statutorily mandated ceiling price. Additionally, our agreement to participate in the 340B program or our Medicaid drug rebate agreement could be terminated, in which case federal payments may not be available under Medicaid or Medicare Part D for our covered outpatient drugs. Additionally, if we overcharge the government in connection with our arrangements with FSS or Tricare Retail Pharmacy, we are required to refund the difference to the government. Failure to make necessary disclosures and/or to identify contract overcharges can result in allegations against us under the FCA and other laws and regulations. Unexpected refunds to the government, and responding to a government investigation or enforcement action, would be expensive and time-consuming, and could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Further, legislation may be introduced that, if passed, would, among other things, further expand the 340B program to additional covered entities or would require participating manufacturers to agree to provide 340B discounted pricing on drugs used in an inpatient setting, and any additional future changes to the definition of average manufacturer price or the Medicaid rebate amount could affect our 340B ceiling price calculations and negatively impact our results of operations. Additionally, certain pharmaceutical manufacturers are involved in ongoing litigation regarding contract pharmacy arrangements under the 340B program. The outcome of those judicial proceedings and the potential impact on the way in which manufacturers extend discounts to covered entities through contract pharmacies remain uncertain.

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

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 United States Food and Drug Administration ("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 new drug application ("NDA") or biologics license application ("BLA") must include comprehensive information regarding the chemistry, manufacturing and controls ("CMC") 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 a submission will be accepted for filing and review by the FDA.

Regulatory authorities outside of the United States, such as the China National Medical Products Administration ("NMPA") and European Medicines Agency ("EMA"), also have requirements for approval of medicines for commercial sale with which we must comply prior to marketing in those areas. Regulatory requirements, approval processes and review periods can vary 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. Seeking regulatory approvals outside of the United States could require additional nonclinical studies or clinical trials, which could be costly and time consuming. For all of these reasons, we may not obtain regulatory approvals on a timely basis, if at all.

The processes required to obtain approval by the FDA, the NMPA, the EMA, and other comparable regulatory authorities is complex, costly, 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. Regulatory approval is never guaranteed. Furthermore, we have limited experience in obtaining regulatory approvals for our drug candidates, including preparing the required materials for regulatory submission and navigating the regulatory approval process. As a result, our ability to successfully 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 substantial experience in obtaining regulatory approvals.

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;

- a delay in or the inability of health authorities to complete regulatory inspections of our development activities, regulatory filings or manufacturing operations, whether as a result of the COVID-19 pandemic or other reasons, or our failure to satisfactorily complete such inspections;
- 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.

For example, in June 2022, the FDA extended the Prescription Drug User Fee Act goal date for the supplemental new drug application ("sNDA") for BRUKINSA as a treatment for adult patients with CLL or SLL by three months to January 2023, to allow time to review additional clinical data submitted by us, which was deemed a major amendment to the sNDA. In July 2022, the FDA deferred action on the BLA for tislelizumab as a second-line treatment for patients with unresectable or metastatic ESCC. In the FDA's general advice letter communicating the deferral of action, the FDA cited only the inability to complete inspections due to COVID-19 related restrictions on travel as the reason for the deferral and did not provide a new anticipated action date as they continue to monitor the public health situation and travel restrictions.

Delays in the completion of a clinical trial of any of our drug candidates will increase our costs, slow down our drug development and approval process, and jeopardize our ability to commence product sales and generate 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, regulatory filings and manufacturing operations also could be harmed or delayed by a shutdown of the U.S. government, including the FDA, or governments and regulatory authorities in other jurisdictions. Since March 2020 when foreign and domestic inspections of facilities were largely placed on hold, the FDA has been working to resume pre-pandemic levels of inspection activities, including routine surveillance, bioresearch monitoring and pre-approval inspections. Should the FDA determine that an inspection is necessary for approval and an inspection cannot be completed during the review cycle due to restrictions on travel, and the FDA does not determine a remote interactive evaluation to be adequate, the agency has stated that it generally intends to issue, depending on the circumstances, a complete response letter or defer action on the application until an inspection can be completed. During the COVID-19 pandemic, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. Regulatory authorities outside the U.S. may adopt similar restrictions or other policy measures in response to the ongoing COVID-19 pandemic and may experience delays in their regulatory activities. If the FDA or other health authorities are delayed or unable to complete required regulatory inspections of our development activities, regulatory filings or manufacturing operations, or we do not satisfactorily complete such inspections, our business could be materially harmed.

We are currently conducting and may in the future conduct clinical trials for our drug candidates outside the U.S., and the FDA and comparable foreign regulatory authorities may not accept data from such trials.

We are currently conducting and may in the future conduct clinical trials for our drug candidates outside the U.S., including in China. The acceptance of data from clinical trials conducted outside the U.S. or another jurisdiction by the FDA or comparable foreign regulatory authority may be subject to certain conditions or may not be accepted at all. The FDA will generally not consider the data from a foreign clinical trial not conducted under an IND unless (i) the trial was well-designed and well-conducted in accordance with GCP requirements, including requirements for the design, conduct, performance, monitoring, auditing, recording, analysis, and reporting of clinical trials in a way that provides assurance that the data and reported results are credible and accurate and that the rights, safety, and well-being of trial subjects are protected, and (ii) the FDA is able to validate the data from the trial through an onsite inspection, if necessary. In cases where data from foreign clinical trials are intended to serve as the sole basis for marketing approval in the U.S., the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the U.S. population and U.S. medical practice; (ii) the trials were performed by clinical investigators of recognized competence; and (iii) the data may be considered valid without the need for an on-site inspection by the FDA or, if the FDA considers such as inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means. Additionally, the FDA’s clinical trial requirements, including sufficient size of patient populations and statistical powering must be met. Many foreign regulatory authorities have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA or any comparable foreign regulatory authority will accept data from trials conducted outside of the U.S. or the applicable jurisdiction. If the FDA or any comparable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which could be costly and time-consuming, and which may result in drug candidates that we may develop not receiving approval for commercialization in the applicable jurisdiction.

Our medicines 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 medicines and drug candidates.

Our medicines 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-marketing information, including both federal and state requirements in the United States and requirements of comparable regulatory authorities in China, Europe and other regions. As such, we and our collaborators will be subject to ongoing review and periodic inspections to assess compliance with applicable post-approval regulations. Additionally, to the extent we want to make certain changes to the approved medicines, product labeling, or manufacturing processes, we will need to submit new applications or supplements to regulatory authorities for approval.

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 GMP regulations. As such, we and our contract manufacturers are and will be subject to continual review and inspections to assess compliance with GMP and adherence to commitments made in any NDA, BLA or 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 failure to comply with these requirements could have a material adverse effect on our business. For example, on March 25, 2020, the NMPA suspended the importation, sales and use of ABRAXANE in China supplied to us by BMS, and the drug was subsequently recalled by BMS and is not currently available for sale in China. This suspension was based on inspection findings at BMS's contract manufacturing facility in the United States. We have not had any sales of ABRAXANE since the suspension and do not expect future revenue from ABRAXANE. For additional information, please see the section of this Annual Report titled "Legal Proceedings".

The regulatory approvals for our medicines 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 medicine may be marketed or to the conditions of approval, which could adversely affect the medicine's commercial potential or contain requirements for potentially costly post-marketing testing and surveillance to monitor the safety and efficacy of the medicine 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 GMP and good clinical practice ("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 medicines 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 medicines, 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 medicines 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 obtain accelerated approval or conditional approval of any of our drug candidates, as we have done with the accelerated approval of BRUKINSA in the United States and China and certain approvals of tislelizumab, pamiparib, XGEVA, BLINCYTO, KYPROLIS and QARZIBA in China, we will be required to conduct a confirmatory study to verify the predicted clinical benefit and may also be required to conduct post-marketing safety studies. The Food and Drug Omnibus Reform Act of 2022 ("FDORA") recently granted the FDA the authority to require, as appropriate, that a post-approval confirmatory study or studies be underway prior to granting accelerated approval or within a specified time period after the date accelerated approval is granted. FDORA also gave the FDA increased authority to withdraw approval of a drug granted accelerated approval on an expedited basis if the sponsor fails to conduct such studies in a timely manner or such studies fail to verify clinical benefit. While operating under accelerated approval, we will be subject to certain restrictions that we would not be subject to upon receiving regular approval. For example, the FDA generally requires that all advertising and promotional materials be submitted to the FDA for review prior to dissemination or publication for products receiving accelerated approval, which could adversely impact the timing of the commercial launch of the product.

Even if we are able to commercialize our medicines and any approved drug candidates, the medicines may become subject to unfavorable pricing regulations or third-party reimbursement practices or healthcare reform initiatives, which could harm our business.

The regulations that govern regulatory approvals, pricing and reimbursement for new therapeutic products vary widely from country to country. Historically, products launched in Europe do not follow price structures of the U.S. and generally prices tend to be significantly lower. Countries in Europe provide options to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost effectiveness of a particular product candidate to currently available therapies. Countries may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market.

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 and results of operations.

Our ability to commercialize our medicines successfully also will depend in part on the extent to which reimbursement for these medicines and related treatments will be available on adequate terms, or at all, from government health administration authorities, private health insurers and other organizations. For additional information, please see the section of this Annual Report titled "Part I — Item 1A — Risk Factors Risks Related to Clinical Development and Commercialization of Our Medicines and Drug Candidates — If we or any third parties with which we may collaborate to market and sell our medicines are unable to achieve and maintain coverage and adequate level of reimbursement, our commercial success and business operations could be adversely affected."

Furthermore, there continues to be scrutiny from federal and state governments over the way drug manufacturers set prices for their marketed products. For example, there are ongoing Congressional investigations, legislation, and regulations to, among other things, bring more transparency to drug pricing, set patient spending caps for Medicare beneficiaries, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer's patient programs, reform federal and state government program reimbursement methodologies for drug products, allow importation of lower-priced drugs from Canada, and set prices based on international reference pricing in other countries. While some of these measures can be done through agency rulemaking, most will require statutory changes by Congress. While addressing drug pricing and patient affordability remains a top priority for Congress, it remains to be seen if any agreement can be reached on a legislative solution. It is therefore unclear if any regulations or legislation will be enacted to implement changes to drug pricing or federal and state government reimbursement programs or what the impact of such changes on the marketing approvals of our drug candidates, if any, may be.

In China, the government launched a national program for volume-based, centralized drug procurement with minimum quantity commitments in an attempt to negotiate lower prices from drug manufacturers and reduce the price of drugs. Under the

program, one of the key determining factors for a successful bid is the price. The government will award a contract to the lowest bidders who are able to satisfy the quality and quantity requirements. The successful bidders will be guaranteed a sale volume for at least a year. A volume guarantee gives the winner an opportunity to gain or increase market share. The volume guarantee is intended to make manufacturers more willing to cut their prices to win a bid. It may also enable manufacturers to lower their distribution and commercial costs. Many types of drugs are covered under the program, including drugs made by international pharmaceutical companies and generics made by domestic Chinese manufacturers. For example, in January 2020, ABRAXANE and its generic forms were included in the program. We won the bid and became one of the three companies who were awarded a government contract, with a price for sales of ABRAXANE under the government contract that would have been significantly lower than the price that we had been charging. On March 25, 2020, the NHSA removed ABRAXANE from the volume-based procurement list due to the NMPA's decision to suspend the importation, sales and use of ABRAXANE, which has adversely impacted our business and results of operations. In August 2020, VIDAZA® and its generic forms were included for bidding in the program. We did not win the bid for VIDAZA, which has resulted in the drug being restricted from use in public hospitals, which account for a large portion of the market, and a decline in sales revenue. Moreover, the program may change how generic drugs are priced and procured in China and is likely to accelerate the replacement of originator drugs with generics. We cannot be sure whether there will be any changes to the program in the future. The implementation of the program may negatively impact our existing commercial operations in China as well as our strategies on how to commercialize our drugs in China, which could have a material adverse effect on our business, financial condition and results of operations.

Although China adopted changes to its patent law to include patent term extension and an early resolution mechanism for pharmaceutical patent disputes, key provisions of the law remain unclear and/or subject to implementing regulations. The absence of effective regulatory exclusivity for pharmaceutical products in China could further increase the risk of early generic or biosimilar competition with our medicines in China.

In the United States, a law commonly referred to as "Hatch-Waxman Act" 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 Act also provides for patent linkage, pursuant to which FDA will stay approval of certain follow-on new drug applications during the pendency of litigation between the follow-on applicant and the patent holder or licensee, for a period of up to 30 months. Finally, the Hatch-Waxman Act provides for regulatory exclusivity that can prevent submission or approval of certain follow-on marketing applications. For example, U.S. law provides a five-year period of exclusivity to the first applicant to obtain approval of a new chemical entity and three years of exclusivity protecting certain innovations to previously approved active ingredients where the applicant was required to conduct new clinical trials to obtain approval for the modification. Similarly, the Orphan Drug Act provides seven years of market exclusivity for certain drugs to treat rare diseases. These provisions, which are designed to promote innovation, can prevent competing products from entering the market for a certain period of time after marketing approval for the innovative product.

In China, however, laws on data exclusivity (referred to as regulatory data protection) are still developing. The PRC Patent Law (as amended in 2020, the "Amended PRC Patent Law") contains both patent term extension and a mechanism for early resolution of patent disputes. Accordingly, NMPA and NIPA jointly issued the Implementation Measures for the Early Settlement Mechanism of Drug Patent Disputes (for Trial Implementation). However, the provisions for patent term extension are unclear and/or remain subject to the approval of implementing regulations that are still in draft form or have not yet been proposed, leading to uncertainty about their scope and implementation. Until the relevant implementing regulations for patent term extension in the Amended PRC Patent Law are implemented, and until data exclusivity is adopted and implemented, we may be subject to earlier generic or biosimilar competition in China than in the United States and other jurisdictions with stronger regulatory data protection for pharmaceutical products.

Undesirable adverse events caused by our medicines 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 ("AEs") caused by our medicines 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, or could result in limitations or withdrawal following 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 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.

As is typical in the development of pharmaceutical products, drug-related AEs and serious AEs ("SAEs") have been reported in our clinical trials. Some of these events have led to patient deaths. 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 ("IRAEs") have been associated with treatment with checkpoint inhibitors such as 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 medicines and drug candidates, or caused by our medicines 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 medicine;
- regulatory authorities may withdraw approvals or revoke licenses of the medicine, 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 implement a Risk Evaluation Mitigation Strategy ("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 regulatory authority;
- we may be required to conduct post-marketing 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, financial condition, and prospects.

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

We plan to develop certain of our medicines and drug candidates for use as a combination therapy. If a regulatory authority revokes its approval of the other therapeutic that we use in combination with our medicines or drug candidates, we will not be able to market our medicines or 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 medicines and 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 medicines or 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 medicines. For example, we have in-licensed drug candidates from third parties to conduct clinical trials in combination with our drug candidates. We may rely on those third parties to manufacture the in-licensed drug candidates and may not have control over their manufacturing process. If these third parties encounter any manufacturing difficulties, disruptions or delays and are not able to supply sufficient quantities of drug candidates, our drug combination study program may be delayed. For additional information, please see the section of this Annual Report titled “Part I — Item 1A — Risk Factors — Risks Related to Our Reliance on Third Parties — We rely on third parties to manufacture some of our commercial and clinical 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.”

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

In the United States, China, Europe 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 medicines 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 medicine. For example, in August 2022, the Inflation Reduction Act of 2022 (the "IRA") was signed into law. The IRA includes several provisions that may impact our business to varying degrees, including provisions that create a $2,000 out-of-pocket cap for Medicare Part D beneficiaries,

impose new manufacturer financial liability on all drugs in Medicare Part D, allow the U.S. government to negotiate Medicare Part B and Part D pricing for certain high-cost drugs and biologics without generic or biosimilar competition, require companies to pay rebates to Medicare for drug prices that increase faster than inflation, and delay the rebate rule that would require pass through of pharmacy benefit manager rebates to beneficiaries. 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 medicines and drug candidates. For additional information, please see the section of this Annual Report titled "Part I — Item 1 — Business – Government Regulation – Healthcare Reform."

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 any regulations, guidance or interpretations will be changed, or what the impact of such changes on the regulatory approvals of our medicines and drug candidates may be.

For example, in the United States, there have been numerous judicial, administrative, executive, and legislative challenges to certain aspects of the Affordable Care Act, and there could be additional challenges and amendments to the Affordable Care Act in the future, which could have a material adverse impact on our business, results of operations and financial condition.

Risks Related to Our Financial Position and Need for Additional Capital

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 not become profitable.

Investment in pharmaceutical drug development is highly capital-intensive and 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 and the first quarter of 2021, when we were profitable due to revenue recognized from up-front license fees from collaboration agreements. As of December 31, 2022, we had an accumulated deficit of $7.1 billion. 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, although we expect these losses to decrease in the near term as product sales growth exceeds expense growth. We expect expenses to continue to increase as we continue to expand our development of, and seek regulatory approvals for, our drug candidates, and our manufacturing facilities, commercialize our medicines and launch new medicines, if approved, maintain and expand regulatory approvals, contribute up to $1.25 billion to the global development of a portfolio of Amgen pipeline assets under our collaboration agreement, and commercialize the medicines that we have licensed from Amgen, BMS and other parties and any other medicines 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. We will also incur costs in support of our growth as a 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 our approved products, our ability to generate revenues and the timing and amount of milestones and other payments we make or receive with arrangements with third parties. If we fail to achieve market acceptance for our medicines or if promising 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, development, manufacturing and commercialization efforts, expand our business or continue our operations.

We may 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 of our drug candidates or achieve profitability.

Our portfolio of 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. Additionally, we are investing in the manufacturing and commercialization of our approved medicines. Our operations have consumed substantial amounts of cash since inception. Our operating activities used $1.5 billion, $1.3 billion and $1.3 billion of net cash during the years ended December 31, 2022, 2021 and 2020, respectively. We recorded negative net cash flows from operating activities in 2022, 2021 and 2020 primarily due to our net losses of $2.0 billion, $1.5 billion and $1.6 billion, respectively. Although we recorded positive net cash flows from operating activities in 2017, primarily

due to the upfront fees received from the BMS 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 financing 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, contributing to the global development of a portfolio of Amgen pipeline assets, developing our manufacturing capabilities and securing drug supply, and launching and commercializing our and our collaborators' medicines and any additional drug candidates for which we receive regulatory approval, including building and maintaining a commercial organization to address markets in China, the United States and other countries.

Since September 2017, we have generated revenues from the sale of medicines in China licensed from BMS, and since the fourth quarter of 2019, we have generated revenues from our internally developed medicines. 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 may not be sufficient to enable us to complete all global development or launch all of our current medicines and drug candidates for the currently anticipated indications and to invest in additional programs. Accordingly, we may require further funding through public or private offerings, debt financing, collaboration and licensing arrangements or other sources.

With uncertainty in the capital markets, 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 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 shares. 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 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. Fluctuations in the value of the U.S. dollar against currencies in countries in which we operate could have a negative impact on our results of operations. 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 PRC, Australia and other governments. It is difficult to predict how market forces or PRC, Australia, other governments outside the U.S. and U.S. government policies may impact the exchange rate of the RMB and the U.S. dollar or any other currencies in the future. There

remains significant international pressure on China 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, 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. 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 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 approval from or registration with appropriate government authorities or designated banks 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 any dividends payable on, our shares in foreign currency terms.

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, 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 $3.9 billion, restricted cash of $5.5 million and short-term investments of $665.3 million as of December 31, 2022, most of which are deposited in financial institutions outside of China. As required by the PRC securities laws, the net proceeds from the STAR Offering must be used in strict compliance with the planned uses as disclosed in the PRC prospectus for the STAR Offering as well as our proceeds management policy for the STAR Offering approved by our board of directors. 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, 2022, our short-term investments consisted of U.S. Treasury securities.

Although we believe that the U.S. Treasury securities 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 medicines and drug candidates through intellectual property rights, or if the scope of such intellectual property rights is not sufficiently broad, third parties may compete against us.

Our success depends in large part on our ability to protect our medicines, drug candidates and proprietary technology from competition by obtaining, maintaining and enforcing our intellectual property rights, including patent rights. We seek to protect the medicines, drug candidates and technology that we consider commercially important by filing patent applications in the United States, the PRC, Europe and other territories, 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, prosecute, maintain, enforce or license all necessary or desirable patents and/or 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 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 the 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.

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, the PRC and other countries. We may be subject to a third-party preissuance submission of prior art to the United States Patent and Trademark Office (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 medicines or drug candidates and compete directly with us without payment to us, or result in our inability to manufacture or commercialize medicines or 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, medicines, 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 medicines 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 BMS in China face competition from generic medications, and we may face similar competition for our approved medicines even if we successfully obtain patent protection. Manufacturers of generic drugs may challenge the scope, validity or enforceability of our patents, 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 medicines and drug candidates are expected to expire on various dates as described in "Part I-Item 1-Business-Intellectual Property" of this Annual Report. 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. If we fail to adequately protect our intellectual property rights, our competitive position could be impaired and our business could be materially harmed.

Filing, prosecuting, maintaining and defending patents on drugs or drug candidates in all countries throughout the world could be prohibitively expensive for us, and our intellectual property rights in some countries can have a different scope and strength than in the United States. In addition, the laws of certain countries do not protect intellectual property rights to the same extent as U.S. laws do, particularly those relating to biopharmaceutical products. 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 other 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-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 medicines 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.

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 medicines and drug candidates could be found invalid or unenforceable if challenged in court or before government patent authorities.

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 challenging the validity or enforceability of our patents or alleging that we infringe their intellectual property rights.

In addition, generic drug companies may in the future file an Abbreviated New Drug Application (“ANDA”) with the FDA seeking approval to market a generic version of our products, or our competitors’ products, before the expiration of the patents covering such products, which may trigger ANDA litigation over the associated patent. Settlements and related licensing agreements resulting from ANDA litigation can be challenged and have the potential to generate additional litigation which can be costly. The success of such litigation depends on the strength of the patents covering the branded product and the manufacturer’s ability to prove infringement. The outcome of such litigation is inherently uncertain and may result in potential loss of market exclusivity for the product which may have a significant financial impact on product revenue. Furthermore, the Federal Trade Commission (“FTC”) has brought lawsuits to challenge ANDA litigation settlements as anti-competitive. If we engage in ANDA litigation, we may also face an FTC challenge with respect to the related settlement which may result in additional expense or penalty.

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 patents, 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 medicines or 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 medicines or 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.

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 medicines or drug candidates.

Our commercial success depends in part on our avoiding infringement of the valid 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 of our medicines and 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 medicines and 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 medicines and drug candidates. 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 medicines and 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 medicines or 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 medicines and 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 patents in the U.S. and some other jurisdictions 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 BRUKINSA for which the patent is expected to expire in 2027; 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; and the use of TIGIT antagonist in combination with PD-1 binding antagonist to treat cancers that are relevant to the use of ociperlimab in combination with tislelizumab for which patents are expected to expire in 2034. 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 medicine was approved for sale in the United States before the expiration of the relevant patents, we would need a license to commercialize the medicine 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 medicine before the expiration of corresponding patents covering that medicine. 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 our shares. 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.

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 other 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 regulatory exclusivity for our medicines, our business may be materially harmed.

Depending upon the timing, duration and specifics of FDA marketing approval of our medicines and drug candidates, one or more of our U.S. patents may be eligible for limited patent term extension under the Hatch-Waxman Act. 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, although the Amended PRC Patent Law includes patent term extension, the patent term extension provision of the law is unclear and/or remains subject to the approval of implementing regulations that are still in draft form and soliciting comments, leading to uncertainty about its scope and implementation. 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 medicines or drug candidates.

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 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 medicines and 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, 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 members of our senior management, executed proprietary rights, non-disclosure and in some cases non-competition agreements in connection with their 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. 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.

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 medicine 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.

Risks Related to Our Reliance on Third Parties

We rely on third parties to manufacture some of our commercial and clinical 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 manufacture commercial supply of tislelizumab, zanubrutinib, and pamiparib at our manufacturing facilities in China, and are constructing a commercial-stage biologics manufacturing and clinical R&D center in New Jersey and a new small molecule manufacturing campus in Suzhou, China, we continue to rely on outside vendors to manufacture supplies and process some of our medicines and drug candidates. For example, we have entered into a commercial supply agreement for tislelizumab with Boehringer Ingelheim Biopharmaceuticals (China) Ltd. ("Boehringer Ingelheim") and entered into a commercial supply agreement for BRUKINSA with Catalent Pharma Solutions, LLC ("Catalent"). In addition, we generally rely on our collaboration partners and their third-party manufacturers for supply of in-licensed medicines in China. We have limited experience in manufacturing or processing our medicines and drug candidates on a commercial scale. Additionally, 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 use 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 medicines 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 regulatory authorities must evaluate and/or approve any manufacturers as part of their regulatory oversight of our medicines and drug candidates. This evaluation would require new testing and GMP-compliance inspections by regulatory authorities;

- our manufacturers may have little or no experience with manufacturing our medicines and 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 medicines and drug candidates;

- our third-party manufacturers might be unable to timely manufacture our medicines and drug candidates or produce the quantity and quality required to meet our clinical and commercial needs, if any. This may, in the future, require us to transfer manufacturing technology to a different manufacturer or use a different process, each of which would be both time consuming and costly and potentially require us to conduct comparative studies to determine bioequivalence of the new and prior manufacturers' products or the new and old processes;

- manufacturers are subject to ongoing periodic unannounced inspection by the FDA and corresponding state agencies in the United States to ensure strict compliance with good manufacturing practice ("GMP") requirements and other government regulations and by other comparable regulatory authorities for corresponding non-U.S. requirements. Manufacturers may be unable to comply with these GMPs which may result in fines and civil penalties, suspension of production, suspension, delay or withdrawal of product approval, or product seizure or recall. 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 some of the technology used and improvements made by our third-party manufacturers in the manufacturing process for our medicines and drug candidates;

- 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;

- our contract manufacturers and drug component suppliers may be subject to disruptions in their business, including unexpected demand for or shortage of raw materials or components, cyber-attacks on supplier systems, labor disputes or shortage and inclement weather, as well as natural or man-made disasters or pandemics; and

- manufacturing partners may require us to fund capital improvements to support scale-up of manufacturing and related activities to the extent our drug candidates or medicines become approved for commercial sale.

For example, on March 25, 2020, the NMPA suspended the importation, sales and use of ABRAXANE in China supplied to us by BMS, and the drug was subsequently recalled by BMS and is not currently available for sale in China. This suspension was based on inspection findings at BMS's contract manufacturing facility in the United States. We have not had any sales of ABRAXANE since the suspension and do not expect future revenue from ABRAXANE. For additional information, please see the section of this Annual Report titled "Legal Proceedings".

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 development of our drug candidates or commercialization of our medicines. In addition, we will rely on third parties to perform certain specification tests on our medicines 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 medicines 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 medicines and 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 medicines 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.

We have entered into licensing and collaboration arrangements and may enter into additional collaborations, licensing arrangements, or strategic alliances in the future, and we may not realize the benefits of such arrangements.

We have entered into licensing and collaboration agreements and may enter into additional collaboration, licensing arrangements, or strategic alliances with third parties that we believe will complement or augment our research, development and commercialization efforts. Any of these relationships may require us to incur non-recurring and other charges, increase our near and long-term expenditures, issue securities that dilute our existing shareholders, or disrupt our management and business.

In August 2017, we acquired Celgene's commercial operations in China and an exclusive license to Celgene's (now BMS's) commercial cancer portfolio in China, REVLIMID, VIDAZA and ABRAXANE. On March 25, 2020, the NMPA suspended the importation, sales and use of ABRAXANE in China supplied to us by BMS, and the drug was subsequently recalled by BMS and is not currently available for sale in China. This suspension was based on inspection findings at BMS's contract manufacturing facility in the United States. We have not had any sales of ABRAXANE since the suspension and do not expect future revenue from ABRAXANE. We have initiated an arbitration proceeding against BMS asserting that it has breached and continues to breach the terms and conditions of the license and supply agreement. For additional information, please see the section of this Annual Report titled "Legal Proceedings".

In 2019, we entered into a strategic collaboration with Amgen with respect to its commercial-stage oncology products XGEVA, BLINCYTO and KYPROLIS and a portfolio of clinical- and late-preclinical-stage oncology pipeline products. In January 2021, we entered into a collaboration and license agreement with Novartis Pharma AG ("Novartis"), granting Novartis rights to develop, manufacture and commercialize our anti-PD-1 antibody tislelizumab in North America, Japan, the EU, and six other European countries. In December 2021, we entered into an option, collaboration and license agreement with Novartis to develop, manufacture and commercialize our investigational TIGIT inhibitor, ociperlimab, in North America, Europe, and Japan.

Our strategic collaborations with Amgen, Novartis and BMS involve numerous risks. We cannot be certain that we will achieve the financial and other benefits that led us to enter into the collaborations. Moreover, we may not achieve the revenue and cost synergies expected from our collaborations for their commercial products in China, and our management's attention may be diverted from our drug discovery and development business. These synergies are inherently uncertain, and are subject to significant business, economic and competitive uncertainties and contingencies, many of which are difficult to predict and are beyond our control. If we achieve the expected benefits, they may not be achieved within the anticipated time frame. Lastly, strategic collaborations can be terminated for various reasons. For example, our strategic collaboration with Celgene for the development and commercialization of tislelizumab, which we entered into in connection with the license agreement in 2017, was terminated in June 2019 in advance of the acquisition of Celgene by BMS, and we received a termination notice in October 2021 to terminate our license agreement for ABRAXANE in China.

Additionally, from time to time, we may enter into joint ventures with other companies. Establishment of a joint venture involves significant risks and uncertainties, including (i) our ability to cooperate with our strategic partner, (ii) our strategic partner having economic, business, or legal interests or goals that are inconsistent with ours, and (iii) the potential that our strategic partner may be unable to meet its economic or other obligations, which may require us to fulfill those obligations alone.

We face significant competition in seeking appropriate strategic partners, and the negotiation process is time-consuming and complex. Moreover, we may not be successful in our efforts to establish a strategic collaboration or other alternative arrangements for our medicines and drug candidates because they may be deemed to be at too early of a stage of development for collaborative effort and third parties may not view our medicines and drug candidates as having the requisite potential to demonstrate safety and efficacy or commercial viability. If and when we collaborate with a third party for development and commercialization of a medicine or drug candidate, we can expect to relinquish some or all of the control over the future success of that medicine or drug candidate to the third party. For any medicines or drug candidates that we may seek to in-license from third parties, we may face significant competition from other pharmaceutical or biotechnology companies with greater resources or capabilities than us, and any agreement that we do enter may not result in the anticipated benefits.

Collaborations involving our medicines and drug candidates are subject to numerous risks, which may include the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to a collaboration;
- collaborators may not pursue development and commercialization of our drug candidates and medicines or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in their strategic focus due to the acquisition of competitive drugs, availability of funding, or other external factors, such as a business combination that diverts resources or creates competing priorities;

- collaborators may delay clinical trials, provide insufficient funding for a clinical trial, stop a clinical trial, abandon a drug candidate, repeat or conduct new clinical trials, or require a new formulation of a drug candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, drugs that compete directly or indirectly with our medicines or drug candidates;
- a collaborator with marketing and distribution rights to one or more medicines may not commit sufficient resources to their marketing and distribution or may set prices that reduce the profitability of the medicines;
- collaborators may not properly maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability;
- disputes may arise between us and a collaborator that cause the delay or termination of the research, development or commercialization of our medicines and drug candidates, or that result in costly litigation or arbitration that diverts management attention and resources;
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable medicines and drug candidates; and
- collaborators may own or co-own intellectual property covering our medicines and drug candidates that results from our collaborating with them, and in such cases, we would not have the exclusive right to commercialize such intellectual property.

As a result, we may not be able to realize the benefit of current or future collaborations, licensing arrangements or strategic alliances for our medicines and drug candidates if we are unable to successfully integrate such products with our existing operations and company culture, which could delay our timelines or otherwise adversely affect our business. We also cannot be certain that, following a strategic transaction or license, we will be able to fulfill all of our contractual obligations in a timely manner or achieve the revenue, specific net income or other goals that justify such transaction. If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms, or at all, we may have to curtail the development of a drug candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense.

If we fail to maintain an effective distribution channel for our medicines, our business and sales could be adversely affected.

We rely on third-party distributors to distribute our approved medicines. For example, we rely on sole third-party distributors to distribute some of our in-licensed approved medicines in China and multiple third-party distributors for the distribution of our internally developed medicines. We also expect to rely on third-party distributors to distribute our other internally developed and in-licensed medicines, if approved. Our ability to maintain and grow our business will depend on our ability to maintain an effective distribution channel that ensures the timely delivery of our medicines. However, we have relatively limited control over our distributors, who may fail to distribute our medicines in the manner we contemplate. For example, while we have long-standing business relationship with our sole distributor for the in-licensed products from BMS, the agreement we entered into with our sole distributor can be terminated by either party upon six months' written notice. If price controls or other factors substantially reduce the margins our distributors can obtain through the resale of our medicines to hospitals, medical institutions and sub-distributors, they may terminate their relationship with us. While we believe alternative distributors are readily available, there is a risk that, if the distribution of our medicines is interrupted, our sales volumes and business prospects could be adversely affected.

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

Before a third party can begin commercial manufacture of our medicines, they 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 products, any potential third-party manufacturer may be unable to initially pass regulatory inspections in a timely or cost-effective manner in order for us to obtain regulatory approval. If contract manufacturers do not pass their inspections by the relevant regulatory authorities, our commercial supply of drug product or substance will be significantly delayed and may result in significant additional costs, including the delay or denial of any marketing application for our drug candidates or disruption in sales. In addition, drug and biological manufacturing facilities are continuously subject to inspection by regulatory authorities, before and after drug approval, and must comply with GMPs. Our or our collaborators' contract manufacturers may

encounter difficulties in achieving quality control and quality assurance and may experience shortages in qualified personnel. In addition, contract manufacturers' failure to achieve and maintain high manufacturing standards in accordance with applicable regulatory requirements, or the incidence of manufacturing errors, could result in patient injury, product liability claims, product shortages, product recalls or withdrawals, delays or failures in product testing or delivery, cost overruns or other problems that could seriously harm our business. If a third-party manufacturer with whom we or our collaborators' contract is unable to comply with manufacturing regulations, we may also be subject to fines, unanticipated compliance expenses, recall or seizure of our drugs, product liability claims, total or partial suspension of production and/or enforcement actions, including injunctions, and criminal or civil prosecution. These possible sanctions could materially adversely affect our financial results and financial condition. On March 25, 2020, the NMPA suspended the importation, sales and use of ABRAXANE in China supplied to us by BMS, and the drug was subsequently recalled by BMS and is not currently available for sale in China. This suspension was based on inspection findings at BMS's contract manufacturing facility in the United States. We have not had any sales of ABRAXANE since the suspension and do not expect future revenue from ABRAXANE. We have initiated an arbitration proceeding against BMS asserting that it has breached and continues to breach the terms and conditions of the license and supply agreement. For additional information, please see the section of this Annual Report titled "Legal Proceedings".

If we are not able to successfully develop and/or commercialize Amgen's oncology products, the expected benefits of the collaboration will not materialize.

We have a collaboration agreement with Amgen pursuant to which we and Amgen have agreed to collaborate on the commercialization of Amgen's oncology products XGEVA, BLINCYTO and KYPROLIS in China, and the global development and commercialization in China of a portfolio of Amgen's clinical- and late-preclinical-stage pipeline products. Amgen has paused or stopped development of some of the pipeline assets due to portfolio prioritization, and the parties expect that the development plan for the pipeline assets will continue to evolve over time. Additionally, Amgen has advised us that its applications to the Human Genetic Resources Administration of China ("HGRAC") to obtain approval to conduct clinical studies in China for the pipeline assets, including its application for LUMAKRAS (sotorasib) ("AMG 510"), a first-in-class KRAS G12C inhibitor, were delayed between 2020 and 2022. Approval from the HGRAC is required for the initiation of clinical trials involving the collection of human genetic materials in China. In connection with our ongoing assessment of the Collaboration Agreement cost-share contributions, we determined that our further investment in the development of AMG 510 was no longer commercially viable for BeiGene. As a result, in February 2023, we entered into an amendment to the Collaboration Agreement to (i) stop sharing costs with Amgen for the further development of AMG 510 during the period starting January 1, 2023 and ending August 31, 2023; and (ii) cooperate in good faith to prepare a transition plan with the anticipated termination of AMG 510 from the Collaboration Agreement. We do not expect the HGRAC delay to affect the conduct of the clinical trials in China for our drug candidates, other than assets that are part of the Amgen collaboration. The Amgen collaboration involves numerous risks, including unanticipated costs and diversion of our management's attention from our other drug discovery and development business. There can be no assurance that we will be able to successfully develop and commercialize Amgen's oncology products in China, which could disrupt our business and harm our financial results.

We rely on third parties to conduct our preclinical studies and clinical trials. 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 medicines and drug candidates and our business could be substantially harmed.

We have relied upon and plan to continue to rely to some extent upon third-party CROs to monitor and manage data and provide other services for our ongoing preclinical and clinical programs. We rely on these parties for execution of our preclinical studies and clinical trials, and control 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 regulatory authorities for all of our drug candidates 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 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 drug product produced under GMP 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 investigations 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.

Risks Related to Our Industry, Business and Operations

We have significantly increased and expect to continue to increase our research, development, manufacturing, and commercial capabilities, and we may experience difficulties in managing our growth.

At the beginning of 2022, we had approximately 8,000 employees, and we ended the year with more than 9,000 employees, an increase of 15%. We expect to continue our growth. Most of our employees are full-time. As our research, development, manufacturing and commercialization plans and strategies evolve, we must add a significant number of additional managerial, operational, drug development, clinical, regulatory affairs, manufacturing, sales, marketing, financial and other personnel in the United States, China, Europe and other regions. Our recent growth and any anticipated future growth will impose significant added responsibilities on members of management, including:

- identifying, recruiting, integrating, maintaining, and motivating additional employees;
- managing the growth in our research, clinical operations, commercial, and supporting functions;
- managing our internal development efforts effectively, including the clinical and regulatory review process for our drug candidates, while complying with our contractual obligations to third parties; and
- improving our operational, financial and management controls, reporting systems and procedures.

Our future financial performance and our ability to develop and commercialize our medicines and drug candidates will depend, in part, on our ability to effectively manage our recent growth and any future growth, and our management may also have to divert a disproportionate amount of its attention away from day-to-day activities in order to devote a substantial amount of time to managing these growth activities.

We currently rely, and for the foreseeable future will continue to rely, on certain independent organizations, advisors and consultants to provide certain services. There can be no assurance that the services of these independent organizations, advisors and consultants will continue to be available to us on a timely basis when needed, or that we can find qualified replacements. There can be no assurance that we will be able to manage our existing consultants or find other competent outside contractors and consultants on economically reasonable terms, if at all.

If we are not able to effectively manage our growth and further expand our organization by hiring new employees and expanding our groups of consultants and contractors as needed, we may not be able to successfully implement the tasks necessary to further develop, manufacture and commercialize our medicines and drug candidates and, accordingly, may not achieve our research, development, manufacturing and commercialization goals.

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

Xiaodong Wang, Ph.D., our Co-Founder, Chairman of our scientific advisory board, and director; John V. Oyler, our Co-Founder, Chief Executive Officer and Chairman of the board of directors; Xiaobin Wu, Ph.D., our President, Chief Operating Officer and General Manager of China; and the other principal members of our management and scientific teams play a critical role in the Company's operation and development. Although we have employment agreements or offer letters with each of our executive officers, these agreements do not prevent our executives from terminating their employment with us at any time. We do not maintain “key person” insurance for any of our executives or other employees. The loss of the services of any of these persons could impede the achievement of our research, development and commercialization objectives.

To induce valuable employees to remain at our company, in addition to salary and cash incentives, we have provided share option, restricted share unit and restricted share grants that vest over time or based on performance conditions. The value to employees of these equity grants that may be significantly affected by movements in our share price that are beyond our control and may be insufficient to counteract more lucrative offers from other companies. Although we have employment agreements or offer letters with our key employees, any of our employees could leave our employment at any time, with or without notice.

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will also be critical to our success. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating and executing our discovery, clinical development, manufacturing and commercialization strategy. The loss of the services of our executive officers or other key employees and consultants could impede the achievement of our research, development, manufacturing and commercialization objectives and seriously harm our ability to successfully implement our business strategy.

Furthermore, replacing executives, key employees or consultants may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel or consultants on acceptable terms, given the competition among numerous pharmaceutical and biotechnology companies for similar personnel.

We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

Our business is subject to complex and evolving industry-specific laws and regulations regarding the collection and transfer of personal data. These laws and regulations can be complex and stringent, and many are subject to change and uncertain interpretation, which could result in claims, changes to our data and other business practices, significant penalties, increased cost of operations, or otherwise adversely impact our business.

Regulatory authorities around the world have implemented industry-specific laws and regulations that affect the collection and transfer of personal data. For example, in China, the Regulation on the Administration of Human Genetic Resources promulgated by the State Council (the “HGR Regulation”), which became effective in 2019, applies to activities that involve sampling, biobanking, use of HGR materials and associated data, in China, and provision of such to foreign parties. The HGR Regulation prohibits both onshore or offshore entities established or actually controlled by foreign entities and individuals from sampling or biobanking any China HGR in China and require approval for the sampling of certain HGR and biobanking of all HGR by Chinese parties. Approval for any export or cross-border transfer of the HGR material is required, and transfer of China HGR data by Chinese parties to foreign parties or entities established or actually controlled by them also requires the Chinese parties to file, before the transfer, a copy of the data to the HGR administration for record. The HGR Regulation also requires that foreign parties ensure the full participation of Chinese parties in international collaborations and all records and data must be shared with the Chinese parties. For information about applications under the HGR Regulation for clinical studies in China that are part of the Amgen- BeiGene Collaboration, see the risk factor entitled “If we are not able to successfully develop and/or commercialize Amgen’s oncology products, the expected benefits of the collaboration will not materialize."

Further to the draft HGR implementing rules, the Cyberspace Administration of China ("CAC") released the final Measures of Cross-Border Data Transfer Security Assessment on July 7, 2022 (effective as of September 1, 2022), under which any transfer of certain "important data" out of China shall trigger a security assessment to be conducted by the government. The term "important data" is a broadly defined term under the Cybersecurity Law and Data Security Law, and further clarifications need to be put in place by the government before international companies could find a practical way to comply. However, under the latest draft Important Data Identification Guidance, HGR data is classified as "important data," and if the guidance is finalized as is, it can be expected that this new cross-border data transfer rule may create considerable additional regulatory burdens on international companies' human gene-involved R&D activities in China (*i.e.*, adding a third layer of CAC's regulatory approval in addition to HGRAC's and NMPA's).

If the Chinese parties fail to comply with data protection laws, regulations and practice standards, and our research data is obtained by unauthorized persons, used or disclosed inappropriately or destroyed, it could result in a loss of our confidential information and subject us to litigation and government enforcement actions. It is possible that these laws may be interpreted and applied in a manner that is inconsistent with our or our collaborators’ practices, potentially resulting in suspension of relevant ongoing clinical trials or the initiation of new trials, confiscation of HGR samples and associated data and administrative fines, disgorgement of illegal gains, or temporary or permanent debarment of our or our collaborators’ entities and responsible persons from further HGR projects and, consequently, a de-facto ban on the debarred entities from initiating new clinical trials in China. So far, the HGR administration has disclosed a number of HGR violation cases. In one case, the sanctioned party was the Chinese subsidiary of a multinational pharmaceutical company that was found to have illegally transferred certain HGR materials to CROs for conducting certain unapproved research. In addition to a written warning and confiscation of relevant HGR materials, the Chinese subsidiary of the multinational pharmaceutical company was requested by the HGR administration to take rectification measures and at the same time banned from submitting any HGR applications until the HGR administration was satisfied with the rectification results, which rendered it unable to initiate new clinical trials in

China until the ban was lifted. In another case, a public hospital was found to have illegally transferred certain HGR data to a university in Europe, and that hospital was eventually subject to the same ban.

To further tighten the control of China HGR, the Chinese government adopted amendments to the Criminal Code, effective as of March 1, 2021, which criminalize the illegal collection of China HGR, the illegal transfer of China HGR materials outside of China, and the transfer of China HGR data to foreign parties or entities established or actually controlled by them without going through security review and assessment. An individual who is convicted of any of these violations may be subject to public surveillance, criminal detention, a fixed-term imprisonment of up to 7 years, and/or a criminal fine. On April 15, 2021, the Biosecurity Law became effective. The Biosecurity Law establishes an integrated system to regulate biosecurity-related activities in China, including the security regulation of HGR and biological resources. The Biosecurity Law for the first time expressly declared that China has sovereignty over its HGR and further endorsed the HGR Regulation by recognizing the fundamental regulatory principles and systems established by it over the utilization of Chinese HGR by foreign entities in China. Although the Biosecurity Law does not provide any specific new regulatory requirements on HGR, as it is a law adopted by China's highest legislative authority, it gives China's major regulatory authority of HGR, i.e., the Ministry of Science and Technology, significantly more power and discretion to regulate HGR and it is expected that the overall regulatory landscape for Chinese HGR will evolve and become even more rigorous. In addition, the interpretation and application of data protection laws in China and elsewhere are often uncertain and in flux.

We expect that these areas will receive greater and continued attention and scrutiny from regulators and the public going forward, which could increase our compliance costs and subject us to heightened risks and challenges associated with data security and protection. If we are unable to manage these risks, we could become subject to significant penalties, including fines, suspension of business and revocation of required licenses, and our reputation and results of operations could be materially and adversely affected.

We manufacture some of our medicines and intend to manufacture some of our drug candidates, if approved. Failure to comply with regulatory requirements could result in sanctions being imposed against us and delays in completing and receiving regulatory approvals for our manufacturing facilities, or damage to, destruction of or interruption of production at such facilities, could delay our development plans or commercialization efforts.

We currently have manufacturing facilities in Beijing, Guangzhou, and Suzhou, China. We are also constructing a commercial-stage biologics manufacturing and clinical R&D center in New Jersey, United States, and a new small molecule manufacturing campus in Suzhou, China. These facilities may encounter unanticipated delays and expenses due to a number of factors, including regulatory requirements. If construction or expansion, regulatory evaluation and/or approval of our facilities are delayed, we may not be able to manufacture sufficient quantities of our medicines and drug candidates, which would limit our development and commercialization activities and our opportunities for growth. Cost overruns associated with constructing or maintaining our facilities could require us to raise additional funds from other sources. For example, we may not be able to complete the construction and validation of and obtain regulatory approval for the new manufacturing and clinical R&D center in New Jersey, the new manufacturing campus in Suzhou and manufacturing facility expansion in Guangzhou in a timely or economic manner.

In addition to the similar manufacturing risks described in "Risks Related to Our Reliance on Third Parties," our manufacturing facilities are subject to inspection in connection with clinical development and new drug approvals and ongoing, periodic inspection by the FDA, NMPA, EMA or other comparable regulatory agencies to ensure compliance with GMP and other regulatory requirements. Historically, some manufacturing facilities in China have had difficulty meeting the FDA's, NMPA's or EMA's standards. Our failure to follow and document our adherence to such GMP regulations or other regulatory requirements may lead to significant delays in the availability of products for clinical or commercial use, may result in the termination of or a hold on a clinical trial, or may delay or prevent filing or approval of marketing applications for our drug candidates or the commercialization of our medicines. We also may encounter problems with the following:

- achieving adequate or clinical-grade materials that meet FDA, NMPA, EMA or other comparable regulatory agency standards or specifications with consistent and acceptable production yield and costs;
- shortages of qualified personnel, raw materials or key contractors; and
- ongoing compliance with GMP regulations and other requirements of the FDA, NMPA, EMA or other comparable regulatory agencies.

Failure to comply with applicable regulations could also result in sanctions being imposed on us, including fines, injunctions, civil penalties, a requirement to suspend or put on hold one or more of our clinical trials, failure of regulatory authorities to grant marketing approval of our drug candidates, delays, suspension or withdrawal of approvals, supply

disruptions, license revocation, seizures or recalls of drug candidates or medicines, operating restrictions and criminal prosecutions, any of which could harm our business.

Developing advanced manufacturing techniques and process controls is required to fully utilize our facilities. Advances in manufacturing techniques may render our facilities and equipment inadequate or obsolete.

To supply commercial quantities for our marketed products, produce our medicines in the quantities that we believe will be required to meet anticipated market demand, and to supply clinical drug material to support the continued growth of our clinical programs, we will need to increase, or "scale up," the production process by a significant factor over the initial level of production, which will require substantial additional expenditures and various regulatory approvals and permits. If we are unable to do so, are delayed, or if the cost of this scale up is not economically feasible for us or we cannot find a third-party supplier, we may not be able to produce our medicines in a sufficient quantity to meet future demand.

If our manufacturing facilities or the equipment in them is damaged or destroyed, we may not be able to quickly or inexpensively replace our manufacturing capacity or replace it at all. In the event of a temporary or protracted loss of the facilities or equipment, we might not be able to transfer manufacturing to a third party. Even if we could transfer manufacturing to a third party, the shift would likely be expensive and time-consuming, particularly since the new facility would need to comply with the necessary regulatory requirements and we would need regulatory agency approval before selling any medicines manufactured at that facility. Any interruption in manufacturing operations at our manufacturing facilities could result in our inability to satisfy the demands of our clinical trials or commercialization. Any disruption that impedes our ability to manufacture our drug candidates or medicines in a timely manner could materially harm our business, financial condition and operating results.

Currently, we maintain insurance coverage against damage to our property, plant and equipment in amounts we believe are reasonable. However, our insurance coverage may not reimburse us, or may not be sufficient to reimburse us, for any expenses or losses we may suffer. We may be unable to meet our requirements for our drug candidates and medicines if there were a catastrophic event or interruption or failure of our manufacturing facilities or processes.

We incur significant costs as a result of operating as a public company, and our management is required to devote substantial time to compliance requirements, including establishing and maintaining internal controls over financial reporting. We may be exposed to potential risks if we are unable to comply with these requirements.

As a public company listed in the United States, Hong Kong and Shanghai, we are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and the listing rules of the Nasdaq Stock Market (Nasdaq), The Stock Exchange of Hong Kong Limited (the "HKEx") and the STAR Market of the Shanghai Stock Exchange (the "SSE"), and incur significant legal, accounting and other expenses to comply with applicable requirements. These rules impose various requirements on public companies, including requiring certain corporate governance practices. Our management and other personnel devote a substantial amount of time to these requirements. Moreover, these rules and regulations increase our legal and financial compliance costs and make some activities more time-consuming and costly.

For example, the Sarbanes-Oxley Act of 2002 (the "Sarbanes-Oxley Act") requires, among other things, that we maintain effective internal controls for financial reporting and disclosure controls and procedures. In particular, we must perform system and process evaluations and testing of our internal controls over financial reporting to allow management to report on the effectiveness of our internal controls over financial reporting, as required by Section 404 of the Sarbanes-Oxley Act. Such compliance may require that we incur substantial accounting expenses and expend significant management efforts. Our testing may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses. In the event we identify significant deficiencies or material weaknesses in our internal controls that we cannot remediate in a timely manner, the market price of our shares could decline if investors and others lose confidence in the reliability of our financial statements, we could be subject to sanctions or investigations by the SEC, HKEx, China Securities Regulatory Commission (the "CSRC"), SSE or other applicable regulatory authorities, and our business could be harmed.

If we engage in acquisitions or strategic collaborations, this may increase our capital requirements, dilute our shareholders, cause us to incur debt or assume contingent liabilities, and subject us to other risks.

From time to time, we may evaluate various acquisitions and strategic collaborations, including licensing or acquiring complementary products, intellectual property rights, technologies or businesses. Any completed, in-process or potential acquisition or strategic collaboration may entail numerous risks, including:

- increased operating expenses and cash requirements;
- the assumption of additional indebtedness or contingent or unforeseen liabilities;

- the issuance of our equity securities;
- assimilation of operations, intellectual property and products of an acquired company, including difficulties associated with integrating new personnel;
- the diversion of our management's attention from our existing product programs and initiatives in pursuing such a strategic merger or acquisition;
- retention of key employees, the loss of key personnel, and uncertainties in our ability to maintain key business relationships;
- risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing drugs or drug candidates and regulatory approvals; and
- our inability to generate revenue from acquired technology and/or products sufficient to meet our objectives in undertaking the acquisition or even to offset the associated acquisition and maintenance costs.

In addition, if we undertake acquisitions or strategic collaborations, we may issue dilutive securities, assume or incur debt obligations, incur large one-time expenses and acquire intangible assets that could result in significant future amortization expense. For example, in connection with our transaction with Amgen, we issued to Amgen a total of 206,635,013 ordinary shares in the form of ADSs in January 2020, representing 20.5% of the then issued share capital of the Company after giving effect to the share issuance, which resulted in Amgen becoming our largest shareholder and the ownership of our existing shareholders being diluted.

PRC regulations and rules concerning mergers and acquisitions, including the Regulations on Mergers and Acquisitions of Domestic Companies by Foreign Investors (the "M&A Rules"), and other regulations and rules with respect to mergers and acquisitions established additional procedures and requirements that could make merger and acquisition activities by foreign investors more time consuming and complex. For example, the M&A Rules require that the Ministry of Commerce of the PRC (the "MOFCOM") be notified in advance of any change-of-control transaction in which a foreign investor takes control of a PRC domestic enterprise, if (i) any important industry is concerned, (ii) such transaction involves factors that have or may have impact on the national economic security, or (iii) such transaction will lead to a change in control of a domestic enterprise which holds a famous trademark or PRC time-honored brand. Moreover, according to the Anti-Monopoly Law of the PRC, which was amended in June 2022 and became effective as of August 1, 2022, and the Provisions on Thresholds for Prior Notification of Concentrations of Undertakings issued by the State Council, the concentration of business undertakings by way of mergers, acquisitions or contractual arrangements that allow one market player to take control of or to exert decisive impact on another market player must also be notified in advance to the State Administration for Market Regulation (the "SAMR") when the threshold is crossed and such concentration shall not be implemented without the clearance of prior notification. In addition, the Measures for Security Review of Foreign Investment jointly issued by the National Development and Reform Commission and MOFCOM and the Regulations on Implementation of Security Review System for the Merger and Acquisition of Domestic Enterprise by Foreign Investors (the "Security Review Rules") issued by the MOFCOM specify that mergers and acquisitions by foreign investors that raise "national defense and security" concerns and mergers and acquisitions through which foreign investors may acquire the de facto control over domestic enterprises that raise "national security" concerns are subject to strict review by the MOFCOM, and the rules prohibit any activities attempting to bypass a security review by structuring the transaction through, among other things, trusts, entrustment or contractual control arrangements.

We may also be subject to similar review and regulations in other jurisdictions, such as the laws and regulations on foreign investment in the United States under the jurisdiction of the Committee on Foreign Investment in the United States (the "CFIUS") and other agencies, including the Foreign Investment Risk Review Modernization Act (the "FIRRMA"), which became effective in February 2020.

Furthermore, according to the Overseas Listing Trial Measures, if a Chinese overseas listed company issues overseas listed securities to acquire assets, such issuance would be subject to filing requirements with the CSRC.

In the future, we may grow our business by acquiring complementary businesses. Complying with the requirements of the above-mentioned regulations and other relevant rules to complete such transactions could be time consuming, and any required approval or filing processes, including obtaining approval from or filing with CFIUS, the SAMR, the MOFCOM, the CSRC or other agencies may delay or inhibit our ability to complete such transactions. It is unclear whether those complementary businesses we may acquire in the future would be deemed to be in an industry that raises "national defense and security" or "national security" concerns.

However, CFIUS, SAMR, MOFCOM, CSRC or other government agencies may publish explanations in the future determining that certain complementary business is in an industry subject to the security review, in which case our future acquisitions in the United States and the PRC, including those by way of entering into contractual control arrangements with target entities, may be closely scrutinized or prohibited. Our ability to expand our business or maintain or expand our market share through future acquisitions would as such be materially and adversely affected.

If we fail to comply with the U.S. Foreign Corrupt Practices Act or other anti-bribery and corruption laws, our reputation may be harmed and we could be subject to penalties and significant expenses that have a material adverse effect on our business, financial condition and results of operations.

We are subject to the U.S. Foreign Corrupt Practices Act (the "FCPA"). The FCPA generally prohibits us from making improper payments to non-U.S. officials for the purpose of obtaining or retaining business. We are also subject to the anti-bribery and corruption laws of other jurisdictions, particularly China. The anti-bribery laws in China generally prohibit companies and their intermediaries from making payments to government officials for the purpose of obtaining or retaining business or securing any other improper advantage. As our business has expanded, the applicability of the FCPA and other anti-bribery and corruption laws to our operations has increased.

We do not fully control the interactions our employees, distributors and third-party promoters have with hospitals, medical institutions and doctors, and they may try to increase sales volumes of our products through means that constitute violations of United States, PRC or other countries' anti-corruption and related laws. Although we have policies and procedures designed to ensure that we, our employees and our agents comply with anti- bribery laws, there is no assurance that such policies or procedures will prevent our agents, employees and intermediaries from engaging in bribery activities. If we, due to either our own deliberate or inadvertent acts or those of others, fail to comply with applicable anti-bribery and corruption laws, our reputation could be harmed and we could incur criminal or civil penalties, including but not limited to imprisonment, criminal and civil fines, suspension of our ability to do business with the government, denial of government reimbursement for our products and/or exclusion from participation in government healthcare programs, other sanctions and/or significant expenses, which could have a material adverse effect on our business.

If we or our CROs or contract manufacturing organizations (CMOs) fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on our business.

We and third parties, such as our CROs or CMOs, are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and waste. In addition, our construction projects can only be put into operation after certain regulatory procedures with the relevant administrative authorities in charge of environmental protection, health and safety have been completed. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and waste. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and such liability could exceed our insurance coverage. We also could incur significant costs associated with civil or criminal fines and penalties.

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

In addition, we may be required to incur substantial costs to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development, manufacturing or commercialization efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Our information technology systems, or those used by our contractors or collaborators, may fail or suffer security breaches, which could result in a material disruption of our product development and commercialization efforts.

Despite the implementation of security measures, our information technology systems and those of our contractors and collaborators, are vulnerable to damage from internal or external events, such as computer viruses, unauthorized access, natural disasters, terrorism, war, and telecommunication and electrical failures, which can compromise the confidentiality, integrity and availability of the systems. Although to our knowledge we have not experienced any material system failure or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our research, development, manufacturing, regulatory and commercialization efforts and our business operations.

In the ordinary course of our business, we collect and store sensitive data, including, among other things, legally protected patient health information, personally identifiable information about our employees, intellectual property, and proprietary business information. We manage and maintain our applications and data utilizing on-site systems and outsourced vendors. These applications and data encompass a wide variety of business-critical information, including research and development information, commercial information and business and financial information. Because information systems, networks and other technologies are critical to many of our operating activities, shutdowns or service disruptions at our company or vendors that provide information systems, networks, or other services to us pose increasing risks. Such disruptions may be caused by events such as computer hacking, phishing attacks, ransomware, dissemination of computer viruses, worms and other destructive or disruptive software, denial of service attacks and other malicious activity, as well as power outages, natural disasters (including extreme weather), terrorist attacks or other similar events. Such events could cause loss of data, damage to systems and data and leave us unable to utilize key business systems or access important data needed to operate our business. Our contractors and collaborators have and in the future may face similar risks, and service disruptions or security breaches of their systems could adversely affect our security, leave us without access to important systems, products, raw materials, components, services or information or expose our confidential data. In addition, system redundancy may be ineffective or inadequate, and our disaster recovery planning may not be sufficient to cover all eventualities. Significant events could result in a disruption of our operations, damage to our reputation or a loss of revenues. In addition, we may not have adequate insurance coverage to compensate for any losses associated with such events.

We could be subject to risks caused by misappropriation, misuse, leakage, falsification or intentional or accidental release or loss of information maintained in the information systems and networks of our company and our vendors, including personal information of our employees and patients, and company and vendor confidential data. In addition, outside parties may attempt to penetrate our systems or those of our vendors or fraudulently induce our personnel or the personnel of our vendors to disclose sensitive information in order to gain access to our data and/or systems. Like other companies, we and our third-party vendors have on occasion experienced, and will continue to experience, threats to our or their data and systems, including malicious codes and viruses, phishing, business email compromise attacks, ransomware, or other cyber-attacks. The number and complexity of these threats continue to increase over time. If a material breach of our information technology systems or those of our vendors occurs, we could be required to expend significant amounts of money and other resources to respond to these threats or breaches and to repair or replace information systems or networks and could suffer financial loss or the loss of valuable confidential information. In addition, we could be subject to regulatory actions and/or claims made by individuals and groups in private litigation involving privacy issues related to data collection and use practices and other data privacy laws and regulations, including claims for misuse or inappropriate disclosure of data, as well as unfair or deceptive practices. Although we develop and maintain systems and controls designed to prevent these events from occurring, and we have processes to identify and mitigate threats, the development and maintenance of these systems, controls and processes is costly and requires ongoing monitoring and updating as technologies change and efforts to overcome security measures become increasingly sophisticated. Moreover, despite our efforts, the possibility of these events occurring cannot be eliminated entirely. As we outsource more of our information systems to vendors, engage in more electronic transactions with payors and patients, and rely more on cloud-based information systems, the related security risks will increase and we will need to expend additional resources to protect our technology and information systems. In addition, there can be no assurance that our internal information technology systems or those of our contractors and collaborators, as well as our and their efforts to implement adequate security and control measures, will be sufficient to protect us against breakdowns, service disruptions, data deterioration or loss in the event of a system malfunction, or prevent data from being stolen or corrupted in the event of a cyberattack, security breach, ransomware, industrial espionage attack or insider threat attack that could adversely affect our business and operations and/or result in the loss or exposure of critical, proprietary, private, confidential or otherwise sensitive data, which could result in financial, legal, business or reputational harm to us.

Our failure to comply with data protection laws and regulations could lead to government enforcement actions and significant penalties against us, and adversely impact our operating results.

In the United States, Europe, China, and many other jurisdictions where we operate, we are subject to laws and regulations that address privacy, personal information protection and data security at both the federal and State levels. Numerous laws and regulations, including, without limitation, privacy laws (such as the European Union's General Data Protection Regulation ("GDPR") or similar laws), security breach notification laws (such as Australia's amendment to the Privacy Act), health information privacy laws (such as the United States' Health Insurance Portability and Accountability Act ("HIPAA") and the Human Genetic Resources Administration of China's rules), and consumer protection laws (such as the United States' Federal Trade Commission's unfair or deceptive practices rules or California's Consumer Privacy Act and California's Privacy Rights Act), govern the collection, use, disclosure and protection of health-related and other personal information. A subset of these laws also have strict requirements governing the cross-border transmission of personal information (see —"*Compliance with the Data Security Law of the People's Republic of China (the "Data Security Law"), Cybersecurity Review Measures, Personal Information Protection Law of the People's Republic of China (the "PIPL"), regulations and guidelines relating to the multi-*

level protection scheme (the "MLPS") and any other future laws and regulations may entail significant expenses and could materially affect our business.").

The legal and regulatory landscape around data privacy is rapidly changing with countries and states passing new laws and regulations every year. Tracking and complying with these laws and regulations requires significant time and expenses and could materially affect our business. By way of example and without limitation, these laws may require updating of contracts, informed consent forms, clinical trial protocols and privacy notices; changes to company procedures; limiting what personal information we collect, who has access to it and how/where we use it; performing internal assessments; changes to the security and hosting solution of our systems; specific reporting and remediation efforts in the event of a data breach; and even opening our business up for external assessments by government bodies.

Given the variability and evolving state of these laws, we face uncertainty as to the exact interpretation of the new requirements, and we may face challenges in implementing all measures required by regulators or courts in their interpretation. Additionally, we may experience a reportable data breach (see —"*Our information technology systems, or those used by our contractors or collaborators, may fail or suffer security breaches, which could result in a material disruption of our product development and commercialization efforts*"). Any failure or perceived failure by us to comply with applicable laws and regulations could subject us to significant administrative, civil or criminal fines or other penalties and negatively impact our reputation. For severe violations, in some countries these laws even allow courts and government agencies to delay or halt transfer of personal information, require deletion of personal information, or even order we stop collection of personal information in that country. All of these could materially harm our business, prospects, and financial condition or even disrupt our operations.

These laws apply not just to us, but also to those vendors working on our behalf, as well as our business partners. Any actual or perceived failure of them to comply with these laws and regulations could impact the services they provide to us, our collaborations with them and our reputation; additionally, there is a risk of liability flowing to us under certain contractual and/or legal conditions.

Compliance with the Data Security Law of the People's Republic of China (the "Data Security Law"), Cybersecurity Review Measures, Personal Information Protection Law of the People's Republic of China (the "PIPL"), regulations and guidelines relating to the multi-level protection scheme (the "MLPS") and any other future laws and regulations may entail significant expenses and could materially affect our business.

China has implemented extensive data protection, privacy and information security rules and is considering a number of additional proposals relating to these subject areas. We face significant uncertainties and risks related to these laws, regulations and policies, some of which were only recently enacted, and the interpretation of these legal requirements by government regulators as applied to biotechnology companies like us. For example, we do not maintain, nor do we intend to maintain in the future, personally identifiable health information of patients in China. We do, however, collect and maintain de-identified or pseudonymized health data for clinical trials in compliance with local regulations. This data could be deemed "personal data" or "important data" by government regulators. With China's growing emphasis of its sovereignty over data derived from China, the outbound transmission of de-identified or pseudonymized health data for clinical trials may be subject to the new national security legal regime, including the Data Security Law, the Cyber Security Law of the People's Republic of China (the "Cyber Security Law"), the PIPL, and various implementing regulations and standards.

China's Data Security Law provides that the data processing activities must be conducted based on "data classification and hierarchical protection system" for the purpose of data protection and prohibits entities in China from transferring data stored in China to foreign law enforcement agencies or judicial authorities without prior approval by the relevant PRC authority. The classification of data is based on its importance in economic and social development, as well as the degree of harm expected to be caused to national security, public interests, or the legitimate rights and interests of individuals or organizations if such data is tampered with, destroyed, leaked, or illegally acquired or used.

The Cyber Security Law requires companies to take certain measures to ensure the security of their networks and data stored on their networks. Specifically, the Cyber Security Law provides that companies adopt an MLPS, under which network operators are required to perform obligations of security protection to ensure that the network is free from interference, disruption or unauthorized access, and prevent network data from being disclosed, stolen or tampered. The CAC released draft amendments to the Cyber Security Law in September 2022, which propose to impose more stringent legal liabilities for violations. Under the MLPS, entities operating information systems must have a thorough assessment of the risks and the conditions of their information and network systems to determine the level to which the entity's information and network systems belong, from the lowest Level 1 to the highest Level 5 pursuant to a series of national standards on the grading and implementation of the classified protection of cybersecurity. The grading result will determine the set of security protection obligations that entities must comply with and when relevant government authority examination and approval is required.

Under the Cyber Security Law and Data Security Law, we are required to establish and maintain a comprehensive data and network security management system that will enable us to monitor and respond appropriately to data security and network security risks. We are obligated to notify affected individuals and appropriate Chinese regulators of and respond to any data security and network security incidents. Establishing and maintaining such systems takes substantial time, effort and cost, and we may not be able to establish and maintain such systems as fully as needed to ensure compliance with our legal obligations. Despite our investment, such systems may not adequately protect us or enable us to appropriately respond to or mitigate all data security and network security risks or incidents we may face.

Furthermore, under the Data Security Law, data categorized as "important data," which will be determined by governmental authorities in the form of catalogs, is to be processed and handled with a higher level of protection. The notion of important data is not clearly defined by the Cyber Security Law or the Data Security Law. In order to comply with the statutory requirements, we will need to determine whether we possess important data, monitor the important data catalogs that are expected to be published by local governments and departments, perform risk assessments and ensure we are complying with reporting obligations to applicable regulators. We may also be required to disclose to regulators business sensitive or network security-sensitive details regarding our processing of important data and may need to pass the government security review or obtain government approval in order to share important data with offshore recipients, which can include foreign licensors, or share data stored in mainland China with judicial and law enforcement authorities outside of mainland China. If judicial and law enforcement authorities outside mainland China require us to provide data stored in mainland China, and we are not able to pass any required government security review or obtain any required government approval to do so, we may not be able to meet the foreign authorities' requirements. The potential conflicts in legal obligations could have adverse impacts on our operations in and outside of mainland China. PRC regulatory authorities have also enhanced the supervision and regulation of cross-border data transmission. The Data Security Law prohibits entities and individuals in China from providing any foreign judicial or law enforcement authority with any data stored in China without approval from competent PRC authority, and sets forth the legal liabilities of entities and individuals found to be in violation of their data protection obligations, including rectification order, warning, fines, suspension of relevant business, and revocation of business permits or licenses. Moreover, the CAC promulgated the Measures for the Security Assessment of Cross-border Data Transmission, which became effective as of September 1, 2022. According to these measures, personal data processors are subject to security assessment prior to any cross-border transfer of data if the transfer involves (i) important data; (ii) personal information transferred overseas by operators of critical information infrastructure or a data processor that has processed personal data of more than one million persons; (iii) personal information transferred overseas by a data processor who has already provided personal data of 100,000 persons or sensitive personal data of 10,000 persons overseas since January 1 of last year; or (iv) other circumstances as requested by the CAC. Any cross-border data transfer activities conducted in violation of the Measures for the Security Assessment of Cross-border Data Transmission before the effectiveness of these measures are required to be rectified by March 2023. Though these measures have already taken effect, substantial uncertainties still exist with respect to the interpretation and implementation of these measures in practice and how they will affect our business operation.

The CAC has taken action against several Chinese internet companies listed on U.S. securities exchanges for alleged national security risks and improper collection and use of the personal information of Chinese data subjects. According to the official announcement, the action was initiated based on the National Security Law of the People's Republic of China (the "National Security Law"), the Cyber Security Law and the Cybersecurity Review Measures. Effective February 15, 2022, the CAC, together with 12 other PRC governmental authorities, promulgated the Revised Cybersecurity Review Measures, pursuant to which critical information infrastructure operators procuring network products and services and online platform operators carrying out data processing activities, which affect or may affect national security, shall conduct a cybersecurity review. In addition, online platform operators possessing personal information of more than one million users seeking to be listed on foreign stock markets must apply for a cybersecurity review. The relevant competent governmental authorities may also initiate a cybersecurity review against the relevant operators if the authorities believe that the network product or service or data processing activities of such operators affect or may affect national security. There are still uncertainties as to the exact scope of network product or service or data processing activities that will or may affect national security, and the PRC government authorities may have discretion in the interpretation and enforcement of these measures.

Additionally, the CAC published the draft Administrative Regulations on Cyber Data Security ("Draft Cyber Data Security Regulations"), pursuant to which data processors shall apply for cybersecurity review if they engage in (i) merger, reorganization or division of internet platform operators with significant data resources related to national security, economic development or public interests that affects or may affect national security; (ii) overseas listing while processing over one million users' personal information; (iii) Hong Kong listing that affects or may affect national security; or (iv) other data processing activities that affect or may affect national security. The Draft Cyber Data Security Regulations further require data processors processing important data or going public overseas to conduct annual data security self-assessment and submit an assessment report to the CAC before January 31 each year. As the Draft Cyber Data Security Regulations were released only for public comment, the final version and the effective date thereof may be subject to change with substantial uncertainty.

It is unclear how widespread the cybersecurity review requirement and the enforcement action will be and what effect they will have on the life sciences sector generally and the Company in particular. China's regulators may impose penalties for non-compliance ranging from fines or suspension of operations, and the imposition of any such penalties on our business could cause a material adverse effect on our business, financial condition, results of operations, prospects and the trading price of our ordinary shares, ADSs and RMB Shares, and could lead to our delisting from the Nasdaq. As of the date of this report, we have not received any notice from any Chinese regulatory authority identifying us as a "critical information infrastructure operator," "online platform operator" or "data processor," or requiring us to go through the cybersecurity review procedures pursuant to the Revised Cybersecurity Review Measures and the Draft Cyber Data Security Regulations. However, there remains uncertainty as to how the regulations if enacted as currently proposed, will be interpreted or implemented and whether the Chinese regulatory authorities will adopt additional regulations. We intend to closely monitor the evolving laws and regulations in this area and take all reasonable measures to mitigate compliance risks, we cannot guarantee that our business and operations will not be adversely affected by the potential impact of the Revised Cybersecurity Review Measures, the Draft Cyber Data Security Regulations or other laws and regulations related to privacy, data protection and information security.

Additionally, the Standing Committee of the National People's Congress of the PRC promulgated the PIPL, which expands data protection compliance obligations to cover the processing of personal information of persons by organizations and individuals in China, and the processing of personal information of persons in China outside of China if such processing is for purposes of providing products and services to, or analyzing and evaluating the behavior of, persons in China. The PIPL also provides that critical information infrastructure operators and personal information processing entities that process personal information meeting a volume threshold are also required to store in China personal information generated or collected in China, and to pass a security assessment for any export of such personal information. Lastly, the PIPL contains proposals for significant fines for serious violations of up to RMB50 million, or 5% of annual revenues from the prior year, and penalties, including that companies found to have violated the PIPL may be ordered to suspend any related activity.

Interpretation, application and enforcement of these laws, rules and regulations evolve from time to time and their scope may continually change, through new legislation, amendments to existing legislation or changes in enforcement. Compliance with the Cyber Security Law, the Data Security Law and the PIPL could significantly increase the cost to us of providing our service offerings, require significant changes to our operations or even prevent us from providing certain service offerings in jurisdictions in which we currently operate or in which we may operate in the future. Despite our efforts to comply with applicable laws, regulations and other obligations relating to privacy, data protection and information security, it is possible that our practices, offerings or platform could fail to meet all of the requirements imposed by the Cyber Security Law, the Data Security Law and/or related implementing regulations. Any failure on our part to comply with such law or regulation, or any compromise of security that results in unauthorized access, use or release of personally identifiable information or other data, or the perception or allegation that any of the foregoing types of failure or compromise has occurred, could damage our reputation, discourage new and existing counterparties from contracting with us or result in investigations, fines, suspension or other penalties by Chinese government authorities and private claims or litigation, any of which could materially adversely affect our business, financial condition and results of operations. Even if our practices are not subject to legal challenge, the perception of privacy concerns, whether or not valid, may harm our reputation and adversely affect our business, financial condition and results of operations. Moreover, the legal uncertainty created by the Data Security Law and the recent Chinese government actions could materially adversely affect our ability, on favorable terms, to raise capital in the U.S. and other markets in the future.

If we or parties on whom we rely fail to maintain the necessary licenses for the development, manufacture, sale and distribution of our products, our ability to conduct our business could be materially impaired.

We are required to obtain, maintain and renew various permits, licenses and certificates to develop, manufacture, promote and sell our products. Third parties, such as distributors, third-party promoters and third-party manufacturers, on whom we may rely to develop, manufacture, promote, sell and distribute our products may be subject to similar requirements. We and third parties on whom we rely may be also subject to regular inspections, examinations, inquiries or audits by the regulatory authorities, and an adverse outcome of such inspections, examinations, inquiries or audits may result in the loss or non-renewal of the relevant permits, licenses and certificates. Moreover, the criteria used in reviewing applications for, or renewals of permits, licenses and certificates may change from time to time, and there can be no assurance that we or the parties on whom we rely will be able to meet new criteria that may be imposed to obtain or renew the necessary permits, licenses and certificates. Many of such permits, licenses and certificates are material to the operation of our business, and if we or parties on whom we rely fail to maintain or renew material permits, licenses and certificates, our ability to conduct our business could be materially impaired. Furthermore, if the interpretation or implementation of existing laws and regulations change, or new regulations come into effect, requiring us or parties on whom we rely to obtain any additional permits, licenses or certificates that were previously not required to operate our business, there can be no assurance that we or parties on whom we rely will successfully obtain such permits, licenses or certificates.

Our financial and operating performance may be adversely affected by public health crises, natural catastrophes, or other disasters outside of our control.

Our global operations and those of our third-party contractors and collaborators expose us to natural or man-made disasters, such as earthquakes, hurricanes, floods, fires, explosions, public health crises, such as epidemics or pandemics, terrorist activity, wars, or other business interruptions outside of our control. Furthermore, we do not maintain any insurance other than property insurance for some of our buildings, vehicles and equipment. Accordingly, unexpected business interruptions resulting from disasters could disrupt our operations and thereby result in substantial costs and diversion of resources. For example, our Guangzhou manufacturing facility was hit by a typhoon in 2019 and although the typhoon did not cause material damage to the facility, the boundary area and the adjacent land were flooded, causing a power outage for a few days. Afterwards, we built a gutter along the boundary and installed waterproof electricity cables to fortify the facility and to help prevent future interruptions. A significant disruption at either our Guangzhou or Suzhou manufacturing facilities, even on a short-term basis, could impair our ability to timely produce products, which could have a material adverse effect on our business, financial position and results of operations.

Our production process requires a continuous supply of electricity. We have encountered power shortages historically in China due to restricted power supply to industrial users during summers when the usage of electricity is high and supply is limited or as a result of damage to the electricity supply network. Because the duration of those power shortages was brief, they had no material impact on our operations. Longer interruptions of electricity supply could result in lengthy production shutdowns, increased costs associated with restarting production and the loss of production in progress. Any major suspension or termination of electricity or other unexpected business interruptions could have a material adverse impact on our business, financial condition and results of operations.

We also rely in part on third-party manufacturers to produce and process our medicines and drug candidates. Our ability to obtain supplies of our medicines and drug candidates could be disrupted if the operations of these suppliers are affected by man-made or natural disasters, public health epidemics or other business interruptions which could cause us to delay or cease development or commercialization of some or all of our medicines and drug candidates. In addition, we partially rely on our third-party research institution collaborators for conducting research and development of our drug candidates, and they may be affected by such business interruptions, government shutdowns or withdrawn funding. For example, the ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, the ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies may also slow the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

In particular, the COVID-19 pandemic has impacted and could continue to negatively impact our business and our financial performance, including causing a delay in or the inability of health authorities to complete regulatory inspections of our development activities, regulatory filings or manufacturing operations. Our clinical development and commercial efforts could be delayed or otherwise negatively impacted, as patients may be reluctant to go to the hospitals to receive treatment, or our regulatory inspections or regulatory filings and approvals could be delayed. We have already experienced delays in clinical trial recruitment. Additionally, the commercial or clinical supply of our medicines and drug candidates could be negatively impacted due to reduced operations or a shutdown of our or our third-party manufacturing facilities, distribution channels and transportation systems, or shortages of raw materials and drug product.

In addition, the COVID-19 pandemic resulted in significant governmental measures being implemented to control the spread of the virus, including quarantines, travel restrictions, social distancing and business shutdowns. The extent to which such measures are removed or new measures are put in place will depend upon how the pandemic evolves, as well as the distribution of available vaccines, the rates at which they are administered and the emergence of new variants of the virus. As needed, we have taken precautionary measures intended to help minimize the risk of the virus to our employees, including temporarily requiring many employees to work remotely or suspending or limiting non-essential travel worldwide for our employees. These measures could negatively affect our business. For instance, temporarily requiring all employees to work remotely may induce absenteeism or employee turnover, disrupt our operations or increase the risk of a cybersecurity incident. COVID-19 has also caused volatility in the global financial markets and threatened a slowdown in the global economy, which may negatively affect our business, results of operations, and financial condition. The extent to which the COVID-19 pandemic may continue to impact our business will depend on future developments, which are highly uncertain, such as the duration of

the pandemic, the severity of COVID-19, including the continued emergence of new variants, developments or perceptions regarding the safety of vaccines, or any additional preventative and protective actions taken to contain the pandemic or treat its impact. Any resulting financial impact cannot be reasonably estimated at this time and may have a material adverse impact on our business, financial condition and results of operations.

Climate change manifesting as physical or transition risks, included related environmental regulation, could have a material adverse impact on our business operations, clients and customers.

The long-term effects of climate change are difficult to assess and predict. Our business and the activities of our clients and customers could be impacted by climate change. Climate change could manifest as a financial risk either through changes in the physical climate or from the process of transitioning to a low-carbon economy, including related environmental regulation of companies with respect to risks posed by climate change.

The physical impacts of climate change may include physical risks (such as rising sea levels or frequency and severity of extreme weather conditions), social and human effects (such as population dislocations or harm to health and well-being), compliance costs and transition risks (such as regulatory or technology changes) and other adverse effects. The effects could impair, for example, the availability and cost of certain products, commodities and energy (including utilities), which in turn may impact our ability to procure goods or services required for the operation of our business at the quantities and levels we require. Furthermore, related environmental regulation as a response to climate change could result in additional costs in the form of taxes and investments of capital to maintain complacent with such laws. We bear losses incurred as a result of, for example, physical damage to or destruction of our facilities, loss or spoilage of inventory, and business interruption due to weather events that may be attributable to climate change and could materially adversely affect our business operations, financial position or results of operation.

Product liability claims or lawsuits could cause us to incur substantial liabilities.

We face an inherent risk of product liability as a result of the commercialization of our medicines in the United States, China, Europe and other markets, and for the clinical testing and any future commercialization of our drug candidates globally. For example, we may be sued if our medicines or drug candidates cause or are perceived to cause injury or are found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the medicine, negligence, strict liability or a breach of warranties. Claims could also be asserted under applicable consumer protection acts. If we cannot successfully defend ourselves against or obtain indemnification from our collaborators for product liability claims, we may incur substantial liabilities or be required to limit commercialization of our medicines and drug candidates. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in: decreased demand for our medicines; injury to our reputation; withdrawal of clinical trial participants and inability to continue clinical trials; initiation of investigations by regulators; costs to defend the related litigation; a diversion of our management's time and resources; substantial monetary awards to trial participants or patients; product recalls, withdrawals or labeling, marketing or promotional restrictions; loss of revenue; exhaustion of any available insurance and our capital resources; the inability to commercialize any medicine or drug candidate; and a decline in our share price.

Our inability to obtain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of our medicines and drug candidates. Although we currently hold product liability coverage which we believe to be sufficient in light of our current products and clinical programs, the amount of such insurance coverage may not be adequate, and we may be unable to maintain such insurance at a reasonable cost or in an amount adequate to satisfy any liability that may arise, or we may not be able to obtain additional or replacement insurance at a reasonable cost, if at all. Our insurance policies may also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Even if our agreements with any future collaborators entitle us to indemnification against losses, such indemnification may not be available or adequate should any claim arise.

We are subject to the risks and challenges of doing business globally, which may adversely affect our business operations.

Our business is subject to risks and challenges associated with doing business globally. Accordingly, our business and financial results could be adversely affected due to a variety of factors, including: changes in a specific country's or region's political and cultural climate or economic condition; unexpected changes in laws and regulatory requirements in local jurisdictions; challenges in replicating or adapting our company policies and procedures to operating environments different from that of the United States; difficulty of effective enforcement of contractual provisions in local jurisdictions; inadequate intellectual property protection in certain countries; enforcement of anti-corruption and anti-bribery laws, such as the FCPA; trade-protection measures or disputes, import or export licensing requirements, and fines, penalties or suspension or revocation

of export privileges; laws and regulations on foreign investment in the United States under the jurisdiction of the CFIUS and other agencies; the effects of applicable local tax regimes and potentially adverse tax consequences; the impact of public health epidemics on employees, our operations and the global economy; restrictions on international travel and commerce; and significant adverse changes in local currency exchange rates. In addition, in 2017 the United Kingdom Financial Conduct Authority ("UKFCA"), which regulates the London Interbank Offered Rate ("LIBOR"), announced that it will no longer require banks to submit rates for the calculation of LIBOR to the LIBOR administrator after 2021. On November 30, 2020, the UKFCA announced a partial extension of this deadline, indicating its intention to cease the publication of the one-week and two-month USD LIBOR settings immediately following December 31, 2021, and the remaining USD LIBOR settings immediately following the LIBOR publication on June 30, 2023. While various replacement reference rates have been proposed, an alternative reference rate to LIBOR has not yet been widely adopted. As such, the replacement of LIBOR could have an adverse effect on the market for, or value of, LIBOR-linked financial instruments. Failure to manage these risks and challenges could negatively affect our ability to expand our businesses and operations as well as materially and adversely affect our business, financial condition and results of operations.

Future operating results could be negatively affected by changes in tax rates, the adoption of new tax legislation in the jurisdictions in which we operate, or exposure to additional tax liabilities.

The nature of our international operations subjects us to local, state, regional and national tax laws in jurisdictions around the world. Our future tax expense could be affected by changes in the mix of earnings in countries with differing statutory tax rates, changes in the valuation of deferred tax assets and liabilities or changes in tax laws or their interpretation. Additionally, tax rules governing cross-border activities are continually subject to modification intended to address concerns over base erosion and profit shifting (BEPS) and other perceived international tax avoidance techniques as a result of both coordinated actions by governments, such as the OECD/G20 Inclusive Framework on BEPS, and unilateral measures designed by individual countries. For example, the Cayman Islands has enacted the International Tax Co-operation (Economic Substance) Law (2020 Revision) (the “Economic Substance Law”), which originally took effect on January 1, 2019, and which is accompanied by Guidance on Economic Substance for Geographically Mobile Activities (Version 2.0; April 30, 2019) published by the Cayman Islands Tax Information Authority. The Economic Substance Law embraces a global initiative to combat BEPS and demonstrates the continued commitment of the Cayman Islands to international best practice. The Economic Substance Law provides that relevant entities that existed before January 1, 2019 and that had been conducting relevant activities by that date must comply with the economic substance requirements from July 1, 2019, and relevant entities that are established from January 1, 2019 onwards must comply with the requirements from the date they commence the relevant activity. Although we believe that we currently are not obliged to meet the economic substance requirements under the Economic Substance Law, we cannot predict any changes to the legislation or its interpretation in the future. If we are obliged to meet certain economic substance requirements in the future, our business and results of operations could be negatively impacted if we are required to make changes to our business in order to gain compliance or if we fail to comply.

We have received tax rulings from various governments that have jurisdictional authority over our operations. If we are unable to meet the requirements of such agreements, or if they expire or are renewed on less favorable terms, the result could negatively impact our future earnings. Additionally, the European Commission has opened formal investigations into specific tax rulings granted by several countries to specific taxpayers. While we believe that our rulings are consistent with accepted tax ruling practices, the ultimate resolution of such activities cannot be predicted and could also have an adverse impact on future operating results.

Risks Related to Our Doing Business in the PRC

Changes in the political and economic policies of the PRC government or in relations between China and the United States or other governments and the significant oversight and discretion the PRC government has over the conduct of the business operations of our PRC subsidiaries may materially and adversely affect our business, financial condition, and results of operations and may result in our inability to sustain our growth and expansion strategies.

Due to our operations in China, our business, results of operations, financial condition and prospects may be influenced to a significant degree by economic, political, legal and social conditions in the PRC or changes in government relations between China and the United States or other governments. There is significant uncertainty about the future relationship between the United States and China with respect to trade policies, treaties, government regulations and tariffs. China’s economy differs from the economies of other countries in many respects, including with respect to the level of development, growth rate, amount of government involvement, control of foreign exchange and allocation of resources. While China's economy has experienced significant growth over the past four decades, growth has been uneven across different regions and among various economic sectors. The Chinese government has implemented various measures to encourage economic development and guide the allocation of resources. Some of these measures may benefit the overall Chinese economy, but may have a negative effect on us. For example, our financial condition and results of operations may be adversely affected by government control over

capital investments or changes in tax regulations that are currently applicable to us. In addition, in the past the Chinese government implemented certain measures, including interest rate increases, to manage the pace of economic growth and prevent the economy from overheating. These measures may cause decreased economic activity in China, which may adversely affect our business and results of operations.

The PRC government has the ability to exert substantial control over any offering of securities conducted overseas and/or foreign investment in China-based issuers, and, as a result, may limit or completely hinder our ability to offer or continue to offer securities to investors, and may cause the value of such securities to significantly decline or be worthless.

The PRC government has recently indicated its intent to exert more oversight and control over securities offerings and other capital markets activities that are conducted overseas and foreign investment in China-based companies. If the PRC authorities attempt to exercise such control or influence through regulation over our PRC subsidiaries, we could be required to restructure our operations to comply with such regulations or potentially cease operations in the PRC entirely, which could adversely affect our business, results of operations and financial condition. Any such action, once taken by the PRC government, could significantly limit or completely hinder our ability to offer or continue to offer securities to investors and cause the value of such securities to significantly decline or in extreme cases, become worthless.

For example, the PRC government recently initiated a series of regulatory actions and statements to regulate business operations in China, including cracking down on illegal activities in the securities market, enhancing supervision over China-based companies listed overseas using the variable interest entity structure, adopting new measures to extend the scope of cybersecurity reviews, and expanding the efforts in anti-monopoly enforcement. For example, in July 2021, the relevant PRC government authorities made public the Opinions on Intensifying Crack Down on Illegal Securities Activities (the "Securities Opinions"), which emphasized the need to strengthen the administration over illegal securities activities and the supervision on overseas listings by China-based companies and proposed to take effective measures, such as promoting the construction of relevant regulatory systems to deal with the risks and incidents faced by China-based overseas listed companies.

Furthermore, in July 2021, the PRC government provided guidance on China-based companies raising capital outside of China, including through arrangements called variable interest entities ("VIEs"). In light of such developments, the SEC has imposed enhanced disclosure requirements on China-based companies seeking to register securities with the SEC. Most recently, on February 17, 2023, the CSRC released the Overseas Listing Trial Measures and five relevant guidelines which will take effect from March 31, 2023. According to the Overseas Listing Trial Measures, where Chinese companies that have directly or indirectly listed securities in overseas markets conduct follow-on offering of equity securities in such overseas markets, they shall fulfill the filing procedures with and report relevant information to the CSRC. As the Overseas Listing Trial Measures have just been promulgated, there are substantial uncertainties as to its interpretation and implementation. We cannot assure you that we would not be deemed as an indirect overseas listed Chinese company under the Overseas Listing Trial Measures. If we are deemed as an indirect overseas listed Chinese company but fail to complete the filing procedures with the CSRC for any of our follow-on offerings or follow relevant reporting requirements thereunder, we may be subject to penalties, sanctions and fines imposed by the CSRC and relevant departments of the State Council. See also “Item 1. Business – Government Regulation – PRC Regulation – Regulations Relating to Overseas Listing”. We are currently evaluating the implications and potential impact of the Overseas Listing Trial Measures and will continue to closely monitor the interpretation and implementation of the Overseas Listing Trial Measures. Due to our operations in China and stock listings in and outside of China, the Overseas Listing Trial Measures and any future PRC, U.S. or other rules and regulations that place restrictions on capital raising could adversely affect our business and results of operations and could significantly limit or completely hinder our ability to offer or continue to offer our ADSs or ordinary shares to investors, and could cause the value of our ADSs or ordinary shares to significantly decline or become worthless.

On February 24, 2023, the CSRC and other PRC governmental authorities jointly issued the revised Provisions on Strengthening Confidentiality and Archives Administration of Overseas Securities Offering and Listing by Domestic Companies (the “Revised Confidentiality Provisions”), which will come into effect on March 31, 2023. According to the Revised Confidentiality Provisions, Chinese companies that directly or indirectly conduct overseas offerings and listings, shall strictly abide by the laws and regulations on confidentiality when providing or publicly disclosing, either directly or through their overseas listed entities, materials to securities services providers. In the event such materials contain state secrets or working secrets of government agencies, the Chinese companies shall first obtain approval from authorities, and file with the secrecy administrative department at the same level with the approving authority; in the event that such materials, if divulged, will jeopardize national security or public interest, the Chinese companies shall comply with procedures stipulated by national regulations. The Chinese companies shall also provide a written statement of the specific sensitive information provided when providing materials to securities service providers, and such written statements shall be retained for inspection. As the Revised Confidentiality Provisions were recently promulgated and has not taken effect, their interpretation and implementation remain substantially uncertain.

Currently, these statements and regulatory actions have had no impact on our daily business operations, the ability to accept foreign investments and list our securities on a U.S. or other foreign exchange. However, since these statements and regulatory actions are new, it is highly uncertain how the legislative or administrative regulation making bodies will further respond and what existing or new laws or regulations or detailed implementations and interpretations will be further modified or promulgated, if any, and the potential impact such modified or new laws and regulations will have on our daily business operations, the ability to accept foreign investments and list our securities on a U.S., Hong Kong, or other stock exchanges. There are still substantial uncertainties as to how PRC governmental authorities will regulate overseas listing in practice and whether we are required to obtain any specific regulatory approvals from the CSRC, CAC or any other PRC governmental authorities for our offshore offerings. If the CSRC, CAC or other regulatory agencies later promulgate new rules or explanations requiring that we obtain their approvals for our future offshore offerings, we may be unable to obtain such approvals in a timely manner, or at all, and such approvals may be rescinded even if obtained. Any such circumstance could significantly limit or completely hinder our ability to continue to offer securities to investors and cause the value of such securities to significantly decline or be worthless. In addition, implementation of industry-wide regulations directly targeting our operations could cause the value of our securities to significantly decline. Therefore, investors of our company face potential uncertainty from actions taken by the PRC government affecting our business.

The audit reports included in our previous annual reports on Form 10-K filed with the SEC have historically been prepared by auditors who are not inspected fully by the Public Company Accounting Oversight Board (the "PCAOB"), and as such, investors have previously been deprived of the benefits of such inspections.

Ernst & Young Hua Ming LLP, our auditor from fiscal year 2014 to fiscal year 2021, is required to undergo regular inspections by the PCAOB as an auditor of companies that are publicly traded in the United States and a firm registered with the PCAOB. Since Ernst & Young Hua Ming LLP is located in China, a jurisdiction where the PCAOB had been unable to conduct inspections without the approval of the Chinese authorities, Ernst & Young Hua Ming LLP has not been and is not currently inspected by the PCAOB. Additionally, because we have substantial operations within the PRC, a jurisdiction where the PCAOB was previously unable to conduct inspections without the approval of the Chinese government authorities, Ernst & Young Hua Ming LLP and the audit work that it has carried out for us in the PRC has not historically been able to be inspected independently and fully by the PCAOB.

Inspections of other auditors conducted by the PCAOB outside the PRC have at times identified deficiencies in those auditors' audit procedures and quality control procedures, which may be addressed as part of the inspection process to improve future audit quality. The lack of PCAOB inspections of audit work undertaken in the PRC prevents the PCAOB from regularly evaluating auditors' audits and their quality control procedures. As a result, to the extent that any components of our auditor's work papers had been located in China, such work papers had not been subject to inspection by the PCAOB. As a result, we and investors of our ADSs, ordinary shares and RMB Shares had been deprived of the benefits of such PCAOB inspections, which could cause investors and potential investors of our securities to lose confidence in our audit procedures and reported financial information and the quality of our financial statements.

Our ADSs may be delisted and our ADSs and ordinary shares prohibited from trading in the over-the-counter market to the extent the Holding Foreign Companies Accountable Act is further revised or similar legislation is enacted. The delisting of our ADSs, or the threat of their being delisted, may materially and adversely affect the value of your investment.

As part of a continued regulatory focus in the United States on access to audit and other information currently protected by national law, in particular China's, the Holding Foreign Companies Accountable Act ("HFCAA"), was signed into law in December 2020. The HFCAA states if the SEC determines that we have filed audit reports issued by a registered public accounting firm that has not been subject to inspection by the PCAOB for three consecutive years beginning in 2021, the SEC shall prohibit securities from being traded on a national securities exchange or in the over-the-counter trading market in the U.S. On March 30, 2022, as expected following its adoption of implementing rules pursuant to the HFCAA, the SEC added us to its conclusive list of issuers identified under HFCAA, after being provisionally named as a Commission-Identified Issuer on March 8, 2022, following the filing of our annual report on Form 10-K, which annual report was audited by Ernst & Young Hua Ming LLP. In December 2022, the Accelerating Holding Foreign Companies Accountable Act ("AHFCAA") was signed into law, which amended the HFCAA to shorten the three-year period to two years.

However, as our global business has expanded, we built substantial organizational capabilities outside of the PRC and we have evaluated, designed and implemented business processes and control changes which has enabled us to engage Ernst & Young LLP, located in Boston, Massachusetts, United States, as our independent registered public accounting firm for the audits of our financial statements and internal control over financial reporting for the fiscal year ending December 31, 2022. We expect that this will satisfy the PCAOB inspection requirements for the audit of our consolidated financial statements, subject to compliance with SEC and other requirements prior to the two-year deadline of the AHFCAA.

On August 26, 2022, the PCAOB signed a Statement of Protocol with the CSRC and the Ministry of Finance of the People's Republic of China, for opening access for the PCAOB to inspect and investigate completely registered public accounting firms in mainland China and Hong Kong. The PCAOB staff members conducted on-site inspections and investigations from September to November 2022. In December 2022, the PCAOB announced that it has secured complete access to inspect and investigate registered public accounting firms headquartered in mainland China and Hong Kong and confirmed that until such time as the PCAOB issues any new determination, there are no Commission-identified Issuers at risk of having their securities subject to a trading prohibition under the HFCAA.

Given that Ernst and Young LLP (United States) now serves as the principal accountant to audit our consolidated financial statements, we expect to be able to comply with the HFCAA and AHFCAA and certify that we have retained a registered public accounting firm that the PCAOB has determined it is able to inspect or investigate, Ernst & Young LLP (United States), which would preclude a further finding by the SEC that we are a Commission-Identified Issuer and therefore the delisting of our ADSs from the Nasdaq Global Select Market.

Additionally, in October 2021, Nasdaq adopted additional listing criteria applicable to companies that primarily operate in jurisdictions where local regulators impose secrecy laws, national security laws or other laws that restrict U.S. regulators from accessing information relating to the issuer (a "Restrictive Market"). Under this rule, whether a jurisdiction permits PCAOB inspection would be a factor in determining whether a jurisdiction is deemed by Nasdaq to be a Restrictive Market. China will likely be determined to be a Restrictive Market and, as a result, Nasdaq may impose on us additional continued listing criteria or deny continued listing of our securities on Nasdaq, and we cannot assure you whether Nasdaq or regulatory authorities would apply additional and more stringent criteria to us after considering the effectiveness of our auditor's audit procedures and quality control procedures, adequacy of personnel and training, or sufficiency of resources, geographic reach or experience as it relates to our audit.

However, these efforts may not be sufficient and ultimately may not be successful. We may also be subject to enforcement under the HFCAA, the rules implementing the act that may be adopted by the SEC, and any other similar legislation that may be enacted into law or executive orders that may be adopted in the future. Although we are committed to complying with the rules and regulations applicable to listed companies in the United States, we are currently unable to predict the potential impact on our listed status by any rules that may be adopted by the SEC under the HFCAA in the future. If we failed to comply with those rules, it is possible that our ADSs would be delisted. The risk and uncertainty associated with a potential delisting would have a negative impact on the price of our ADSs, ordinary shares and RMB Shares. Delisting of our ADSs would force holders of our ADSs to sell their ADSs or convert them into our ordinary shares, which are listed for trading on the HKEx. Although our ordinary shares are listed in Hong Kong, investors may face difficulties in converting their ADSs into ordinary shares and migrating the ordinary shares to Hong Kong, or may have to incur increased costs or suffer losses in order to do so. Failure to adopt effective contingency plans may also have a material adverse impact on our business and the price of our ADSs, ordinary shares and RMB Shares.

Proceedings instituted by the SEC against five PRC-based accounting firms and any negative news about the proceedings against these audit firms, including Ernst & Young Hua Ming LLP, could adversely affect the market price of our ADSs, ordinary shares and/or RMB Shares.

In 2012, the SEC brought administrative proceedings against five accounting firms in China, including Ernst & Young Hua Ming LLP, alleging that they had refused to produce audit work papers and other documents related to certain other PRC-based companies under investigation by the SEC. In 2014, an initial administrative law decision was issued, censuring these accounting firms and suspending four of these firms from practicing before the SEC for a period of six months. In 2015, each of the four PRC-based accounting firms agreed to a censure and to pay a fine to the SEC to settle the dispute and avoid suspension of their ability to practice before the SEC. These firms' ability to continue to serve their clients was not affected by the settlement. The settlement required these firms to follow detailed procedures to seek to provide the SEC with access to Chinese firms' audit documents via the CSRC. If these firms do not follow these procedures, the SEC could impose penalties such as suspensions, or it could restart the administrative proceedings. Our audit committee has been aware of the policy restriction and communicated with Ernst & Young Hua Ming LLP to ensure compliance during the completion of our audits from fiscal year 2014 to fiscal year 2021. The settlement did not require these firms to admit to any violation of law and preserves these firms' legal defenses in the event the administrative proceeding is restarted. In the event that the SEC restarts the administrative proceedings, depending upon the final outcome, listed companies in the United States with major PRC operations may find it difficult or impossible to retain auditors in respect of their operations in the PRC, which could result in financial statements being determined to not be in compliance with the requirements of the Exchange Act, including possible delisting. Moreover, any negative news about the proceedings against these audit firms may cause investor uncertainty regarding PRC-based, U.S.-listed companies and the market price of the ADSs, ordinary shares and/or RMB Shares may be adversely affected. As discussed above, we have engaged Ernst & Young LLP, located in Boston, Massachusetts, United States, as our independent

registered public accounting firm for the audits of our financial statements and internal control over financial reporting for the fiscal year ending December 31, 2022 to be filed with the SEC.

There are uncertainties regarding the interpretation and enforcement of Chinese laws, rules and regulations.

A large portion of our operations are conducted in China through our Chinese subsidiaries. Our Chinese subsidiaries are subject to laws, rules and regulations applicable to foreign investment in China. The Chinese legal system is a civil law system based on written statutes. Unlike the common law system, prior court decisions may be cited for reference but have limited precedential value.

In 1979, the Chinese government began to promulgate a comprehensive system of laws, rules and regulations governing economic matters in general. The overall effect of legislation over the past four decades has significantly enhanced the protections afforded to various forms of foreign investment in China. However, China's legal system is still developing. The laws, rules and regulations are subject to interpretation and enforcement by PRC regulatory agencies and courts. In particular, because these laws, rules and regulations are relatively new, because of the limited number of published decisions and the non-precedential nature of such decisions, and because the laws, rules and regulations often give the relevant regulator significant discretion in how to enforce them, the interpretation and enforcement of these laws, rules and regulations involve uncertainties and can be inconsistent and unpredictable. In addition, the legal system is based in part on government policies and internal rules, some of which are not published on a timely basis or at all, and which may have a retroactive effect. The regulations in China can change quickly. As a result, we may not be aware of our violation of these policies and rules until after the occurrence of the violation.

China's Foreign Investment Law and its implementing rule came into force in January 2020. The Foreign Investment Law and its implementing rules embody an expected regulatory trend to rationalize China’s foreign investment regulatory regime in line with prevailing international practice and the legislative efforts to unify the legal requirements for both foreign and domestic investments. There are still uncertainties with respect to the interpretation and implementation of the Foreign Investment Law and its implementing rules. For example, the Foreign Investment Law and its implementing rules provide that foreign invested entities established according to the previous laws regulating foreign investment prior to its implementation may maintain their structure and corporate governance for a five-year transition period. It is uncertain whether governmental authorities may require us to adjust the structure and corporate governance of certain of our Chinese subsidiaries in such transition period. Failure to take timely and appropriate measures to meet any of these or similar regulatory requirements could materially affect our current corporate governance practices and business operations and our compliance costs may increase significantly. In addition, the Security Review Rules, effective from January 18, 2021, embody China's continued efforts to provide a legal regime for national security review comparable to similar procedures in other jurisdictions, such as CFIUS review in the United States. There are still uncertainties with respect to the interpretation, implementation and enforcement of the Security Review Rules. For example, national security remains undefined and there is no clear guidance on whether the biotechnology industry requires security review and what factors the regulatory authority may consider in determining whether there are security concerns. It is difficult to evaluate the impact of the Security Review Rules on our existing investments or potential investments in China.

It may be difficult for overseas regulators to conduct investigations or collect evidence within China. In China, there are significant legal and other obstacles to providing information needed for regulatory investigations or litigations initiated outside China. According to Article 177 of the PRC Securities Law, which became effective in March 2020, no overseas securities regulator is allowed to directly conduct investigation or evidence collection activities within the PRC territory. According to the Revised Confidentiality and Archives Administration Provisions, where overseas securities regulators or relevant competent authorities request to inspect, investigate or collect evidence from Chinese domestic companies concerning their overseas offering and listing or their securities firms and securities service providers that undertake securities business for such Chinese domestic companies, such inspection, investigation and evidence collection must be conducted under the cross-border regulatory cooperation mechanism, and the CSRC or competent authorities of the Chinese government will provide necessary assistance pursuant to bilateral and multilateral cooperation mechanism. Although the authorities in China may establish a regulatory cooperation mechanism with the securities regulatory authorities of another country or region to implement cross-border supervision and administration, such cooperation with the securities regulatory authorities in the Unities States may not be efficient in the absence of a mutual and practical cooperation mechanism. While detailed interpretation of or implementation rules under Article 177 have yet to be promulgated, the inability for an overseas securities regulator to directly conduct investigations or evidence collection activities within China may further increase the difficulties you face in protecting your interests. For risks associated with investing in us as a Cayman Islands company, see also “—Risks Related to Our Ordinary Shares, ADSs, and RMB Shares—We are a Cayman Islands company. Because judicial precedent regarding the rights of shareholders is more limited under Cayman Islands law than under Hong Kong law, Chinese law or U.S. law, our shareholders may have fewer shareholder rights than they would have under Hong Kong law, Chinese law or U.S. law and may face difficulties in protecting their interests.”

Any administrative and court proceedings in China may be protracted, resulting in substantial costs and diversion of resources and management attention. Since administrative and court authorities have significant discretion in interpreting and implementing statutory and contractual terms, it may be more difficult to evaluate the outcome of administrative and court proceedings and the level of legal protection we enjoy than in more developed legal systems. These uncertainties may impede our ability to enforce the contracts we have entered and could materially and adversely affect our business, financial condition and results of operations.

In addition, the PRC government has announced its plans to enhance its regulatory oversight of China-based companies listed overseas and cross-border law enforcement cooperation. The Securities Opinions called for:

- tightening oversight of data security, cross-border data flow and administration of classified information, as well as amendments to relevant regulation to specify responsibilities of overseas listed China-based companies with respect to data security and information security;
- enhanced oversight of overseas listed companies as well as overseas equity fundraising and listing by China-based companies; and
- extraterritorial application of China's securities laws.

There are great uncertainties with respect to the interpretation and implementation of the Securities Opinions and the newly promulgated Overseas Listing Trial Measures. The PRC government may promulgate relevant laws, rules and regulations to impose additional and significant obligations and liabilities on overseas listed China-based companies regarding data security, cross-border data flow, and compliance with China's securities laws. As a company with operations in China and stock listings in and outside of China, it is uncertain whether or how these laws, rules and regulations and their interpretation and implementation may affect us. However, among other things, our ability to obtain external financing through the issuance of equity securities overseas could be adversely affected if restrictions on overseas fundraising are imposed on companies like us.

The filing or other procedures with, the CSRC or other Chinese regulatory authorities may be required in connection with issuing our equity securities to foreign investors under Chinese law, and, if required, we cannot predict whether we will be able, or how long it will take us, to complete such filing or other procedures. If we fail to complete a filing with the CSRC, our future offering application may be impacted and we may be subject to penalties, sanctions and fines imposed by the CSRC and relevant departments of the State Council.

Pursuant to the Securities Opinions, Chinese regulators are required to accelerate rulemaking related to the overseas issuance and listing of securities outside of China, and update the existing laws and regulations related to data security, cross-border data flow, and administration of classified information. The Securities Opinions emphasized the need to strengthen the administration over illegal securities activities and the need to strengthen the supervision over overseas listings by Chinese companies.

Numerous regulations, guidelines and other measures have been or are expected to be adopted under the umbrella of or in addition to the Cyber Security Law and Data Security Law. As there are still uncertainties regarding the interpretation and implementation of such regulatory guidance, we cannot assure investors that we will be able to comply with new regulatory requirements relating to our future overseas capital-raising activities outside of China and we may become subject to more stringent requirements with respect to matters including data privacy and cross-border investigation and enforcement of legal claims.

Furthermore, on February 17, 2023, the CSRC released the Overseas Listing Trial Measures and five relevant guidelines, which will take effect from March 31, 2023, requiring Chinese companies that have already directly or indirectly offered and listed securities in overseas markets to fulfil their filing obligations and report relevant information to the CSRC within three working days after conducting a follow-on offering of equity securities on the same overseas market. As the Overseas Listing Trial Measures are newly promulgated and have not yet come into effect, their interpretation and implementation are subject to substantial uncertainty. After the effectiveness of the Overseas Listing Trial Measures, we may have to go through the filing process for any follow-on offerings we conduct on the NASDAQ Global Select Market or Hong Kong Stock Exchange within three working days of the completion of our follow-on offerings. If we fail to complete a filing with the CSRC for any of our follow-on offerings, we may be subject to penalties, sanctions and fines imposed by the CSRC and relevant departments of the State Council.

As of the date of this report, we have not received any inquiry, notice, warning or sanction regarding completing filing or other procedures in connection with offering our equity securities on the Nasdaq Global Select Market or Hong Kong Stock Exchange from the CSRC or any other Chinese regulatory authorities that have jurisdiction over our operations. However, there

remains significant uncertainty as to the interpretation and implementation of regulatory requirements related to securities offerings and other capital markets activities outside of China. If it is determined in the future that the filing or other procedure with the CSRC or any other regulatory authority is required for issuing our equity securities on the Nasdaq Global Select Market or Hong Kong Stock Exchange, it is uncertain whether we will be able to and how long it would take for us to complete the filing or other procedure, despite our best efforts. If we, for any reason, are unable to complete, or experience significant delays in completing, the requisite relevant filing or other procedure(s), we may face sanctions by the CSRC or other Chinese regulatory authorities. These regulatory authorities may impose fines and penalties on our operations in China, limit our ability to pay dividends outside of China, limit our operations in China, delay or restrict the repatriation of funds into China or take other actions that could have a material adverse effect on our business, financial condition, results of operations and prospects, as well as the trading price of our ADSs, ordinary shares, and RMB Shares. In addition, if the CSRC or other regulatory authorities later promulgate new rules requiring that we obtain their approvals or complete filing or other procedures for any future public offerings on the Nasdaq Global Select Market or Hong Kong Stock Exchange, we may be unable to obtain a waiver of such requirements, if and when procedures are established to obtain such a waiver. Any uncertainties and/or negative publicity regarding such a requirement could have a material adverse effect on the trading price of our ADSs, ordinary shares, and RMB Shares.

To operate our general business activities currently conducted in China, each of our Chinese subsidiaries is required to obtain a business license from the local counterpart of the SAMR. Each of our Chinese subsidiaries has obtained a valid business license from the local counterpart of the SAMR, and no application for any such license has been denied. The pharmaceutical industry in which we operate is also highly regulated in China. Our Chinese subsidiaries are required to obtain applicable licenses from competent Chinese government authorities for our operations in China, including drug manufacturing licenses, drug trade license, clinical trial authorizations, drug registration certificates, licenses for use of experimental animals, pollutant discharge licenses and permits for urban sewage discharge into drainage pipe network. We believe our PRC subsidiaries have obtained all applicable licenses and permits which are material to our business operations in China.

PRC regulations establish complex procedures for some acquisitions conducted by foreign investors, which could make it more difficult for us to pursue growth through acquisitions in China.

PRC regulations and rules concerning mergers and acquisitions set forth additional procedures and requirements that could make merger and acquisition activities of PRC-based companies by foreign investors more time-consuming and complex. See also "—Risks Related to Our Industry, Business and Operations—We incur significant costs as a result of operating as a public company, and our management is required to devote substantial time to compliance requirements, including establishing and maintaining internal controls over financial reporting. We may be exposed to potential risks if we are unable to comply with these requirements." These rules, among others, specify that mergers and acquisitions by foreign investors that raise "national defense and security" concerns and mergers and acquisitions through which foreign investors may acquire the de facto control over domestic enterprises that raise "national security" concerns are subject to strict review by the MOFCOM, and the rules prohibit any activities attempting to bypass a security review by structuring the transaction through, among other things, trusts, entrustment or contractual control arrangements. Although we believe that our business is not in an industry related to national security, we cannot preclude the possibility that the competent PRC government authorities may publish explanations contrary to our understanding or broaden the scope of such security reviews in the future, in which case our future acquisitions and investment in the PRC, including those by way of entering into contractual control arrangements with target entities, may be closely scrutinized or prohibited. Moreover, according to the Anti-Monopoly Law, the SAMR shall be notified in advance of any concentration of undertaking if certain filing thresholds are triggered. We may grow our business in part by acquiring complementary businesses in China. Complying with the requirements of the laws and regulations mentioned above and other PRC regulations to complete such transactions could be time-consuming, and any required approval processes, including obtaining approval from the SAMR, may delay or inhibit our ability to complete such transactions, which could affect our ability to expand our business or maintain or expand our market share. Our ability to expand our business or maintain or expand our market share through future acquisitions would as such be materially and adversely affected.

In December 2020, the NDRC and the MOFCOM promulgated the Foreign Investment Security Review Measures, which came into effect on January 18, 2021. Under the Foreign Investment Security Review Measures, investments in military, national defense-related areas or in locations in proximity to military facilities, or investments that would result in acquiring the actual control of assets in certain key sectors, such as critical agricultural products, energy and resources, equipment manufacturing, infrastructure, transport, cultural products and services, IT, Internet products and services, financial services and technology sectors, are required to be approved by designated governmental authorities in advance. As these measures are recently promulgated, official guidance has not been issued by the designated office in charge of such security review yet, therefore there are great uncertainties with respect to the interpretation and implementation of the Foreign Investment Security Review Measures. If any of our business operations were to fall under the foregoing categories, we would need to take further actions in order to comply with these laws, regulations and rules, which may materially and adversely affect our current corporate structure, business, financial condition and results of operations.

We may rely on dividends and other distributions on equity paid by our PRC subsidiaries to fund any cash and financing requirements we may have, and any limitation on the ability of our PRC subsidiaries to make payments to us could have a material and adverse effect on our ability to conduct our business.

We are a holding company incorporated in the Cayman Islands, and we may rely on dividends and other distributions on equity paid by our PRC subsidiaries for our cash and financing requirements, including the funds necessary to pay dividends and other cash distributions to our shareholders or to service any debt we may incur. If any of our PRC subsidiaries incur debt on their own behalf in the future, the instruments governing the debt may restrict their ability to pay dividends or make other distributions to us. Under PRC laws and regulations, our PRC subsidiaries may pay dividends only out of their respective accumulated profits as determined in accordance with PRC accounting standards and regulations. In addition, a wholly foreign-owned enterprise is required to set aside at least 10% of its accumulated after-tax profits each year, if any, to fund a certain statutory reserve fund, until the aggregate amount of such fund reaches 50% of its registered capital. Such reserve funds cannot be distributed to us as dividends until the liquidation of the enterprise. At its discretion, a wholly foreign-owned enterprise may allocate a portion of its after-tax profits based on PRC accounting standards to an enterprise expansion fund, or a staff welfare and bonus fund. In addition, registered share capital and capital reserve accounts are also restricted from withdrawal in the PRC, up to the amount of net assets held in each operating subsidiary. As of December 31, 2022, these restricted assets totaled $3.5 billion.

Our PRC subsidiaries generate primarily all of their revenue in RMB, which is not freely convertible into other currencies. As a result, any restriction on currency exchange may limit the ability of our PRC subsidiaries to use their RMB revenues to pay dividends to us.

In response to the persistent capital outflow in the PRC and RMB's depreciation against the U.S. dollar in the fourth quarter of 2016, the People's Bank of China ("PBOC") and China's State Administration of Foreign Exchange ("SAFE") promulgated a series of capital control measures, including stricter vetting procedures for domestic companies to remit foreign currency for overseas investments, dividends payments and shareholder loan repayments.

The PRC government may continue to strengthen its capital controls, and more restrictions and substantial vetting process may be put forward by the SAFE for cross-border transactions falling under both the current account and the capital account. Any limitation on the ability of our PRC subsidiaries to pay dividends or make other kinds of payments to us could materially and adversely limit our ability to grow, make investments or acquisitions that could be beneficial to our business, pay dividends, or otherwise fund and conduct our business.

The PRC Enterprise Income Tax Law (the "EIT Law") and its implementation rules provide that China-sourced income of foreign enterprises, such as dividends paid by a PRC subsidiary to its equity holders that are non-PRC resident enterprises, will normally be subject to PRC withholding tax at a rate of 10%, unless any such foreign investor's jurisdiction of tax residency has a tax treaty with China that provides for a reduced withholding rate arrangement and such non-PRC resident enterprises constitute the beneficiary of such income.

Pursuant to an arrangement between mainland China and the Hong Kong Special Administrative Region (the "Hong Kong Tax Treaty") and relevant tax regulations of the PRC, subject to certain conditions, a reduced withholding tax rate of 5% will be available for dividends from PRC entities provided that the recipient holds at least 25% shares of the PRC entities and can demonstrate it is a Hong Kong tax resident and it is the beneficial owner of the dividends. The China government has adopted multiple regulations which stipulate that in determining whether a non-resident enterprise has the status as a beneficial owner, comprehensive analysis shall be conducted based on the factors listed therein and the actual circumstances of the specific case shall be taken into consideration. Specifically, it expressly excludes an agent or a designated payee from being considered as a "beneficial owner." We own the PRC subsidiaries through BeiGene (Hong Kong) Co., Limited ("BeiGene HK"), a company incorporated under the laws of Hong Kong on November 22, 2010 and a wholly owned subsidiary of the Company. BeiGene HK currently does not hold a Hong Kong tax resident certificate from the Inland Revenue Department of Hong Kong, and there is no assurance that the reduced withholding tax rate will be available.

We may be treated as a resident enterprise for PRC tax purposes under the EIT Law and we may therefore be subject to PRC income tax on our worldwide taxable income. Dividends payable to foreign investors and gains on the sale of our ADSs or ordinary shares by our foreign investors may become subject to PRC tax.

Under the EIT Law, an enterprise established outside the PRC with "de facto management bodies" within the PRC is considered a "resident enterprise," meaning that it is treated in a manner similar to a Chinese enterprise for PRC enterprise income tax purposes. The implementing rules of the EIT Law define "de facto management bodies" as "management bodies that exercise substantial and overall management and control over the production and operations, personnel, accounting, and properties" of the enterprise. In addition, PRC regulations specify that certain Chinese-controlled offshore incorporated enterprises, defined as enterprises incorporated under the laws of foreign countries or territories and that have PRC enterprises

or enterprise groups as their primary controlling shareholders, will be classified as resident enterprises if all of the following are located or resident in China: (i) senior management personnel and departments that are responsible for daily production, operation and management; (ii) financial and personnel decision-making bodies; (iii) key properties, accounting books, company seal, and minutes of board meetings and shareholders' meetings; and (iv) half or more of senior management or directors having voting rights.

Although BeiGene, Ltd. does not have a PRC enterprise or enterprise group as its primary controlling shareholder and is therefore not a Chinese-controlled offshore incorporated enterprise within the meaning of these regulations, in the absence of guidance specifically applicable to us, we have applied the guidance set forth in the regulations to evaluate the tax residence status of BeiGene, Ltd. and its subsidiaries organized outside of the PRC.

We are not aware of any offshore holding company with a corporate structure similar to ours that has been deemed a PRC "resident enterprise" by the PRC tax authorities. Accordingly, we do not believe that our company or any of our overseas subsidiaries should be treated as a PRC resident enterprise. However, the tax resident status of an enterprise is subject to determination by the PRC tax authorities and uncertainties remain with respect to the interpretation of the term "de facto management body." If the PRC tax authorities determine that our Cayman Islands holding company is a resident enterprise for PRC enterprise income tax purposes, a number of unfavorable PRC tax consequences could follow and we may be subject to enterprise income tax at a rate of 25% on our worldwide taxable income, as well as to PRC enterprise income tax reporting obligations. If we are deemed a PRC resident enterprise, dividends paid on our shares and any gain realized from the transfer of our ordinary shares may be treated as income derived from sources within the PRC. As a result, dividends paid to non-PRC resident enterprise ADS holders or shareholders may be subject to PRC withholding tax at a rate of 10% (or 20% in the case of non-PRC individual ADS holders or shareholders) and gains realized by non-PRC resident enterprises ADS holders or shareholders from the transfer of our ordinary shares or ADSs may be subject to PRC tax at a rate of 10% (or 20% in the case of non-PRC individual ADS holders or shareholders), which may be reduced or exempted according to relevant tax treaties between PRC and the non-PRC resident enterprise/individual ADS holders' or shareholders' tax resident jurisdictions.

We and our shareholders face uncertainties with respect to indirect transfers of equity interests in PRC resident enterprises or other assets attributed to a PRC establishment of a non-PRC company, or other assets attributable to a PRC establishment of a non-PRC company.

Pursuant to Chinese regulations, an "indirect transfer" of "PRC taxable assets," including equity interests in a PRC resident enterprise, by non-PRC resident enterprises may be recharacterized and treated as a direct transfer of PRC taxable assets, if such arrangement does not have a reasonable commercial purpose and was established for the purpose of avoiding payment of PRC enterprise income tax. As a result, gains derived from such indirect transfer may be subject to PRC enterprise income tax. When determining whether there is a "reasonable commercial purpose" of the transaction arrangement, factors to be taken into consideration include: whether the main value of the equity interest of the relevant offshore enterprise derives from PRC taxable assets; whether the assets of the relevant offshore enterprise mainly consists of direct or indirect investment in the PRC or if its income mainly derives from the PRC; whether the offshore enterprise and its subsidiaries directly or indirectly holding PRC taxable assets have real commercial nature which is evidenced by their actual function and risk exposure; the duration of existence of the business model and organizational structure; the replicability of the transaction by direct transfer of PRC taxable assets; and the tax situation of such indirect transfer and applicable tax treaties or similar arrangements. In respect of an indirect offshore transfer of assets of a PRC establishment, the resulting gain is to be reported on with the enterprise income tax filing of the PRC establishment or place of business being transferred and would consequently be subject to PRC enterprise income tax at a rate of 25%. Where the underlying transfer relates to equity investments in a PRC resident enterprise, which is not related to a PRC establishment or place of business of a non-resident enterprise, a PRC enterprise income tax at the rate of 10% would apply, subject to available preferential tax treatment under applicable tax treaties or similar arrangements. Late payment of applicable tax will subject the transferor to default interest. Gains derived from the sale of shares by investors through a public stock exchange are not subject to the PRC enterprise income tax where such shares were acquired in a transaction through a public stock exchange. As such, the sale of the ADSs or ordinary shares on a public stock exchange will not be subject to PRC enterprise income tax. However, the sale of our ordinary shares or ADSs originally purchased from a stock exchange by a non-PRC resident enterprise outside a public stock exchange may be subject to PRC enterprise income tax under these regulations.

There are uncertainties as to the application of these regulations, which may be determined by the tax authorities to be applicable to sale of the shares of our offshore subsidiaries or investments where PRC taxable assets are involved. The transferors and transferees may be subject to the tax filing and withholding or tax payment obligation, while our PRC subsidiaries may be requested to assist in the filing. Furthermore, we, our non-resident enterprises and PRC subsidiaries may be required to spend valuable resources to comply with these regulations or to establish that we and our non-resident enterprises should not be taxed under these regulations, for our previous and future restructuring or disposal of shares of our offshore subsidiaries, which may have a material adverse effect on our financial condition and results of operations.

The PRC tax authorities have the discretion to make adjustments to the taxable capital gains based on the difference between the fair value of the taxable assets transferred and the cost of investment. If the PRC tax authorities make adjustments to the taxable income of the transactions under these regulations, our income tax costs associated with such potential acquisitions or disposals will increase, which may have an adverse effect on our financial condition and results of operations.

Restrictions on currency exchange may limit our ability to utilize our revenue effectively.

The PRC government imposes controls on the conversion of RMB into foreign currencies and, in certain cases, the remittance of currency out of the PRC. A portion of our revenue is denominated in RMB. Shortages in availability of foreign currency may restrict the ability of our PRC subsidiaries to remit sufficient foreign currency to our offshore entities for our offshore entities to pay dividends or make other payments or otherwise to satisfy our foreign currency denominated obligations. The RMB is currently convertible under the "current account," which includes dividends, trade and service-related foreign exchange transactions, but not under the "capital account," which includes foreign direct investment and loans, including loans we may secure from our onshore subsidiaries. Currently, our PRC subsidiaries may purchase foreign currency for settlement of "current account transactions," including payment of dividends to us, without the approval of SAFE by complying with certain procedural requirements. However, the relevant PRC governmental authorities may limit or eliminate our ability to purchase foreign currencies in the future for current account transactions. Since a portion of our revenue is denominated in RMB, any existing and future restrictions on currency exchange may limit our ability to utilize revenue generated in RMB to fund our business activities outside of the PRC or pay dividends in foreign currencies to holders of our ordinary shares and the ADSs. Foreign exchange transactions under the capital account remain subject to limitations and require approvals from, or registration with, SAFE and other relevant PRC governmental authorities or designated banks. This could affect our ability to obtain foreign currency through debt or equity financing for our subsidiaries.

Our business benefits from certain financial incentives and discretionary policies granted by local governments. Expiration of, or changes to, these incentives or policies would have an adverse effect on our results of operations.

Local governments in the PRC have granted certain financial incentives from time to time to our PRC subsidiaries as part of their efforts to encourage the development of local businesses. The timing, amount and criteria of government financial incentives are determined within the sole discretion of the local government authorities and cannot be predicted with certainty before we actually receive any financial incentive. We generally do not have the ability to influence local governments in making these decisions. Local governments may decide to reduce or eliminate incentives at any time. In addition, some of the government financial incentives are granted on a project basis and subject to the satisfaction of certain conditions, including compliance with the applicable financial incentive agreements and completion of the specific project therein. We cannot guarantee that we will satisfy all relevant conditions, and if we do so we may be deprived of the relevant incentives. We cannot assure you of the continued availability of the government incentives currently enjoyed by us. Any reduction or elimination of incentives would have an adverse effect on our results of operations.

Any failure to comply with PRC regulations regarding our employee equity plans and investments in offshore companies by PRC residents may subject the PRC plan participants and PRC-resident beneficial owners or us to fines and other legal or administrative sanctions.

We and our directors, executive officers and other employees who are PRC residents have participated in our employee equity plans. We are an overseas listed company, and therefore, we and our directors, executive officers and other employees who are PRC citizens or who have resided in the PRC for a continuous period of not less than one year and who have been granted restricted share units, restricted shares, options or other forms of equity incentives or rights to acquire equity are subject to the PRC regulations, according to which, employees, directors, supervisors and other management members participating in any share incentive plan of an overseas publicly listed company who are PRC citizens or who are non-PRC citizens residing in the PRC for a continuous period of not less than one year, subject to limited exceptions, are required to register with the SAFE through a domestic qualified agent, which could be a PRC subsidiary of such overseas listed company, and complete certain other procedures. We also face regulatory uncertainties that could restrict our ability to adopt additional equity incentive plans for our directors and employees under PRC law. Moreover, failure to comply with the various foreign exchange registration requirements could result in liability under PRC law for circumventing applicable foreign exchange restrictions.

The pharmaceutical industry in China is highly regulated, and such regulations are subject to change, which may affect approval and commercialization of our medicines and drug candidates.

A large portion of our business is conducted in China. The pharmaceutical industry in China is subject to comprehensive government regulation and supervision, encompassing the approval, registration, manufacturing, packaging, licensing and marketing of new medicines. In recent years, the regulatory framework in China for pharmaceutical companies has undergone significant changes, which we expect will continue. While we believe our strategies regarding research, development, manufacturing and commercialization in China are aligned with the Chinese government's policies, they may in the future

diverge, requiring a change in our strategies. Any such change may result in increased compliance costs on our business or cause delays in or prevent the successful research, development, manufacturing or commercialization of our drug candidates or medicines in China and reduce the current benefits we believe are available to us from developing and manufacturing medicines in China.

Chinese authorities have become increasingly vigilant in enforcing laws affecting the pharmaceutical industry. Any failure by us or our partners to maintain compliance with applicable laws and regulations or obtain and maintain required licenses and permits may result in the suspension or termination of our business activities in China. Reports of what have come to be viewed as significant quality-control failures by Chinese vaccine manufacturers have led to enforcement actions against officials responsible for implementing national reforms favorable to innovative drugs (such as ours). While not directly affecting us, this macro-industry event could cause state or private resources to be diverted away from fostering innovation and be redirected toward regulatory enforcement, which could adversely affect our research, development, manufacturing and commercialization activities and increase our compliance costs.

Risks Related to Our Ordinary Shares, ADSs, and RMB Shares

The trading prices of our ordinary shares, ADSs, and/or RMB Shares can be volatile, which could result in substantial losses to you.

The trading price of our ordinary shares, ADSs, and/or RMB Shares can be volatile and fluctuate widely in response to a variety of factors, many of which are beyond our control, including: announcements of regulatory approval or a complete response letter, or specific label indications or patient populations for its use, or changes or delays in the regulatory review process; announcements of therapeutic innovations, new products, acquisitions, strategic relationships, joint ventures or capital commitments by us or our competitors; adverse actions taken by regulatory agencies with respect to our clinical trials, manufacturing supply chain or sales and marketing activities; any adverse changes to our relationship with manufacturers or suppliers; the results of our testing and clinical trials; the results of our efforts to acquire or license additional medicines or drug candidates; variations in the level of expenses related to our existing medicines and drug candidates or preclinical, clinical development and commercialization programs; any intellectual property infringement actions in which we may become involved; announcements concerning our competitors or the pharmaceutical industry in general; the performance and fluctuation of the market prices of other companies with significant business operations in China that have listed their securities in Hong Kong, Shanghai or the United States; fluctuations in product revenue, sales and marketing expenses and profitability; manufacture, supply or distribution shortages; variations in our results of operations; announcements about our results of operations that are not in line with analyst expectations, the risk of which is enhanced because it is our policy not to give guidance on results of operations; publication of operating or industry metrics by third parties, including government statistical agencies, that differ from expectations of industry or financial analysts; changes in financial estimates by securities research analysts; media reports, whether or not true, about our business, our competitors or our industry; additions to or departures of our management; fluctuations of exchange rates between the RMB, the U.S. dollar and Hong Kong dollar; release or expiry of lock-up or other transfer restrictions on our outstanding ordinary shares, ADSs or RMB Shares; sales or perceived potential sales of additional ordinary shares, ADSs or RMB Shares by us, our executive officers and directors or our shareholders; general economic and market conditions and overall fluctuations in the United States, Hong Kong or Shanghai equity markets; changes in accounting principles; trade disputes or U.S.-China government relations; and changes or developments in the United States, PRC, EU or global regulatory environment.

In addition, the stock market, in general, and pharmaceutical and biotechnology companies, in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our ordinary shares, ADSs, and/or RMB Shares, regardless of our actual operating performance.

The characteristics of capital markets in the United States, Hong Kong and Shanghai are different, which may cause volatility in the market price of our ordinary shares, ADSs, and RMB Shares.

Our ordinary shares are listed on the HKEx in Hong Kong under the stock code "06160", our ADSs are listed on the Nasdaq in the United States under the symbol “BGNE”, and our RMB Shares are listed on the STAR Market in the PRC under the stock code "688235". Under current PRC laws and regulations, our ADSs and ordinary shares listed on the Nasdaq and the HKEx are not interchangeable or fungible with the RMB Shares listed on the STAR Market, and there is no trading or settlement between either the Nasdaq or the HKEx on the one hand, and the STAR Market on the other hand. The three markets have different trading hours, trading characteristics (including trading volume and liquidity), trading and listing rules, and investor bases (including different levels of retail and institutional participation). As a result of these major differences, the trading prices of our ordinary shares, ADSs, and RMB Shares might not be the same, even allowing for currency differences. Fluctuations in the price of our ADSs due to circumstances peculiar to its home capital market could materially and adversely

affect the price of the ordinary shares and/or RMB Shares, and vice versa. Because of the different characteristics of the U.S., Hong Kong and Shanghai equity markets, the historic market prices of our ordinary shares, ADSs, and RMB Shares may not be indicative of the performance of our securities going forward.

We may be subject to securities litigation, which is expensive and could divert management attention.

Companies that have experienced volatility in the volume and market price of their shares have been subject to an increased incidence of securities class action litigation, particularly in our industry in recent years. We may be the target of this type of litigation in the future. Securities litigation against us could result in substantial costs and divert our management's attention from other business concerns, and, if adversely determined, could have a material adverse effect on our business, financial condition, and results of operations.

Future sales of our ordinary shares, ADSs, and/or RMB Shares in the public market could cause the ordinary share, ADS, and/or RMB Share price to fall.

The price of our ordinary shares, ADSs, and/or RMB Shares could decline as a result of sales of a large number of the ordinary shares, ADSs, and/or RMB Shares or the perception that these sales could occur. These sales, or the possibility that these sales may occur, also might make it more difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate.

As of February 14, 2023, 1,356,140,180 ordinary shares, par value $0.0001 per share, were outstanding, of which 863,876,312 ordinary shares were held in the form of 66,452,024 ADSs, each representing 13 ordinary shares, and 115,055,260 were RMB Shares.

We filed a registration statement on Form S-3 with the SEC on behalf of certain shareholders on May 11, 2020, registering 300,197,772 ordinary shares, including 224,861,338 ordinary shares in the form of 17,297,026 ADSs to be resold by the selling shareholders identified therein and in any related prospectus supplement from time to time. Amgen also has specified registration rights upon expiration of a lock-up period. Furthermore, we have registered or plan to register the offer and sale of all securities that we have issued and may issue in the future under our equity compensation plans, including upon the exercise of share options and vesting of restricted share units and under our employee share purchase plan. If these additional securities are sold, or if it is perceived that they will be sold, in the public market, the trading price of our ordinary shares, ADSs and/or RMB Shares could decline.

In addition, in the future, we may issue additional ordinary shares, ADSs, RMB Shares, or other equity or debt securities convertible into ordinary shares, ADSs, or RMB Shares in connection with a financing, acquisition, license, litigation settlement, employee arrangements or otherwise. Any such issuance could result in substantial dilution to our existing shareholders and could cause the ordinary share, ADS, and/or RMB Share price to decline.

The triple listing of our ADSs, ordinary shares and RMB Shares may adversely affect the liquidity and value of our ADSs, ordinary shares and/or RMB Shares.

Our ADSs are traded on the Nasdaq, our existing ordinary shares maintained on our Cayman register in Cayman Islands and Hong Kong register in Hong Kong, are traded on the HKEx, and our RMB Shares are traded on the STAR Market. The triple listing of our ADSs, ordinary shares and RMB Shares may dilute the liquidity of these securities in one or all three markets and may adversely affect the maintenance of an active trading market for ADSs in the United States, the ordinary shares in Hong Kong, and/or the RMB Shares in the PRC. The price of our ADSs, ordinary shares and/or RMB Shares could also be adversely affected by trading of our securities on other markets. We may decide at some point in the future to delist our RMB Shares from the STAR Market, and our shareholders may approve such delisting. We cannot predict the effect such delisting of our RMB Shares on the STAR Market would have on the market price of our ADSs on the Nasdaq or our ordinary shares on the HKEx.

We face increased regulatory scrutiny and compliance costs due to our listing on the STAR Market of the SSE.

We are subject to the applicable laws, rules and regulations governing public companies listed on the STAR Market in addition to the various laws, rules and regulations that we are subject to in the United States and Hong Kong. The listing and trading of our equity securities in multiple jurisdictions and multiple markets will lead to increased compliance obligations and costs for us, and we may face the risk of significant intervention by regulatory authorities in these jurisdictions and markets, such as inquiries, investigations, enforcement actions and other regulatory proceedings by regulatory authorities. In addition, we may be subject to securities litigation filed with the courts in China by the investors with respect to the RMB Shares traded on the STAR Market.

Because we do not expect to pay dividends in the foreseeable future, you must rely on price appreciation of the ordinary shares, ADSs and/or RMB Shares for return on your investment.

We intend to retain most, if not all, of our available funds and earnings to fund the development and growth of our business. As a result, we do not expect to pay any cash dividends in the foreseeable future. Therefore, you should not rely on an investment in the ordinary shares, ADSs and/or RMB Shares as a source for any future dividend income.

Our board of directors has significant discretion as to whether to distribute dividends. Even if our board of directors decides to declare and pay dividends, the timing, amount and form of future dividends, if any, will depend on, among other things, our future results of operations and cash flow, our capital requirements and surplus, the amount of distributions, if any, received by us from our subsidiaries, our financial condition, contractual and regulatory restrictions and other factors deemed relevant by our board of directors. Accordingly, the return on your investment in the ordinary shares, ADSs and/or RMB Shares will likely depend entirely upon any future price appreciation of the ordinary shares, ADSs and/or RMB Shares. There is no guarantee that the ordinary shares, ADSs and/or RMB Shares will appreciate in value or even maintain the price at which you purchased the ordinary shares, ADSs and/or RMB Shares. You may not realize a return on your investment in the ordinary shares, ADSs and/or RMB Shares and you may even lose your entire investment in the ordinary shares, ADSs and/or RMB Shares.

If securities or industry analysts do not continue to publish research or publish inaccurate or unfavorable research about our business, the market price for the ordinary shares, ADSs and/or RMB Shares and trading volume could decline.

The trading market for the ordinary shares, ADSs and RMB Shares relies in part on the research and reports that equity research analysts publish about us or our business. We do not control these analysts. If research analysts do not maintain adequate research coverage or if one or more of the analysts who covers us downgrades the ordinary shares, ADSs and/or RMB Shares or publishes inaccurate or unfavorable research about our business, the market price for the ordinary shares, ADSs and/or RMB Shares would likely decline. If one or more of these analysts cease coverage of our company or fail to publish reports on us regularly, we could lose visibility in the financial markets, which, in turn, could cause the market price or trading volume for the ordinary shares, ADSs and/or RMB Shares to decline significantly.

Because we are a Cayman Islands company, our shareholders may have fewer shareholder rights than they would have under Hong Kong law, Chinese law or U.S. law and may face difficulties in protecting their interests.

We are an exempted company with limited liability incorporated in the Cayman Islands. Our corporate affairs are governed by our amended and restated memorandum and articles of association (as may be further amended from time to time), the Companies Law (as amended) of the Cayman Islands, and the common law of the Cayman Islands. The rights of shareholders to take action against the directors, actions by minority shareholders and the fiduciary responsibilities of our directors are to a large extent governed by the common law of the Cayman Islands. This common law is derived in part from comparatively limited judicial precedent in the Cayman Islands as well as from English common law, which has persuasive, but not binding, authority on courts in the Cayman Islands. The rights of our shareholders and the fiduciary responsibilities of our directors under Cayman Islands law are not as clearly established as they would be under statutes or judicial precedent in some jurisdictions in Hong Kong, mainland China and the United States. In particular, the Cayman Islands has a less developed body of securities law than Hong Kong, mainland China or the United States. In addition, some states in the United States, such as Delaware, have more fully developed and judicially interpreted bodies of corporate law than the Cayman Islands.

In addition, as a Cayman Islands exempted company, our shareholders have no general rights under Cayman Islands law to inspect corporate records and accounts or to obtain copies of lists of shareholders, with the exception that shareholders may request a copy of the current amended and restated memorandum and articles of association. Our directors have discretion under our amended and restated articles of association to determine whether or not, and under what conditions, our corporate records may be inspected by our shareholders, but are not obliged to make them available to our shareholders. This may make it more difficult for shareholders to obtain the information needed to establish facts necessary for a shareholder action or to solicit proxies from other shareholders in connection with a proxy contest. As a Cayman Islands company, we may not have standing to initiate a derivative action in a Hong Kong, mainland China or U.S. federal court. As a result, shareholders may be limited in their ability to protect their interests if they are harmed in a manner that would otherwise enable them to sue in a United States federal court. In addition, shareholders of Cayman Islands companies may not have standing to initiate a shareholder derivative action in Hong Kong, mainland China or U.S. federal courts.

Some of our directors and executive officers reside outside of Hong Kong and the United States and a substantial portion of their assets are located outside of Hong Kong and the United States. As a result, it may be difficult or impossible for shareholders to bring an action against us or against these individuals in Hong Kong or in the United States in the event that shareholders believe that their rights have been infringed under the securities laws of Hong Kong, the United States or otherwise. In addition, some of our directors and executive officers reside outside of China. To the extent our directors and

executive officers reside outside of China or their assets are located outside of China, it may not be possible for investors to effect service of process upon us or our management inside China. Even if shareholders are successful in bringing an action, the laws of the Cayman Islands and China may render them unable to enforce a judgment against our assets or the assets of our directors and officers. There is no statutory recognition in the Cayman Islands of judgments obtained in the United States, Hong Kong or China, although the courts of the Cayman Islands will generally recognize and enforce a non-penal judgment of a foreign court of competent jurisdiction without retrial on the merits.

As a result of the above, shareholders may have more difficulty protecting their interests in the face of actions taken by management, members of the board of directors or controlling shareholders than they would as shareholders of a Hong Kong company, a Chinese company or a U.S. company.

Voting rights of our ADS holders are limited by the terms of the deposit agreement. The depositary for the ADSs will give us a discretionary proxy to vote the ordinary shares underlying our ADS holders' ADSs if they do not vote at shareholders' meetings, except in limited circumstances, which could adversely affect their interests.

Holders of our ADSs may exercise their voting rights with respect to the ordinary shares underlying their ADSs only in accordance with the provisions of the deposit agreement. Upon receipt of voting instructions from ADS holders in the manner set forth in the deposit agreement, the depositary for the ADSs will endeavor to vote the holder's underlying ordinary shares in accordance with these instructions. Under our articles of association, the minimum notice period required for convening an annual general meeting is 21 calendar days and the minimum notice period required for convening an extraordinary general meeting is 14 calendar days. When a general meeting is convened, ADS holders may not receive sufficient notice of a shareholders' meeting to permit them to withdraw their ordinary shares to allow them to cast their vote with respect to any specific matter at the meeting. In addition, the depositary and its agents may not be able to send voting instructions to ADS holders or carry out their voting instructions in a timely manner. We will make reasonable efforts to cause the depositary to extend voting rights to our ADS holders in a timely manner, but our ADS holders may not receive the voting materials in time to ensure that they can vote or instruct their agent to vote their shares.

Furthermore, the depositary and its agents will not be responsible for any failure to carry out any instructions to vote, for the manner in which any vote is cast or for the effect of any such vote. As a result, ADS holders may not be able to exercise their right to vote and they may lack recourse if the ordinary shares underlying their ADSs are not voted as they requested.

Under the deposit agreement for the ADSs, the depositary will give us a discretionary proxy to vote the ordinary shares underlying ADS holders' ADSs at shareholders' meetings if such holders do not give voting instructions to the depositary, unless:

- we have failed to timely provide the depositary with our notice of meeting and related voting materials;
- we have instructed the depositary that we do not wish a discretionary proxy to be given;
- we have informed the depositary that there is substantial opposition as to a matter to be voted on at the meeting; or
- a matter to be voted on at the meeting would have a material adverse impact on shareholders.

The effect of this discretionary proxy is that, if ADS holders fail to give voting instructions to the depositary, they cannot prevent the ordinary shares underlying their ADSs from being voted, absent the situations described above, and it may make it more difficult for such ADS holders to influence our management. Holders of our ordinary shares are not subject to this discretionary proxy.

Anti-takeover provisions in our constitutional documents may discourage our acquisition by a third party, which could limit our shareholders' opportunity to sell their shares at a premium.

Our amended and restated memorandum and articles of association include provisions that could limit the ability of others to acquire control of our company, could modify our structure or could cause us to engage in change-of-control transactions. These provisions could have the effect of depriving our shareholders of an opportunity to sell their shares, at a premium over prevailing market prices by discouraging third parties from seeking to obtain control in a tender offer or similar transaction.

For example, our board of directors has the authority, without further action by our shareholders, to issue preferred shares in one or more series and to fix the powers and rights of these shares, including dividend rights, conversion rights, voting rights, terms of redemption and liquidation preferences, any or all of which may be greater than the rights associated with our ordinary shares. Preferred shares could thus be issued quickly with terms calculated to delay or prevent a change in control or make removal of management more difficult. In addition, if our board of directors authorizes the issuance of preferred shares, the

market price of the ordinary shares and/or ADSs may fall and the voting and other rights of the holders of our ordinary shares and/or ADSs may be materially and adversely affected.

Furthermore, our amended and restated articles of association permit our directors to vary all or any of the rights attaching to any class of shares in issue without the consent of shareholders but only if such variation is considered by the directors not to have a material adverse effect upon such holders. The amended and restated articles of association provide that the holders must consent to any such material adverse changes in the manner set out therein.

Because our directors are divided into three classes with staggered terms of three years each, shareholders can only elect or remove a limited number of our directors in any given year. The length of these terms could present an obstacle to certain actions, such as a merger or other change of control, which could be in the interest of our shareholders.

Our amended and restated memorandum and articles of association designate specific courts as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our shareholders, which could limit our shareholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or other employees.

Our amended and restated memorandum and articles of association provide that, unless we consent in writing to the selection of an alternative forum, the courts of Cayman Islands will be the sole and exclusive forum for any derivative action or proceeding brought on behalf of us, any action asserting a claim of breach of a fiduciary duty owed by any director, officer or other employee of us to us or our shareholders, any action asserting a claim arising pursuant to any provision of the Companies Law of the Cayman Islands as amended from time to time, or the amended and restated memorandum and articles of association, or any action asserting a claim governed by the internal affairs doctrine (as such concept is recognized under the U.S. laws). In connection with our offering and listing on the STAR Market, our shareholders approved the Sixth Amended and Restated Memorandum and Articles of Association, which became effective on December 15, 2021. The Sixth Amended and Restated Memorandum and Articles of Association provide that unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States shall be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act of 1933, as amended (the "Securities Act"). In addition, the Sixth Amended and Restated Memorandum and Articles of Association provide that any person or entity purchasing or otherwise acquiring any interest in any of our securities is deemed to have notice of and consented to these provisions; provided, however, that shareholders cannot and will not be deemed to have waived our compliance with the U.S. federal securities laws and rules and regulations thereunder.

These provisions may limit a shareholder’s ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits. Alternatively, if a court were to find these provisions of our amended and restated memorandum and articles of association inapplicable to, or unenforceable in respect of, one or more of the specified types of actions or proceedings, we may incur additional costs associated with resolving such matters in other jurisdictions.

Our amended and restated memorandum and articles of association provide that any shareholder bringing an unsuccessful action against us may be obligated to reimburse us for any costs we have incurred in connection with such unsuccessful action.

Our amended and restated memorandum and articles of association provide that under certain circumstances the fees, costs, and expenses that we incur in connection with actions or proceedings brought by any person or entity, which we refer to as claiming parties, may be shifted to such person or entity. If a claiming party asserts any claim; initiates any proceeding; or joins, offers substantial assistance to, or has a direct financial interest in any claim or proceeding against us, and such claiming party or the third party that received substantial assistance from the claiming party or in whole claim the claiming party had a direct financial interest is unsuccessful in obtaining a judgment on the merits in which the claiming party prevails, then such claiming party shall (to the fullest extent permitted by law) be obligated to reimburse us for all fees, costs, and expenses, including but not limited to all reasonable attorneys’ fees and other litigation expenses, that we may incur in connection with such claim or proceeding.

Fee-shifting articles are relatively new and untested in the Cayman Islands, the United States, Hong Kong and mainland China. The case law and potential legislative action on fee-shifting articles are evolving and there exists considerable uncertainty regarding the validity of, and potential judicial and legislative responses to, such articles. The application of our fee-shifting article in connection with claims under the Cayman Islands, the United States, Hong Kong or Chinese securities laws, if any, will depend in part on future developments of the law. We cannot assure you that we will or will not invoke our fee-shifting article in any particular dispute. Consistent with our directors’ fiduciary duties to act in the best interests of the Company, the directors may in their sole discretion from time to time decide whether or not to enforce this article. In addition, given the unsettled state of the law related to fee-shifting articles, such as ours, we may incur significant additional costs associated with resolving disputes with respect to such articles, which could adversely affect our business and financial condition.

If a shareholder that brings any such claim or proceeding is unable to obtain the judgment sought, the attorneys' fees and other litigation expenses that might be shifted to a claiming party may be significant. This fee-shifting article, therefore, may dissuade or discourage current or former shareholders (and their attorneys) from initiating lawsuits or claims against us. In addition, it may impact the fees, contingency or otherwise, required by potential plaintiffs' attorneys to represent our shareholders or otherwise discourage plaintiffs' attorneys from representing our shareholders at all. As a result, this article may limit the ability of shareholders to affect the management and direction of our company, particularly through litigation or the threat of litigation.

Holders of ADSs may be subject to limitations on transfer of their ADSs.

ADSs are transferable only on the books of the depositary. However, the depositary may close its books at any time or from time to time when it deems expedient in connection with the performance of its duties. The depositary may refuse to deliver, transfer or register transfers of ADSs generally when our books or the books of the depositary are closed, or at any time if we or the depositary think it is advisable to do so because of any requirement of law, government or governmental body, or under any provision of the deposit agreement, as amended, or for any other reason, subject to ADS holders' right to cancel their ADSs and withdraw the underlying ordinary shares. Temporary delays in the cancellation of ADSs and withdrawal of the underlying ordinary shares may arise because the depositary has closed its transfer books or we have closed our transfer books, the transfer of ordinary shares is blocked to permit voting at a shareholders' meeting or we are paying a dividend on our ordinary shares.

In addition, holders of ADSs may not be able to cancel their ADSs and withdraw the underlying ordinary shares when they owe money for fees, taxes and similar charges and when it is necessary to prohibit withdrawals in order to comply with any laws or governmental regulations that apply to ADSs or to the withdrawal of ordinary shares or other deposited securities.

The depositary for the ADSs is entitled to charge holders fees for various services, including annual service fees.

The depositary for the ADSs is entitled to charge holders fees for various services, including for the issuance of ADSs upon deposit of ordinary shares, cancellation of ADSs, distributions of cash dividends or other cash distributions, distributions of ADSs pursuant to share dividends or other free share distributions, distributions of securities other than ADSs, and annual service fees. In the case of ADSs issued by the depositary into The Depository Trust Company ("DTC"), the fees will be charged by the DTC participant to the account of the applicable beneficial owner in accordance with the procedures and practices of the DTC participant as in effect at the time.

Dealings in ordinary shares registered in our Hong Kong register of members will be subject to Hong Kong stamp duty. There is uncertainty as to whether Hong Kong stamp duty will apply to the trading or conversion of the ADSs.

In connection with our Hong Kong public offering in 2018, we established a branch register of members in Hong Kong (the "Hong Kong share register"). Our ordinary shares that are traded on the HKEx, including those that may be converted from ADSs, are registered on the Hong Kong share register, and the trading of these ordinary shares on the HKEx are subject to Hong Kong stamp duty. To facilitate ADS to ordinary share conversion and trading between the Nasdaq and the HKEx, we moved a portion of our issued ordinary shares from our Cayman share register to our Hong Kong share register.

Under the Hong Kong Stamp Duty Ordinance, any person who effects a sale or purchase of Hong Kong stock, defined as stock the transfer of which is required to be registered in Hong Kong, is required to pay Hong Kong stamp duty. The stamp duty is currently set at a total rate of 0.2% of the greater of the consideration for, or the value of, shares transferred, with 0.1% payable by each of the buyer and the seller.

To the best of our knowledge, Hong Kong stamp duty has not been levied in practice on the trading or conversion of ADSs of companies that are listed in both the United States and Hong Kong and that have maintained all or a portion of their ordinary shares, including ordinary shares underlying ADSs, in their Hong Kong share registers. However, it is unclear whether, as a matter of Hong Kong law, the trading or conversion of ADSs of these dual-listed companies constitutes a sale or purchase of the underlying Hong Kong registered ordinary shares that is subject to Hong Kong stamp duty. We advise investors to consult their own tax advisors on this matter. If Hong Kong stamp duty is determined by the competent authority to apply to the trading or conversion of the ADSs, the trading price and the value of your investment in our ADSs or ordinary shares may be affected.

Holders of ADSs may not receive distributions on our ordinary shares or any value for them if it is illegal or impractical to make them available.

The depositary of the ADSs has agreed to ADS holders the cash dividends or other distributions it or the custodian for the ADSs receives on our ordinary shares or other deposited securities after deducting its fees and expenses. ADS holders will receive these distributions in proportion to the number of our ordinary shares that their ADSs represent. However, the

depositary is not responsible for making such payments or distributions if it is unlawful or impractical to make a distribution available to any holders of ADSs. For example, it would be unlawful to make a distribution to a holder of ADSs if it consists of securities that require registration under the Securities Act, but that are not properly registered or distributed pursuant to an applicable exemption from registration. The depositary is not responsible for making a distribution available to any holders of ADSs if any government approval or registration required for such distribution cannot be obtained after reasonable efforts made by the depositary. We have no obligation to take any other action to permit the distribution of the ADSs, ordinary shares, rights or anything else to holders of the ADSs. This means that holders of ADSs may not receive the distributions we make on our ordinary shares or any value for them if it is illegal or impractical for us to make them available to such holders. These restrictions may materially reduce the value of our ADSs.

Holders of ADSs may not be able to participate in rights offerings and may experience dilution of their holdings.

From time to time, we may distribute rights to our shareholders, including rights to acquire securities. Under the deposit agreement, the depositary will not distribute rights to holders of ADSs unless the distribution and sale of rights and the securities to which these rights relate are either exempt from registration under the Securities Act with respect to all holders of ADSs or are registered under the Securities Act. The depositary may, but is not required to, attempt to sell these undistributed rights to third parties and may allow the rights to lapse. We may be unable to establish an exemption from registration under the Securities Act, and we are under no obligation to file a registration statement with respect to these rights or underlying securities or to try to have a registration statement declared effective. Accordingly, holders of ADSs may be unable to participate in our rights offerings and may experience dilution of their holdings as a result.

Our corporate actions are substantially controlled by our directors, executive officers and other principal shareholders, who can exert significant influence over important corporate matters, which may reduce the price of our ordinary shares, ADSs, and/or RMB Shares and deprive shareholders of an opportunity to receive a premium for their ordinary shares, ADSs, and/or RMB Shares.

Our directors, executive officers and principal shareholders beneficially owned approximately 55% of our outstanding ordinary shares as of February 14, 2023. These shareholders, if acting together, could exert substantial influence over matters such as electing directors and approving material mergers, acquisitions or other business combination transactions. This concentration of ownership may also discourage, delay or prevent a change in control of our company, which could have the dual effect of depriving our shareholders of an opportunity to receive a premium for their shares as part of a sale of our company and reducing the price of our ordinary shares, ADSs, and/or RMB Shares. These actions may be taken even if they are opposed by our other shareholders. In addition, these persons could divert business opportunities away from us to themselves or others.

We may be a passive foreign investment company in future taxable years, which may have adverse U.S. federal income tax consequences for U.S. shareholders.

A non-U.S. corporation will be classified as a “passive foreign investment company” ("PFIC") for any taxable year if either (1) 75% or more of its gross income consists of certain types of passive income or (2) 50% or more of the average quarterly value of its assets during such year produce or are held for the production of passive income. Based upon the composition of our income and assets, we believe that we were not a PFIC for the taxable year ended December 31, 2022. Nevertheless, because our PFIC status must be determined annually with respect to each taxable year and will depend on the composition and character of our assets and income, including our use of proceeds from any equity offerings, and the value of our assets (which may be determined, in part, by reference to the market value of our ADSs and ordinary shares, which may be volatile) over the course of such taxable year, we may be a PFIC in any taxable year. The determination of whether we will be or become a PFIC may also depend, in part, on how, and how quickly, we use our liquid assets and the cash raised in equity offerings. If we determine not to deploy significant amounts of cash for active purposes, our risk of being a PFIC may substantially increase. Because there are uncertainties in the application of the relevant rules and PFIC status is a factual determination made annually after the close of each taxable year, there can be no assurance that we will not be a PFIC for the current taxable year or any future taxable year. In addition, it is possible that the Internal Revenue Service may challenge our classification of certain income and assets as non-passive, which may result in our being or becoming a PFIC in the current or subsequent years.

If we are a PFIC for any taxable year during a U.S. shareholder’s holding period of the ordinary shares or ADSs, then such U.S. shareholder may incur significantly increased United States income tax on gain recognized on the sale or other disposition of the ordinary shares or ADSs and on the receipt of distributions on the ordinary shares or ADSs to the extent such distribution is treated as an “excess distribution” under the United States federal income tax rules. In addition, such holders may be subject to burdensome reporting requirements.

Further, if we are classified as a PFIC for any year during which a U.S. shareholder holds our ordinary shares or ADSs, we generally will continue to be treated as a PFIC for all succeeding years during which such U.S. shareholder holds such ordinary

shares or ADSs. Each U.S. shareholder should consult its tax advisor regarding the PFIC rules and the U.S. federal income tax consequences of the acquisition, ownership and disposition of the ordinary shares and ADSs.

If you are a "Ten Percent Shareholder," you may be subject to adverse U.S. federal income tax consequences if we are classified as a Controlled Foreign Corporation.

Each "Ten Percent Shareholder" (as defined below) in a non-U.S. corporation that is classified as a "controlled foreign corporation" ("CFC"), for U.S. federal income tax purposes is generally required to include in income for U.S. federal tax purposes such Ten Percent Shareholder's pro rata share of the CFC's "Subpart F income" and investment of earnings in U.S. property, even if the CFC has made no distributions to its shareholders. Each Ten Percent Shareholder is also required to include in gross income its "global intangible low-taxed income," which is determined by reference to the income of CFCs of which such Ten Percent Shareholder is a Ten Percent Shareholder. Ten Percent Shareholders that are corporations may be entitled to a deduction equal to the foreign portion of any dividend when a dividend is paid. A non-U.S. corporation will generally be classified as a CFC for U.S. federal income tax purposes if Ten Percent Shareholders own in the aggregate, directly or indirectly, more than 50% of either the total combined voting power of all classes of stock of such corporation entitled to vote or of the total value of the stock of such corporation. A "Ten Percent Shareholder" is a U.S. person (as defined by the Internal Revenue Code of 1986, as amended), who owns or is considered to own 10% or more of the total combined voting power of all classes of stock entitled to vote of such corporation or 10% of the value of all classes of stock of such corporation. The determination of CFC status is complex and includes attribution rules, the application of which is not entirely certain.

Although we believe we are not a CFC now, we may become one or own interests in one in the future. Holders are urged to consult their own tax advisors with respect to our potential CFC status and the consequences thereof.

Item 1B. Unresolved Staff Comments

Not applicable.

Item 2. Properties

We lease all of our facilities, other than the following facilities that we own: our offices and laboratories in Changping, Beijing, our manufacturing facility in Guangzhou, China, and the site for our planned manufacturing facility and clinical R&D center at the Princeton Innovation Park in Hopewell, New Jersey. We lease an aggregate of approximately 91,000 square meters of office space at approximately 42 other locations across the United States, China, and Europe, in cities such as Cambridge, Massachusetts; Ridgefield Park, New Jersey; and Emeryville and San Mateo, California in the United States; Beijing, Shanghai, Suzhou, and Guangzhou in China; and Basel, Switzerland, primarily for our offices and for our manufacturing facility in Suzhou, China, pursuant to leases with various expiration dates, with the latest expiring in 2027. We believe that our facilities are currently suitable and sufficient to meet our needs. We intend to add new facilities or expand existing facilities as we add employees and enter new locations, and we believe that suitable additional or substitute space will be available as needed to accommodate any such expansion of our operations.

Please refer to "Note 9: Leases" in the notes to our consolidated financial statements in this Annual Report for further information on our real property leases.

Item 3. Legal Proceedings

From time to time we may become involved in legal proceedings or be subject to claims arising in the ordinary course of our business. We are not presently a party to any legal proceedings that, if determined adversely to us, would individually or taken together have a material adverse effect on our business, results of operations, financial condition or cash flows. Regardless of the outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

On June 26, 2020, following the suspension and recall of ABRAXANE® in China supplied to us by Celgene Logistics Sàrl, a Bristol Myers Squibb Company (referred to elsewhere in this report as BMS, but for this paragraph only, "BMS-Celgene"), we initiated an arbitration proceeding at the International Chamber of Commerce (the ICC) against BMS-Celgene asserting that it had breached and continues to breach the terms and conditions of the License and Supply Agreement entered into by BeiGene and BMS-Celgene in July 2017 and a related quality agreement (collectively, the "BMS-Celgene License"). Under the BMS-Celgene License, we allege that BMS-Celgene is obligated, among other things, to ensure the continuity and adequacy of its supply of ABRAXANE to us. In the arbitration proceeding, we are seeking (i) a declaration that BMS-Celgene was and is in breach of the BMS-Celgene License, (ii) a declaration that BMS-Celgene acted with gross negligence and/or willful misconduct, (iii) an award of damages, and (iv) such other relief as the arbitrators deem appropriate. BMS-Celgene responded in part by submitting a counterclaim against us seeking to recover approximately $30 million in costs that it contends it incurred

as part of the ABRAXANE recall. We believe that the allegations contained in the counterclaim are without merit and are defending the counterclaim vigorously. On October 6, 2021, BMS-Celgene delivered a notice to us purporting to terminate the BMS-Celgene License with respect to ABRAXANE and providing 180-days' notice that it was withdrawing ABRAXANE from the range of products for sale or distribution in China pursuant to Section 2.6 of the BMS-Celgene License. We believe that the reasons stated in the notice do not provide a valid basis for terminating the BMS-Celgene License with respect to ABRAXANE, and that the notice is a tactical maneuver on the part of BMS-Celgene to reduce its damages in the arbitration proceedings, and we have amended our claims to add a claim for wrongful termination of the BMS-Celgene License with respect to ABRAXANE. A hearing was held in the arbitration in June 2022, and no decision has been issued.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

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

Market Information

Our American Depositary Shares ("ADSs") have been publicly traded on the NASDAQ Global Select Market under the symbol "BGNE" since February 3, 2016. Our ordinary shares have been publicly traded on the Stock Exchange of Hong Kong Limited under the stock code "06160" since August 8, 2018. Our ordinary shares traded in Renminbi (the "RMB Shares") have been publicly traded on the Science and Technology Innovation Board of the Shanghai Stock Exchange in China under the stock code "688235" since December 15, 2021.

Shareholders

As of January 31, 2023, we had approximately 47,084 holders of record of our ordinary shares, 46,932 of which are holders of record of our RMB Shares, and 8 holders of record of our ADSs. These number do not include beneficial owners whose ordinary shares or ADSs are held by nominees in street name. Because many ordinary shares and ADSs are held by broker nominees, we are unable to estimate the total number of beneficial holders represented by these record holders.

Dividend Policy

Our board of directors has adopted a dividend policy which provides that we currently intend to retain all available funds and earnings, if any, to fund the development and expansion of our business, and we do not anticipate paying any cash dividends in the foreseeable future. Subject to applicable law and our amended and restated articles of association, any future determination to pay dividends will be made at the discretion of our board of directors and may be based on a number of factors, including our future operations and earnings, capital requirements and surplus, general financial condition, contractual restrictions and other factors that our board of directors may deem relevant. This dividend policy reflects our board of directors' current views on our financial and cash flow position. We intend to continue to review our dividend policy from time to time, and there can be no assurance that dividends will be paid in any particular amount, if at all, for any given period.

We have never declared or paid any dividends on our ordinary shares or any other securities. If we pay dividends in the future, in order for us to distribute dividends to our shareholders and holders of ADSs, we may rely to some extent on dividends distributed by our PRC subsidiaries. PRC regulations may restrict the ability of our PRC subsidiaries to pay dividends to us, and such distributions will be subject to PRC withholding tax. In addition, PRC regulations currently permit payment of dividends of a PRC company only out of accumulated distributable after-tax profits, as determined in accordance with our articles of association and the accounting standards and regulations in the PRC.

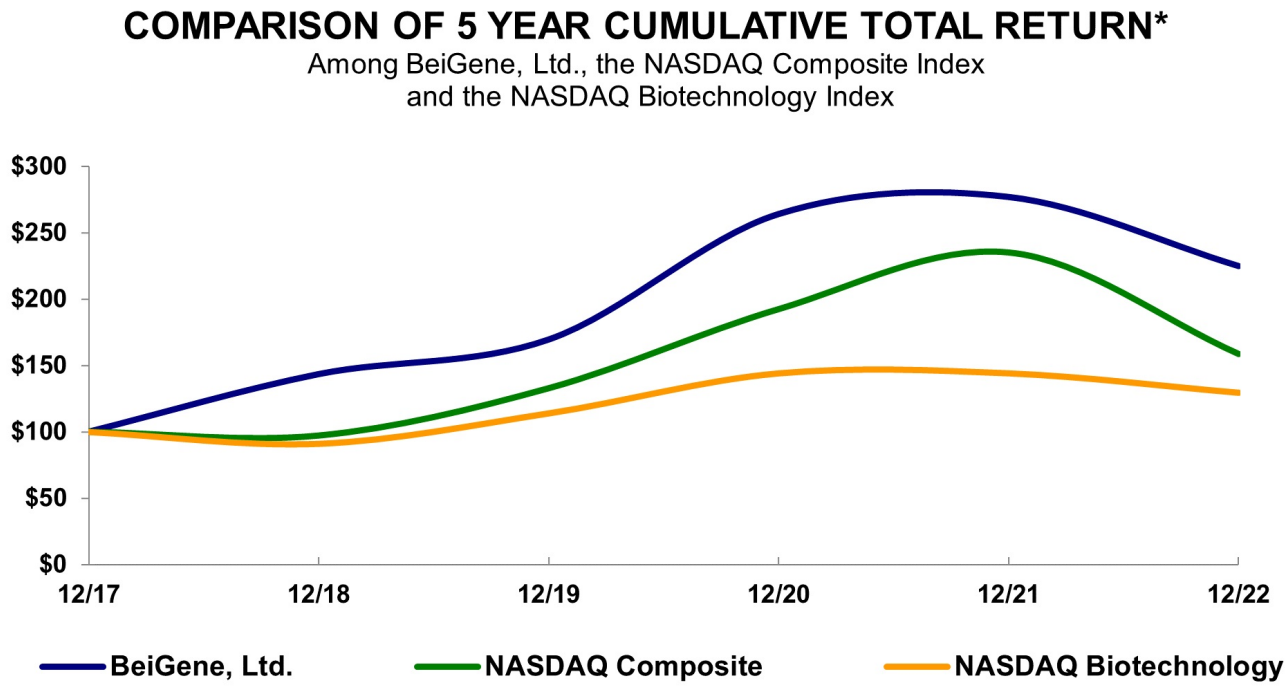
Investors should not purchase our ordinary shares, RMB Shares, or ADSs with the expectation of receiving cash dividends.

Performance Comparison Graph

This graph is not "soliciting material," is not deemed "filed" with the SEC and is not to be incorporated by reference into any of our filings under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing.

The following graph shows the total shareholder return of an investment of $100 in cash at market close on December 31, 2017 through December 31, 2022 for our ADSs, the NASDAQ Composite Index (U.S.), and the NASDAQ Biotechnology Index.

Pursuant to applicable SEC rules, all values assume reinvestment of the full amount of any dividends, although no dividends have been declared or paid to date. The shareholder return shown on the graph below is not necessarily indicative of future performance, and we do not make or endorse any predictions as to future shareholder returns.



	12/31/17	12/31/18	12/31/19	12/31/20	12/31/21	12/31/22
BeiGene, Ltd.	**100.00**	**143.53**	**169.63**	**264.42**	**277.25**	**225.07**
NASDAQ Composite	**100.00**	**97.16**	**132.81**	**192.47**	**235.15**	**158.65**
NASDAQ Biotechnology	**100.00**	**91.14**	**114.02**	**144.15**	**144.18**	**129.59**

Equity Compensation Plan Information

Our equity compensation plan information required by this item is incorporated by reference to the information in "Part III—Item 12—Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters" of this Annual Report.

Recent Sales of Unregistered Securities

None.

Issuer Purchases of Equity Securities

None.

Taxation

Cayman Islands Taxation

The Cayman Islands currently levies no taxes on individuals or corporations based upon profits, income, gains or appreciation, and there is no taxation in the nature of inheritance tax or estate duty or withholding tax applicable to us or to any holder of the ADSs, ordinary shares and RMB Shares. There are no other taxes likely to be material to us levied by the Government of the Cayman Islands except for stamp duties which may be applicable on instruments executed in, or after execution brought within, the jurisdiction of the Cayman Islands. No stamp duty is payable in the Cayman Islands on the issue of shares by, or any transfers of shares of, Cayman Islands companies (except those which hold interests in land in the Cayman Islands). The Cayman Islands is not party to any double tax treaties that are applicable to any payments made to or by our company. There are no exchange control regulations or currency restrictions in the Cayman Islands.

Payments of dividends and capital in respect of the ADSs, ordinary shares and RMB Shares will not be subject to taxation in the Cayman Islands and no withholding will be required on the payment of a dividend or capital to any holder of the ADSs, ordinary shares or RMB Shares, as the case may be, nor will gains derived from the disposal of the ADSs, ordinary shares or RMB Shares be subject to Cayman Islands income or corporation tax.

PRC Taxation

Under the Enterprise Income Tax Law ("EIT Law"), an enterprise established outside the PRC with a "de facto management body" within the PRC is considered a "resident enterprise," which means that it is treated in a manner similar to a Chinese enterprise for PRC enterprise income tax purposes. The implementation rules of the EIT Law define "de facto management body" as a managing body that exercises substantial and overall management and control over the production and operations, personnel, accounting and properties of an enterprise. In addition, the Notice Regarding the Determination of Chinese-Controlled Offshore Incorporated Enterprise as PRC Tax Resident Enterprises on the Basis of De Facto Management Bodies ("Circular 82)", issued by the State Administration of Taxation, which provides guidance on the determination of the tax residence status of a Chinese-controlled offshore incorporated enterprise, defines Chinese-controlled offshore incorporated enterprise as an enterprise that is incorporated under the laws of a foreign country or territory and that has a PRC enterprise or enterprise group as its primary controlling shareholder. Although BeiGene, Ltd. does not have a PRC enterprise or enterprise group as our primary controlling shareholder and is therefore not a Chinese-controlled offshore incorporated enterprise within the meaning of Circular 82, in the absence of guidance specifically applicable to us, we have applied the guidance set forth in Circular 82 to evaluate the tax residence status of BeiGene, Ltd. and its subsidiaries organized outside the PRC.

According to Circular 82, a Chinese-controlled offshore incorporated enterprise will be regarded as a PRC tax resident by virtue of having a "de facto management body" in China and will be subject to PRC enterprise income tax on its worldwide income only if all of the following criteria are met:

- the primary location of the enterprise's senior executives of the day-to-day operational management and senior management departments performing their duties is in the PRC;
- decisions relating to the enterprise's financial and human resource matters are made or are subject to approval by organizations or personnel in the PRC;
- the enterprise's primary assets, accounting books and records, company seals, and board and shareholder meeting minutes are located or maintained in the PRC; and
- 50% or more of voting board members or senior executives habitually reside in the PRC.

Currently, some of the members of our management team are located in China. However, we do not believe that we meet all of the conditions outlined in the immediately preceding paragraph. BeiGene, Ltd. and its offshore subsidiaries are incorporated outside the PRC. As a holding company, our key assets and records, including the resolutions and meeting minutes of our board of directors and the resolutions and meeting minutes of our shareholders, are located and maintained outside the PRC. We are not aware of any offshore holding companies with a corporate structure similar to ours that has been deemed a PRC "resident enterprise" by the PRC tax authorities. Accordingly, we believe that BeiGene, Ltd. and its offshore subsidiaries should not be treated as a "resident enterprise" for PRC tax purposes if the criteria for "de facto management body" as set forth in Circular 82 were deemed applicable to us. However, as the tax residency status of an enterprise is subject to determination by

the PRC tax authorities and uncertainties remain with respect to the interpretation of the term "de facto management body" as applicable to our offshore entities, we will continue to monitor our tax status.

The implementation rules of the EIT Law provide that, (1) if the enterprise that distributes dividends is domiciled in the PRC or (2) if gains are realized from transferring equity interests of enterprises domiciled in the PRC, then such dividends or capital gains are treated as China-sourced income. It is not clear how "domicile" may be interpreted under the EIT Law, and it may be interpreted as the jurisdiction where the enterprise is a tax resident. Therefore, if we are considered as a PRC tax resident enterprise for PRC tax purposes, any dividends we pay to our overseas shareholders or ADS holders as well as gains realized by such shareholders or ADS holders from the transfer of our shares or ADSs may be regarded as China-sourced income. As a result, dividends paid to non-PRC resident enterprise ADS holders or shareholders may be subject to PRC withholding tax at a rate of up to 10% (or 20% in the case of non-PRC individual ADS holders or shareholders) and gains realized by non-PRC resident enterprise ADS holders or shareholders from the transfer of our ordinary shares or ADSs may be subject to PRC tax at a rate of 10% (or 20% in the case of non-PRC individual ADS holders or shareholders). It is also unclear whether, if we are considered a PRC resident enterprise, holders of our shares or ADSs would be able to claim the benefit of income tax treaties or agreements entered into between China and other countries or areas.

Item 6. Reserved

Not applicable.

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

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and related notes appearing elsewhere in this Annual Report. In addition to historical information, this discussion and analysis contains forward-looking statements that involve risks, uncertainties and assumptions. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of certain factors. We discuss factors that we believe could cause or contribute to these differences below and elsewhere in this report, including those set forth under "Part I—Item 1A—Risk Factors" and under "Forward-Looking Statements and Market Data" in this Annual Report.

Overview

We are a global biotechnology company that is developing and commercializing innovative and affordable oncology medicines to improve treatment outcomes and access for patients worldwide.

We currently have three approved medicines that were discovered and developed in our own labs, including BRUKINSA®, a small molecule inhibitor of Bruton's Tyrosine Kinase (BTK) for the treatment of various blood cancers; tislelizumab, an anti-PD-1 antibody immunotherapy for the treatment of various solid tumor and blood cancers; and pamiparib, a selective small molecule inhibitor of PARP1 and PARP2. We have obtained approvals to market BRUKINSA in the United States, China, EU, the UK, Canada, Australia and additional international markets, and tislelizumab in China. By leveraging our China commercial capabilities, we have in-licensed the rights to distribute 13 approved medicines for the China market. Supported by our global clinical development and commercial capabilities, we have entered into collaborations with world-leading biopharmaceutical companies such as Amgen Inc. ("Amgen") and Novartis Pharma AG ("Novartis") to develop and commercialize innovative medicines.

We are committed to advancing best and first-in-class clinical candidates internally or with like-minded partners to develop impactful and affordable medicines for patients across the globe. Our internal clinical development capabilities are deep, including a more than 2,700-person global clinical development team that is running close to 80 ongoing or planned clinical trials in over 50 medicines and drug candidates. This includes more than 30 pivotal or potentially registration-enabling trials across our portfolio, including our three internally discovered, approved medicines. We have enrolled in our clinical trials more than 18,000 subjects, of which approximately one-half have been outside of China.

We have built, and are expanding, our internal manufacturing capabilities through our state-of-the-art biologic and small molecule manufacturing facilities in China to support current and potential future demand of our medicines, and are building a commercial-stage biologics manufacturing and clinical R&D center in New Jersey. We also work with high quality contract manufacturing organizations (CMOs) to manufacture our internally developed clinical and commercial products.

Since our inception in 2010, we have become a fully integrated global organization of over 9,000 employees in 29 countries and regions, including the United States, China, Europe, and Australia.

Recent Business Developments

On February 24, 2023, we announced that the China National Medical Products Administration ("NMPA") granted approval for our PD-1 inhibitor, tislelizumab, in combination with fluoropyrimidine and platinum chemotherapy, for the first-line treatment of patients with locally advanced unresectable or metastatic gastric or gastroesophageal junction adenocarcinoma with high PD-L1 expression.

On January 19, 2023, we announced that the U.S. Food and Drug Administration ("FDA") approved our Bruton's tyrosine kinase inhibitor BRUKINSA (zanubrutinib) for the treatment of adult patients with chronic lymphocytic leukemia ("CLL") or small lymphocytic lymphoma ("SLL").

On January 19, 2023, we announced that the Medicines and Healthcare products Regulatory Agency granted marketing authorizations for BRUKINSA in Great Britain for both the treatment of adult patients with CLL and the treatment of adult patients with marginal zone lymphoma ("MZL") who have received at least one prior anti-CD20-based therapy.

On January 18, 2023, we announced that the National Reimbursement Drug List ("NRDL") released by China's National Healthcare Security Administration ("NHSA") was updated to include four new indications for our PD-1 inhibitor tislelizumab. KYPROLIS® (carfilzomib), a proteosome inhibitor licensed-in from Amgen, is included for the first time and XGEVA® (denosumab), a RANKL inhibitor and another Amgen asset, successfully renewed this year. The updated NRDL will officially take effect on March 1, 2023.

On December 30, 2022, we announced that the Center for Drug Evaluation of the China National Medical Products Administration accepted a supplemental biologics license application for tislelizumab in patients with first-line unresectable or metastatic hepatocellular carcinoma.

On November 17, 2022, we announced that the European Commission approved BRUKINSA for the treatment of adult patients with treatment-naïve or relapsed/refractory ("R/R") CLL.

On November 10, 2022, we announced that BRUKINSA was approved in Brazil for the treatment of adult patients with Waldenström's macroglobulinemia ("WM") and adult patients with R/R MZL who have received at least one anti-CD20-based regimen.

Components of Operating Results

Revenue

Product Revenue

We generate product revenue through the sale of our three internally developed products and our in-licensed medicines from our partners.

Revenues from product sales are recognized when there is a transfer of control from the Company to the customer. The Company determines transfer of control based on when the product is delivered, and title passes to the customer. Revenues from product sales are recognized net of variable consideration resulting from rebates, chargebacks, trade discounts and allowances, sales returns allowances and other incentives. Provisions for estimated reductions to revenue are provided for in the same period the related sales are recorded and are based on contractual terms, historical experience and trend analysis.

Collaboration Revenue

We recognize collaboration revenue for amounts earned under collaborative and out-licensing arrangements. In January 2021, we entered into a collaboration and license agreement with Novartis, granting Novartis rights to develop, manufacture and commercialize tislelizumab in the United States, Canada, Mexico, member countries of the European Union, United Kingdom, Norway, Switzerland, Iceland, Liechtenstein, Russia, and Japan (the Novartis Territory). There were two performance obligations identified at the outset of the agreement: (1) the exclusive license to develop, manufacture, and commercialize tislelizumab in the Novartis Territory, transfer of know-how and use of the tislelizumab trademark and (2) conducting and completing tislelizumab R&D services. Under this agreement, we received an upfront cash payment, which was allocated between the two performance obligations identified in the agreement based on the relative standalone selling prices of the performance obligations. The portion allocated to the license was recognized upon the delivery of the license right and transfer of know-how. The portion of the upfront payment allocated to the tislelizumab R&D services was deferred and is being recognized as collaboration revenue as the tislelizumab R&D services are performed using a percentage of completion method. Estimated costs to complete are reassessed on a periodic basis and any updates to the revenue earned are recognized on a prospective basis.

In December 2021, we expanded our collaboration with Novartis by entering into an option, collaboration and license agreement with Novartis to develop, manufacture and commercialize our investigational TIGIT inhibitor ociperlimab in the Novartis Territory. In addition, we entered into an agreement with Novartis which granted us rights to market, promote and detail five approved Novartis oncology products, TAFINLAR® (dabrafenib), MEKINIST® (trametinib), VOTRIENT® (pazopanib), AFINITOR® (everolimus), and ZYKADIA® (ceritinib), across designated regions of China referred to as "broad markets." There were three performance obligations identified at the outset of the arrangement: (1) a material right for the option to the exclusive product license, (2) the right to access ociperlimab in clinical trials during the option period provided to Novartis, combined with the initial transfer of BeiGene know-how, and (3) conducting ociperlimab R&D services. The market development activities are considered immaterial in the context of the agreements. Under this agreement, we received an upfront cash payment, which was allocated between the three performance obligations identified in the agreement based on the relative standalone selling prices of the performance obligations. The portion allocated to the material right was deferred and will be recognized at the earlier of when Novartis exercises the option and the license is delivered or the expiration of the option period. The portion of the transaction price allocated to Novartis' right to access ociperlimab in its own clinical trials during the option period and the initial transfer of BeiGene know-how was deferred and is being recognized over the expected option period. The portion of the transaction price allocated to the ociperlimab R&D services was deferred and is being recognized as collaboration revenue as the ociperlimab R&D services are performed over the expected option period.

The option exercise fee under the ociperlimab agreement is contingent upon Novartis exercising its right, and is considered fully constrained until the option is exercised. The potential milestone payments that we are eligible to receive under both of the

Novartis collaborations were excluded from the initial transaction prices, as all milestone amounts are variable consideration and were fully constrained due to uncertainty of achievement. Performance-based milestones will be recognized when the milestone event is achieved or when the risk of revenue reversal is remote. Sales-based milestones and royalties will be recognized when the underlying sales occur.

Expenses

Cost of Sales

Cost of sales includes the costs to manufacture our internally developed commercial products, as well as costs to purchase tislelizumab from Boehringer Ingelheim. Additionally, cost of sales included the cost of in-licensed products purchased for sale in the PRC. Costs to manufacture inventory in preparation for commercial launch of a product incurred prior to regulatory approval are expensed to research and development expense as incurred. Cost of sales for newly launched products will not be recorded until the initial pre-launch inventory is depleted and additional inventory is manufactured. To date, the Company's initial pre-launch inventory for its commercial products has been immaterial and has not had a significant impact on the Company's gross margin.

Research and Development Expenses

Research and development expenses consist of the costs associated with our research and development activities, conducting preclinical studies and clinical trials, and activities related to regulatory filings. Our research and development expenses consist of:

- expenses incurred under agreements with contract research organizations (CROs), CMOs, and consultants that conduct and support clinical trials and preclinical studies;
- costs of comparator drugs in certain of our clinical trials;
- manufacturing costs related to pre-commercial activities;
- costs associated with preclinical activities and development activities;
- costs associated with regulatory operations;
- employee-related expenses, including salaries, benefits, travel and share-based compensation expense for research and development personnel;
- in-process research and development costs expensed as part of collaboration agreements entered into; and
- other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance and other supplies used in research and development activities.

Our current research and development activities mainly relate to the clinical advancement of our internally developed medicines and drug candidates:

- BRUKINSA (zanubrutinib), a small molecule inhibitor of BTK;
- tislelizumab, a humanized monoclonal antibody against PD-1;
- ociperlimab, an investigational humanized monoclonal antibody against TIGIT;
- pamiparib, a selective small molecule inhibitor of PARP1 and PARP2;
- BGB-15025, an investigational hematopoietic progenitor kinase 1 (HPK1) inhibitor;
- BGB-11417, an investigational small molecular inhibitor of Bcl-2;
- BGB-A445, an investigational non-ligand competing OX40 monoclonal antibody;
- BGB-16673, an investigational Chimeric Degradation Activating Compound ("CDAC"), targeting BTK; and
- BGB-A425, an investigational humanized monoclonal antibody against TIM-3;
- BGB-10188, an investigational PI3Kδ inhibitor;

- BGB-23339, a potent, allosteric investigational tyrosine kinase 2 (TYK2) inhibitor; and
- LBL-007, a novel investigational antibody targeting the LAG-3 pathway

Research and development activities also include costs associated with in-licensed drug candidates, including:

- R&D expense related to the co-development of pipeline assets under the Amgen collaboration agreement. Our total cost share obligation to Amgen is split between R&D expense and a reduction to the R&D cost share liability;
- sitravatinib, an investigational, spectrum-selective kinase inhibitor, licensed from Mirati Therapeutics, Inc. ("Mirati");
- ZW25 (zanidatamab) and ZW49, two investigational bispecific antibody-based product candidates targeting HER2, licensed from Zymeworks Inc. ("Zymeworks"); and
- POBEVCY® (BAT1706), a biosimilar to Avastin® (bevacizumab), licensed from Bio-Thera Solutions, Ltd. (Bio-Thera).

We expense research and development costs when incurred. We record costs for certain development activities, such as clinical trials, based on an evaluation of the progress to completion of specific tasks using data such as subject enrollment, clinical site activations or information our vendors provide to us. We expense the manufacturing costs of our internally developed products that are used in clinical trials as they are incurred as research and development expense. We do not allocate employee-related costs, depreciation, rental and other indirect costs to specific research and development programs because these costs are deployed across multiple product programs under research and development and, as such, are separately classified as unallocated research and development expenses.

At this time, it is difficult to estimate or know for certain, the nature, timing and estimated costs of the efforts that will be necessary to complete the development of our internally developed and in-licensed medicines and drug candidates. This is due to the numerous risks and uncertainties associated with developing such medicines and drug candidates, including the uncertainty of:

- successful enrollment in and completion of clinical trials;
- establishing an appropriate safety and efficacy profile;
- establishing and maintaining commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- receipt of marketing and other required approvals from applicable regulatory authorities;
- successfully launching and commercializing our medicines and drug candidates, if and when approved, whether as monotherapies or in combination with our medicines and drug candidates or third-party products;
- market acceptance, pricing and reimbursement;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our medicines and drug candidates;
- continued acceptable safety and efficacy profiles of the products following approval;
- sufficient supply of the products following approval;
- competition from competing products; and
- retention of key personnel.

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

Research and development activities are central to our business model. We expect continued substantial investment in research and development for the foreseeable future as our discovery and development programs progress, as we continue to support the clinical trials of our medicines and drug candidates as treatments for various cancers and as we move these medicines and drug candidates into additional clinical trials, including potential pivotal trials. There are numerous factors associated with the successful commercialization of any of our medicines and drug candidates, including future trial design and

various regulatory requirements, many of which cannot be determined with accuracy at this time based on our stage of development. Additionally, future commercial and regulatory factors beyond our control may impact our clinical development and commercial programs and plans.

Selling, General and Administrative Expenses

Selling, general and administrative expenses consist primarily of product promotion costs, distribution costs, salaries and related benefit costs, including share-based compensation for selling, general and administrative personnel. Other selling, general and administrative expenses include professional fees for legal, consulting, auditing and tax services as well as other direct and allocated expenses for rent and maintenance of facilities, travel costs, insurance and other supplies used in selling, general and administrative activities. We anticipate that our selling, general and administrative expenses will increase in future periods to support planned increases in commercialization activities for our approved medicines, and the preparation for potential launch and commercialization of additional in-licensed products from our collaborations and internally developed products, if approved. We also incur significant legal, compliance, accounting, insurance and investor and public relations expenses associated with being a public company with our ADSs, ordinary shares and RMB Shares listed for trading on The Nasdaq Global Select Market, The Hong Kong Stock Exchange and The STAR Market of the Shanghai Stock Exchange, respectively.

Interest Income (Expense), Net

Interest Income

Interest income consists primarily of interest generated from our RMB-denominated cash deposits and short-term investments in money market funds, time deposits, U.S. Treasury securities and U.S. agency securities.

Interest Expense

Interest expense consists primarily of interest on our bank loans and related party loan.

Other (Expense) Income, Net

Other (expense) income consists primarily of gains and losses recognized related to fluctuations in foreign currency exchange rates, gains and losses on equity investments, government grants and subsidies received that involve no conditions or continuing performance obligations by us, unrealized gains and losses on equity securities, and realized gains and losses on the sale of investments. We hold significant cash in the form of RMB-denominated deposits at U.S. functional currency entities, including a large portion of the cash generated from the STAR Market offering in December 2021. Other (expense) income includes the revaluation gains and losses of these cash deposits based on foreign currency exchange rates.

Results of Operations

Comparison of the Years Ended December 31, 2022 and 2021

The following table summarizes our results of operations for the years ended December 31, 2022 and 2021:

	Year Ended December 31,		Change	
	2022	2021	$	%
	(dollars in thousands)			
Revenues				
Product revenue, net	$ 1,254,612	$ 633,987	$ 620,625	97.9 %
Collaboration revenue	161,309	542,296	(380,987)	(70.3)%
Total revenues	1,415,921	1,176,283	239,638	20.4 %
Expenses				
Cost of sales - product	286,475	164,906	121,569	73.7 %
Research and development	1,640,508	1,459,239	181,269	12.4 %
Selling, general and administrative	1,277,852	990,123	287,729	29.1 %
Amortization of intangible assets	751	750	1	0.1 %
Total expenses	3,205,586	2,615,018	590,568	22.6 %
Loss from operations	(1,789,665)	(1,438,735)	(350,930)	24.4 %
Interest income (expense), net	52,480	(15,757)	68,237	(433.1)%
Other (expense) income, net	(223,852)	15,904	(239,756)	(1,507.5)%
Loss before income tax expense	(1,961,037)	(1,438,588)	(522,449)	36.3 %
Income tax expense	42,778	19,228	23,550	122.5 %
Net loss	(2,003,815)	(1,457,816)	(545,999)	37.5 %
Less: Net loss attributable to noncontrolling interest	—	—	—	NM
Net loss attributable to BeiGene, Ltd.	$ (2,003,815)	$ (1,457,816)	$ (545,999)	37.5 %

Revenue

Total revenue increased by $239.6 million to $1.4 billion for the year ended December 31, 2022, from $1.2 billion for the year ended December 31, 2021, primarily due to increases in sales of our internally developed products and in-licensed products, partially offset by a decrease in collaboration revenue, as the prior year period included the recognition of the majority of the $650 million upfront payment from Novartis as license revenue.

The following table summarizes the components of revenue for the year ended December 31, 2022 and 2021, respectively:

	Year Ended December 31,		Changes	
	2022	2021	$	%
	(dollars in thousands)			
Product revenue	$ 1,254,612	$ 633,987	$ 620,625	97.9 %
Collaboration revenue:				
License revenue	—	484,646	(484,646)	(100.0)%
Research and development service revenue	46,822	53,671	(6,849)	(12.8)%
Right to access intellectual property revenue	104,994	3,979	101,015	2,538.7 %
Other	9,493	—	9,493	NM
Total collaboration revenue	161,309	542,296	(380,987)	(70.3)%
Total Revenue	$ 1,415,921	$ 1,176,283	$ 239,638	20.4 %

Net product revenue consisted of the following:

	Year Ended December 31,		Changes	
	2022	2021	$	%
	(dollars in thousands)			
BRUKINSA®	$ 564,651	$ 217,987	$ 346,664	159.0 %
Tislelizumab	422,885	255,119	167,766	65.8 %
REVLIMID®	79,049	70,065	8,984	12.8 %
XGEVA®	63,398	45,956	17,442	38.0 %
POBEVCY®	38,124	1,353	36,771	2,717.7 %
BLINCYTO®	36,107	12,515	23,592	188.5 %
VIDAZA®	15,213	19,591	(4,378)	(22.3)%
KYPROLIS®	13,696	—	13,696	NM
Pamiparib	5,460	3,661	1,799	49.1 %
Other	16,029	7,740	8,289	107.1 %
Total product revenue	$ 1,254,612	$ 633,987	$ 620,625	97.9 %

Net product revenue was $1.3 billion for the year ended December 31, 2022, compared to $634.0 million in the prior year, primarily due to increased sales of BRUKINSA in the United States and China and tislelizumab in China, in-licensed sales of Amgen's BLINCYTO®, which we began distributing in August 2021, and XGEVA, as well as Bio-Thera's POBEVCY. During 2022, we continued to see increased patient demand in China for tislelizumab and BRUKINSA due to the inclusion on the National Reimbursement Drug List ("NRDL"), and this demand more than offset the effect of the related price reductions.

Global sales of BRUKINSA totaled $564.7 million for the year ended December 31, 2022, representing a 159.0% increase compared to the prior year; U.S. sales of BRUKINSA totaled $389.7 million for the year ended December 31, 2022 compared to $115.7 million in the prior year, representing growth of 237.0%. U.S. sales accelerated in the period, driven by increased uptake in MCL, WM and MZL. BRUKINSA sales in China totaled $150.3 million for the year ended December 31, 2022, representing growth of 48.6% compared to the prior year, driven by a significant increase in all approved indications, including CLL/SLL.

Sales of tislelizumab in China totaled $422.9 million for the year ended December 31, 2022, representing a 65.8% increase compared to the prior year. During the year ended December 31, 2022, new patient demand from broader reimbursement and further expansion of our salesforce and hospital listings continued to drive increased market penetration and market share for tislelizumab. Full year 2021 sales of tislelizumab included two negative adjustments totaling $45.6 million for distributor channel inventory compensation as a result of inclusion in the March 2021 and January 2022 NRDL lists.

Product revenues for the year ended December 31, 2021 were negatively impacted by adjustments of $57.5 million as a result of compensating distributors for products previously sold at the pre-NRDL price, which remained in the distribution channel, due to the first inclusion of tislelizumab, BRUKINSA, and XGEVA in the updated NRDL effective March 1, 2021 and additional indications for tislelizumab, BRUKINSA and pamiparib effective January 1, 2022. During the year ended December 31, 2021, the inclusion of tislelizumab, BRUKINSA, XGEVA, and pamiparib in the NRDL significantly increased patient demand that more than offset the net effect of price reductions as a result of NRDL inclusion.

Collaboration revenue totaled $161.3 million for the year ended December 31, 2022, of which $46.8 million was recognized from deferred revenue for R&D services performed during the year ended December 31, 2022 under both the tislelizumab and ociperlimab collaborations, $105.0 million was recognized from deferred revenue for Novartis' right to access ociperlimab over the option period, and $9.5 million was recognized related to the sale of tislelizumab clinical supply to Novartis. Collaboration revenue totaled $542.3 million for the year ended December 31, 2021, of which $484.6 million was recognized upon delivery of the tislelizumab license right and transfer of know-how to Novartis, $53.7 million was recognized from deferred revenue for R&D services performed during the year ended December 31, 2021 under both the tislelizumab and ociperlimab collaborations, and $4.0 million was recognized from deferred revenue for Novartis' right to access ociperlimab over the option period (see Note 4 to our consolidated financial statements included in this Annual Report on Form 10-K).

Cost of Sales

Cost of sales increased to $286.5 million for the year ended December 31, 2022 from $164.9 million for the year ended December 31, 2021, primarily due to increased product sales of tislelizumab, BRUKINSA and XGEVA, as well as initial sales of BLINCYTO®, which we began selling in August 2021, and initial sales of KYPROLIS and POBEVCY.

Gross Margin

Gross margin on global product sales increased to $968.1 million for the year ended December 31, 2022, compared to $469.1 million for the year ended December 31, 2021, primarily due to increased product revenue in the current year period. Gross margin as a percentage of product sales increased to 77.2% for the year ended December 31, 2022, from 74.0% in the prior year. The increase is primarily due to proportionally higher sales mix of global BRUKINSA sales and sales of tislelizumab in China compared to lower margin sales of in-licensed products and lower costs per unit for both BRUKINSA and tislelizumab, partially offset by a lower average selling price for both BRUKINSA and tislelizumab.

Research and Development Expense

Research and development expense increased by $181.3 million, or 12.4%, to $1.6 billion for the year ended December 31, 2022, from $1.5 billion for the year ended December 31, 2021. The following table summarizes the external cost of development programs, upfront license fees, and internal research and development expense for the years ended December 31, 2022 and 2021:

	Year Ended December 31,		Changes	
	2022	2021	$	%
	(dollars in thousands)			
External research and development expense:				
Cost of development programs	$ 469,497	$ 477,761	$ (8,264)	(1.7)%
Upfront license fees	68,665	83,500	(14,835)	(17.8)%
Amgen co-development expenses[1]	98,955	115,464	(16,509)	(14.3)%
Total external research and development expenses	637,117	676,725	(39,608)	(5.9)%
Internal research and development expenses	1,003,391	782,514	220,877	28.2 %
Total research and development expenses	$ 1,640,508	$ 1,459,239	$ 181,269	12.4 %

1. Our co-funding obligation for the development of the pipeline assets under the Amgen collaboration for the year ended December 31, 2022 totaled $195.4 million, of which $99.0 million was recorded as R&D expense. The remaining $96.4 million was recorded as a reduction for the R&D cost share liability.

The decrease in external research and development expenses for the year ended December 31, 2022 was primarily attributable to lower upfront license fees under collaboration agreements, lower external spending related to fees paid to CROs as we internalize previously outsourced activities, and a decrease in the expense recognized on co-development fees to Amgen.

Internal research and development expense increased $220.9 million, or 28.2%, to $1.0 billion and was primarily attributable to the expansion of our global development organization and our clinical and preclinical drug candidates, as well as our continued efforts to internalize research and clinical trial activities, and included the following:

- $114.7 million increase of employee salary and benefits, primarily attributable to hiring more research and development personnel to support our expanding research and development activities;
- $57.6 million increase of materials and reagent expenses, primarily in connection with the in-house manufacturing of drug candidates used for clinical purposes;
- $47.6 million increase of facilities, depreciation, office expense, rental fees, and other expenses to support the growth of our organization;
- $25.0 million increase of share-based compensation expense, primarily attributable to our increased headcount of research and development employees, resulting in more awards being expensed; and
- $24.0 million decrease of consulting fees, including decreased meeting expense related to scientific, regulatory and development consulting activities, in connection with the advancement of our drug candidates.

Selling, General and Administrative Expense

Selling, general and administrative expense increased by $287.7 million, or 29.1%, to $1,277.9 million for the year ended December 31, 2022, from $990.1 million for the year ended December 31, 2021. The increase was primarily attributable to the following:

- $176.4 million increase of employee salary and benefits, which was primarily attributable to the hiring of personnel to support our growing business, including the expansion of our commercial organizations in China, the United States, Canada, Europe and emerging markets;
- $46.0 million increase in external commercial-related expenses, including market research, market access studies and promotional activities, related to the growth of our global commercial organization, as we continue to build our worldwide footprint and capabilities;
- $37.5 million increase of share-based compensation expense, primarily attributable to our increased headcount of sales and administrative employees, resulting in more awards being expensed; and
- $27.8 increase of professional fees, consulting, recruiting, information technology, tax, accounting and audit services, and facility expenses, rental fees, office expenses, and other administrative expenses, primarily attributable to the global expansion of our business, including the expansion of our commercial operations in China, the United States and Europe.

Interest Income (Expense), Net

Interest income (expense), net increased by $68.2 million, or 433.1%, to $52.5 million of net interest income for the year ended December 31, 2022, from $15.8 million of net interest expense for the year ended December 31, 2021. The increase in interest income (expense), net, was primarily attributable to increased interest income resulting from the increase in cash balances resulting from the STAR Offering proceeds in the fourth quarter of 2021, as well as higher interest rates earned on our cash, cash equivalents and short-term investments.

Other (Expense) Income, Net

Other (expense) income, net decreased by $239.8 million to $223.9 million of expense for the year ended December 31, 2022, from $15.9 million of income for the year ended December 31, 2021. The increase in expense for the year ended December 31, 2022 was primarily related to foreign exchange losses resulting from the strengthening of the U.S. dollar and the revaluation impact of foreign currencies held in U.S. functional currency subsidiaries. Also contributing to the increase in expense was an increase in the unrealized loss on our equity investments. These losses were partially offset by increased income from government subsidies.

Income Tax Expense

Income tax expense was $42.8 million for the year ended December 31, 2022 compared with $19.2 million for the year ended December 31, 2021. The income tax expense for the year ended December 31, 2022 was primarily attributable to current China tax expense for certain subsidiaries determined after certain non-deductible expenses and current U.S. tax expense, as a result of amendments to Internal Revenue Code (IRC) Section 174 pursuant to the 2017 Tax Cuts and Jobs Act, which took effect January 1, 2022, and eliminates the ability to fully deduct research and development expenditures in the year incurred, and requires capitalization and amortization. Other current tax expense was primarily attributable to foreign non-creditable withholding taxes.

Liquidity and Capital Resources

The following table represents our cash, short-term investments, and debt balances as of December 31, 2022:

	Year Ended December 31,	
	2022	2021
	(in thousands)	
Cash, cash equivalents and restricted cash	$ 3,875,037	$ 4,382,887
Short-term investments	$ 665,251	$ 2,241,962
Total debt	$ 538,117	$ 629,678

We have incurred annual net losses and negative cash flows from operations since inception, resulting from the funding of our research and development programs and selling, general and administrative expenses associated with our operations, as well as to support the commercialization of our products globally. We incurred net losses of $2.0 billion and $1.5 billion for the years ended December 31, 2022 and 2021, respectively. As of December 31, 2022, we had an accumulated deficit of $7.1 billion.

To date, we have financed our operations principally through proceeds from public and private offerings of our securities and proceeds from our collaborations, together with product sales since September 2017. Based on our current operating plan, we expect that our existing cash, cash equivalents and short-term investments as of December 31, 2022 will enable us to fund our operating expenses and capital expenditure requirements for at least the next 12 months after the date that the financial statements included in this report are issued.

On December 15, 2021, we completed the initial public offering on the SSE. The shares offered in the STAR Offering were issued to and subscribed for by permitted investors in the People's Republic of China ("PRC") in Renminbi ("RMB Shares"). The public offering price of the RMB Shares was RMB192.60 per ordinary share, or $391.68 per ADS. In this offering, we sold 115,055,260 ordinary shares. Net proceeds after deducting underwriting commissions and offering expenses were $3.4 billion. As required by the PRC securities laws, the net proceeds from the STAR Offering must be used in compliance with the planned uses as disclosed in the PRC prospectus as well as our proceeds management policy for the STAR Offering approved by our board of directors.

In January 2021, we entered into a collaboration and license agreement with Novartis, granting Novartis rights to develop, manufacture and commercialize tislelizumab in North America, Europe, and Japan. Under the agreement, we received an upfront cash payment of $650 million from Novartis. In December 2021, we expanded our collaboration with Novartis by entering into an option, collaboration and license agreement with Novartis to develop, manufacture and commercialize our investigational TIGIT inhibitor ociperlimab in the Novartis Territory. In addition, we and Novartis entered into an agreement granting us rights to market, promote and detail five approved Novartis oncology products. Under the terms of the agreement, we received an upfront cash payment of $300 million in January 2022.

The following table provides information regarding our cash flows for the years ended December 31, 2022 and 2021:

	Year Ended December 31,	
	2022	2021
	(in thousands)	
Cash, cash equivalents and restricted cash at beginning of period	$ 4,382,887	$ 1,390,005
Net cash used in operating activities	(1,496,619)	(1,298,723)
Net cash provided by investing activities	1,077,123	640,659
Net cash (used in) provided by financing activities	(18,971)	3,636,911
Net effect of foreign exchange rate changes	(69,383)	14,035
Net (decrease) increase in cash, cash equivalents and restricted cash	(507,850)	2,992,882
Cash, cash equivalents and restricted cash at end of period	$ 3,875,037	$ 4,382,887

Operating Activities

Cash flows from operating activities is net loss adjusted for certain non-cash items and changes in assets and liabilities.

Operating activities used $1.5 billion of cash for the year ended December 31, 2022, which resulted principally from our net loss of $2.0 billion, inclusive of $223.9 million of other losses due primarily to the strengthening of the U.S. dollar and the related revaluation of foreign currencies held by U.S. functional currency subsidiaries, partially offset by non-cash charges and adjustments of $374.8 million, and by a decrease in our net operating assets and liabilities of $132.4 million. The non-cash charges and adjustments were primarily driven by share-based compensation expense, charges for acquired in-process research and development costs, and depreciation and amortization expense, offset by amortization of the research and development cost share liability. The decrease in working capital was driven largely by decreases in accounts receivable and prepaid expenses and an increase in taxes payable, partially offset by a decrease in deferred revenue and an increase in inventories.

Operating activities used $1.3 billion of cash for the year ended December 31, 2021, which resulted principally from our net loss of $1.5 billion and an increase in our net operating assets and liabilities of $118.3 million, partially offset by non-cash charges and adjustments of $277.4 million. The non-cash charges and adjustments were primarily driven by share-based compensation expense, charges for acquired in-process research and development costs, and depreciation and amortization expense, offset by amortization of the research and development cost share liability. The increase in working capital was driven

largely by increases in accounts receivable, inventory and prepaid expenses, offset by increases in accounts payable, accrued expenses and other liabilities and deferred revenue resulting from the upfront option payment from Novartis.

Investing Activities

Cash flows from investing activities consist primarily of capital expenditures, investment purchases, sales, maturities, and disposals, and upfront payments related to our collaboration agreements.

Investing activities provided $1.1 billion of cash for the year ended December 31, 2022, consisting of $1.6 billion in sales and maturities of investment securities, partially offset by $325.4 million of capital expenditures, $143.7 million upfront collaboration payments, $15.9 million in purchases of long-term investments and $1.5 million in purchases of short-term investment securities.

Investing activities provided $640.7 million of cash for the year ended December 31, 2021, consisting of $2.1 billion in purchases of short-term investment securities, $262.9 million of capital expenditures, $43.4 million in purchases of intangible assets, $43.5 million in purchases of long-term investments and $8.5 million upfront collaboration payments, all of which were offset by sales and maturities of investment securities of $3.1 billion.

Financing Activities

Cash flows from financing activities consist primarily of sale of ordinary shares, RMB Shares, and ADSs through equity offerings, issuance and repayment of short-term and long-term debt, and proceeds from the sale of ADSs through employee equity compensation plans.

Financing activities used $19.0 million of cash for the year ended December 31, 2022, consisting primarily of $417.1 million of repayment of short-term loans, partially offset by $313.8 million from proceeds of short-term loans, $47.0 million from the exercise of employee share options and proceeds from the issuance of shares through our employee share purchase plan and $37.4 million from proceeds of long-term bank loans.

Financing activities provided $3.6 billion of cash for the year ended December 31, 2021, consisting primarily of $3.4 billion of net proceeds from our STAR Offering in December 2021, $406.4 million from proceeds of short-term loans, $92.8 million from the exercise of employee share options and proceeds from the issuance of shares through our employee share purchase plan, $50.0 million from the sale of our shares to Amgen, and $16.8 million from proceeds of long-term bank loans. These inflows were partially offset by $321.8 million of repayment of short-term loans.

Effects of Exchange Rates on Cash

We have substantial operations in the PRC, which generate a significant amount of RMB-denominated cash from product sales and require a significant amount of RMB-denominated cash to pay our obligations. Additionally, on December 15, 2021, we received RMB21.7 billion in net proceeds from the STAR Offering. Since the reporting currency of the Company is the U.S. dollar, periods of volatility in exchange rates may have a significant impact on our consolidated cash balances.

Future Liquidity and Material Cash Requirements

Until such time, if ever, as we can generate substantial product revenue sufficient to cover our costs and capital investments, we may be required to finance our cash needs through a combination of equity offerings, debt financings, collaboration agreements, strategic alliances, licensing arrangements, government grants, and other available sources. Under the rules of the SEC, we currently qualify as a “well-known seasoned issuer,” which allows us to file shelf registration statements to register an unspecified amount of securities that are effective upon filing. In May 2020, we filed such a shelf registration statement with the SEC for the issuance of an unspecified amount of ordinary shares (including in the form of ADSs), preferred shares, various series of debt securities and/or warrants to purchase any of such securities, either individually or in units, from time to time at prices and on terms to be determined at the time of any such offering. This registration statement was effective upon filing and will remain in effect for up to three years from filing, prior to which time we may file another shelf registration statement that will be effective for up to three years from filing.

To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our shareholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a holder of ADSs, ordinary shares, or RMB Shares. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures, or declaring dividends, and may require the issuance of warrants, which could potentially dilute your ownership interest. If we raise additional funds through collaboration agreements, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our medicines or drug candidates, future revenue streams or

research programs, or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings, collaborations or other sources when needed, we may be required to delay, limit, reduce or terminate our product development or commercialization efforts or grant rights to develop and market products or drug candidates that we would otherwise prefer to develop and market ourselves.

Our material cash requirements in the short- and long-term consist of the following operational, capital, and manufacturing expenditures, a portion of which contain contractual or other obligations. We plan to fund our material cash requirements with our current financial resources together with our anticipated receipts of accounts receivable, product sales and royalty revenues, and reimbursements we expect to receive under our existing collaboration and license agreements.

Contractual and Other Obligations

The following table summarizes our significant contractual obligations as of December 31, 2022:

		Payments Due by Period	
	Total	Short-term	Long-term
		(in thousands)	
Contractual obligations:			
Operating lease commitments	$ 63,024	$ 26,278	$ 36,746
Purchase commitments	117,293	74,449	42,844
Debt obligations	538,117	328,969	209,148
Interest on debt	45,947	16,632	29,315
Co-development funding commitment	595,702	231,697	364,005
Funding commitment	16,000	7,000	9,000
Research and development commitment	22,327	5,829	16,498
Pension plan	7,760	2,553	5,207
Capital commitments	404,914	404,914	—
Total	$ 1,811,084	$ 1,098,321	$ 712,763

Operating Lease Commitments

We lease office or manufacturing facilities in Beijing, Shanghai, Suzhou and Guangzhou in China; office facilities in California, Massachusetts, Maryland, and New Jersey in the United States; and in Basel, Switzerland under non-cancelable operating leases expiring on various dates. Payments under operating leases are expensed on a straight-line basis over the respective lease terms. The aggregate future minimum payments under these non-cancelable operating leases are summarized in the table above.

Purchase Commitments

As of December 31, 2022, purchase commitments amounted to $117.3 million, of which $55.3 million related to minimum purchase requirements for supply purchased from CMOs and $61.9 million related to binding purchase order obligations of inventory from BMS and Amgen. We do not have any minimum purchase requirements for inventory from BMS or Amgen.

Debt Obligations and Interest

Total debt obligations coming due in the next twelve months is $329.0 million. Total long-term debt obligations are $209.1 million. See Note 14 in the Notes to the Financial Statements for further detail of our debt obligations.

Interest on bank loans is paid quarterly until the respective loans are fully settled. For the purpose of contractual obligations calculation, current interest rates on floating rate obligations were used for the remainder contractual life of the outstanding borrowings.

Co-Development Funding Commitments

Under our collaboration with Amgen, we are responsible for co-funding global clinical development costs for the licensed oncology pipeline assets, up to a total cap of $1.25 billion. We are funding our portion of the co-development costs by contributing cash and/or development services. As of December 31, 2022, our remaining co-development funding commitment was $0.6 billion.

Funding Commitment

Funding commitment represents our committed capital related to two of our equity method investments in the amount of $19.0 million. As of December 31, 2022, our remaining capital commitment was $16.0 million and is expected to be paid from time to time over the investment period.

Research and Development Commitment

We entered into long-term research and development agreements, which includes obligations to make upfront payments and fixed quarterly payments over the next four years. As of December 31, 2022, the total research and development commitment amounted to $22.3 million.

Pension Plan

We maintain a defined benefit pension plan in Switzerland. Funding obligations under the defined benefit pension plan are equivalent to $2.6 million per year based on annual funding contributions in effect as of December 31, 2022 to achieve fully funded status where the market value of plan assets equals the projected benefit obligations. Future funding requirements will be subject to change as a result of future changes in staffing and compensation levels, various actuarial assumptions and actual investment returns on plan assets.

Capital Commitments

We had capital commitments amounting to $404.9 million for the acquisition of property, plant and equipment as of December 31, 2022, which were mainly for our manufacturing and clinical R&D campus in Hopewell, NJ, additional capacity at the Guangzhou and Suzhou manufacturing facilities, and new building for Beijing Innerway Bio-tech Co., Ltd.

Other Obligations

We expect to make a significant investment in our future manufacturing facility in the United States, a 42-acre site that will be constructed in Hopewell, NJ, and for which we purchased for $75.2 million. We expect significant capital expenditures as we build out the Hopewell facility over the next several years.

We also enter into agreements in the ordinary course of business with CROs to provide research and development services. These contracts are generally cancellable at any time by us with prior written notice.

We also enter into collaboration agreements with institutions and companies to license intellectual property. We may be obligated to make future development, regulatory and commercial milestone payments and royalty payments on future sales of specified products associated with these agreements. Payments under these agreements generally become due and payable upon achievement of such milestones or sales. These commitments are not recorded on our balance sheet because the achievement and timing of these milestones are not fixed and determinable. When the achievement of these milestones or sales have occurred, the corresponding amounts are recognized in our financial statements.

Critical Accounting Estimates

Our discussion and analysis of our financial condition and results of operations is based on our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States of America (GAAP). The preparation of these financial statements requires us to make estimates, assumptions and judgments that affect the reported amounts of assets, liabilities, revenues, costs and expenses. We evaluate our estimates and judgments on an ongoing basis, and our actual results may differ from these estimates. We base our estimates on historical experience, known trends and events, contractual milestones and other various factors that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources.

Certain of these estimates are considered critical as they involve a significant level of estimation uncertainty and have had or are reasonably likely to have a material impact on our consolidated financial statements. Our critical accounting estimates are summarized below. See Note 2 to our consolidated financial statements included in this Annual Report for a description of our significant accounting policies.

Revenue Recognition

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

Product Revenue

To determine the appropriate transaction price for our product sales at the time we recognize a sale to a direct customer, we estimate any rebates, chargebacks or discounts that ultimately will be due to the direct customer and other customers in the distribution chain under the terms of our contracts. Significant judgments are required in making these estimates. We include variable consideration in the transaction price to the extent it is probable that a significant reversal will not occur and estimate variable consideration from rebates, chargebacks, trade discounts and allowances, sales returns allowances, and other incentives using the expected value method.

Estimates for variable consideration for which reserves are established at the time of sale include government and commercial rebates, provisions for acceptance of NRDL pricing, chargebacks, trade discounts and allowances, sales returns allowances and other incentives that are offered within contracts between the Company and our customers, health care providers and other indirect customers. Where appropriate, these estimates take into consideration a range of possible outcomes that are probability-weighted for relevant factors such as our historical experience, current contractual and statutory requirements, channel inventory levels, specific known market events and trends, industry data and forecasted customer buying and payment patterns.

We base our sales returns allowance on estimated distributor inventories, customer demand as reported by third-party sources, and actual returns history, as well as other factors, as appropriate. For newly launched products where actual returns history is not yet available, the sales returns allowance is initially calculated based on benchmarking data from similar products and industry experience. If the historical or benchmarking data we use to calculate these estimates do not properly reflect future returns, then a change in the allowance would be made in the period in which such a determination is made and revenues in that period could be materially affected. Any changes from the historical trend rates are considered in determining the current sales return allowance. To date, sales returns have not been significant.

Actual amounts of consideration ultimately received may differ from our estimates. We will reassess estimates for variable consideration periodically. If actual results in the future vary from our estimates, we will adjust these estimates, which would affect net product revenue and earnings in the period such variances become known.

Collaboration Revenue

Our collaborative arrangements may contain more than one unit of account, or performance obligation, including grants of licenses to intellectual property rights, agreements to provide research and development services and other deliverables. As part of the accounting for these arrangements, we must develop assumptions that require significant judgments to determine the standalone selling price for each performance obligation identified in the contract.

Standalone selling prices for licenses of intellectual property and the right to access and use intellectual property during an option period performance obligations are determined based on the probability-weighted present value of forecasted cash flows associated with the intellectual property. Stand-alone selling prices for research and development services performance obligations are based on the present value of estimated clinical trial costs plus a reasonable margin.

The estimates of standalone selling prices involve management's key assumptions such as revenue growth rate, estimated clinical trial costs, mark-up rate, probability of technical and regulatory success, and discount rates. These significant assumptions are forward looking and could be affected by future economic, regulatory and market conditions.

Research and Development Expenses

Clinical trial costs are a significant component of our research and development expenses. We have a history of contracting with third parties that perform various clinical trial activities on behalf of us in the ongoing development of our product candidates. Expenses related to clinical trials are accrued based on our estimates of the actual services performed by the third parties for the respective period. If the contracted amounts are modified (for instance, as a result of changes in the clinical trial protocol or scope of work to be performed), we will modify the related accruals accordingly on a prospective basis. Revisions in the scope of a contract are charged to expense in the period in which the facts that give rise to the revision become reasonably certain.

The process of estimating our external research and development expenses involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated costs incurred for the services when we have not yet been invoiced or otherwise notified of the actual costs. The majority of our service providers invoice us in arrears for services performed, on a pre-determined schedule or when contractual milestones are met; however, some require advanced payments. We make estimates of our expenses as of each balance sheet date in our financial statements based on facts and circumstances known to

us at that time. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in us reporting expenses that are too high or too low in any particular period. To date, we have not made any material adjustments to our prior estimates of research and development expenses.

Income Taxes

Deferred tax assets represent amounts available to reduce income taxes payable on taxable income in future years. Such assets arise because of temporary differences between the financial reporting and tax basis of assets and liabilities, as well as from net operating losses and tax credit carryforwards. We evaluate the recoverability of these future tax deductions and credits by assessing the adequacy of future expected taxable income from all sources, including reversal of temporary differences, forecasted operating earnings and available tax planning strategies. These sources of income rely heavily on estimates that are based on a number of factors, including historical experience and short-range and long-range business forecasts. A valuation allowance is provided when it is more likely than not that some portion or all of a deferred tax asset will not be realized.

Recent Accounting Pronouncements

See Note 2 to our consolidated financial statements included in this Annual Report for information regarding recent accounting pronouncements.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

Interest and Credit Risk

Financial instruments that are potentially subject to credit risk consist of cash and cash equivalents, restricted cash, short term investments and accounts receivable.

We had cash and cash equivalents of $3.9 billion, $4.4 billion and $1.4 billion, restricted cash of $5.5 million, $7.2 million and $8.1 million, and short-term investments of $0.7 billion, $2.2 billion and $3.3 billion, at December 31, 2022, 2021 and 2020, respectively. Our cash and cash equivalents are deposited with various major reputable financial institutions located within or without the PRC. 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. We believe that these financial institutions are of high credit quality, and we continually monitor the credit worthiness of these financial institutions. At December 31, 2022, our short-term investments consisted primarily of U.S. treasury securities. We believe that U.S. treasury securities are of high credit quality and continually monitor the credit worthiness of these institutions.

The primary objectives of our investment activities are to preserve principal, provide liquidity, and maximize income without significant increasing risk. Our primary exposure to market risk relates to fluctuations in the interest rates, which are affected by changes in the general level of PRC and U.S. interest rates. Given the short-term nature of our cash equivalents, we believe that a sudden change in market interest rates would not be expected to have a material impact on our financial condition and/or results of operation. We estimate that a hypothetical 100-basis point increase or decrease in market interest rates would result in a decrease of $2.1 million or increase of $2.1 million, respectively, in the fair value of our investment portfolio as of December 31, 2022.

We do not believe that our cash, cash equivalents, and short-term investments have significant risk of default or illiquidity. While we believe our cash, cash equivalents, and short-term investments do not contain excessive risk, we cannot provide absolute assurance that in the future investments will not be subject to adverse changes in market value.

We had accounts receivable, net of $173.2 million, $483.1 million and $60.4 million at December 31, 2022, 2021 and 2020, respectively. Accounts receivable at December 31, 2021 included the upfront fee from Novartis of $300.0 million under the ociperlimab agreement. Accounts receivable, net represent amounts arising from product sales and amounts due from the our collaboration partners. We monitor economic conditions to identify facts or circumstances that may indicate receivables are at risk of collection. To date, we have not experienced any significant losses with respect to the collection of our accounts receivable.

Currency Convertibility Risk

A significant portion of our expenses, assets, and liabilities are denominated in RMB. In 1994, the PRC government abolished the dual rate system and introduced a single rate of exchange as quoted daily by the People's Bank of China (the PBOC). However, the unification of exchange rates does not imply that the RMB may be readily convertible into U.S. dollars or other foreign currencies. All foreign exchange transactions continue to take place either through the PBOC or other banks

authorized to buy and sell foreign currencies at the exchange rates quoted by the PBOC. Approvals of foreign currency payments by the PBOC or other institutions require submitting a payment application form together with suppliers' invoices, shipping documents and signed contracts.

Additionally, the value of the RMB is subject to changes in central government policies and international economic and political developments affecting supply and demand in the PRC foreign exchange trading system market.

Foreign Currency Exchange Rate Risk

We are exposed to foreign exchange risk arising from various currency exposures. Our reporting currency is the U.S. dollar, but a portion of our operating transactions and assets and liabilities are in other currencies, such as RMB, Euro, and Australian dollar.

RMB is not freely convertible into foreign currencies for capital account transactions. The value of RMB against the U.S. dollar and other currencies is affected by, among other things, changes in China's political and economic conditions and China's foreign exchange prices. Since 2005, the RMB has been permitted to fluctuate within a narrow and managed band against a basket of certain foreign currencies. The RMB compared to the U.S. dollar depreciated approximately 8.2%, appreciated approximately 2.3%, and appreciated approximately 6.3% for the years ended December 31, 2022, 2021 and 2020, respectively. It is difficult to predict how market forces or PRC or U.S. government policy may impact the exchange rate between the RMB and the U.S. dollar in the future.

To the extent that we need to convert U.S. dollars into RMB for capital expenditures, working capital and other business purposes, appreciation of RMB against the U.S. dollar would have an adverse effect on the RMB amount we would receive from the conversion. Conversely, if we decide to convert RMB into U.S. dollars for the purpose of making payments for dividends on our ordinary shares, strategic acquisitions or investments or other business purposes, appreciation of the U.S. dollar against RMB would have a negative effect on the U.S. dollar amount available to us.

In addition, a significant depreciation of the RMB against the U.S. dollar may significantly reduce the U.S. dollar equivalent of our foreign cash balances and trade receivables. Further, volatility in exchange rate fluctuations may have a significant impact on the foreign currency translation adjustments recorded in other comprehensive income (loss). We have not used derivative financial instruments to hedge exposure to foreign exchange risk.

Effects of Inflation

Inflation generally affects us by increasing our cost of labor and clinical development costs. We do not believe that inflation has had a material effect on our results of operations during the year ended December 31, 2022.

Item 8. Financial Statements and Supplementary Data

The financial statements required to be filed pursuant to this item are appended to this Annual Report. An index of those financial statements is in "Part IV—Item 15—Exhibits, Financial Statement Schedules."

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

None.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

Based on their evaluation, required by paragraph (b) of Rules 13a-15 or 15d-15, promulgated under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), our principal executive officer and principal financial officer have concluded that our disclosure controls and procedures as defined in Rules 13a-15(e) and 15d-15(e) of the Exchange Act are effective, at a reasonable assurance level, as of December 31, 2022, to ensure that information required to be disclosed in reports that we file or submit under the Exchange Act is recorded, processed, summarized, and reported within the time periods specified in U.S. Securities and Exchange Commission rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is accumulated and communicated to our management, including our principal executive and principal financial officers, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, our management recognized that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurances of achieving the desired

control objectives, and management necessarily was required to apply its judgment in designing and evaluating the controls and procedures.

Management's Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act). Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with U.S. generally accepted accounting principles. Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting based on the framework in Internal Control-Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on our assessment and those criteria, management concluded that we maintained effective internal control over financial reporting as of December 31, 2022.

The effectiveness of our internal control over financial reporting as of December 31, 2022, has been tested by Ernst & Young LLP, our independent registered public accounting firm, as stated in their report which is included in "Item 8—Financial Statements and Other Supplementary Data" in this Annual Report.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting identified in connection with the evaluation required by Rule 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the three months ended December 31, 2022 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

On October 31, 2019, our wholly-owned subsidiary, BeiGene Switzerland GmbH ("BeiGene Switzerland"), entered into a collaboration agreement with Amgen Inc. ("Amgen"), which became effective on January 2, 2020 (as amended, the "Collaboration Agreement"). Pursuant to the Collaboration Agreement, we agreed to collaborate on the commercialization of Amgen's oncology products XGEVA®, BLINCYTO® and KYPROLIS® in China, and the global development and commercialization in China of a portfolio of Amgen's clinical- and late-preclinical-stage pipeline products. In connection with our ongoing assessment of the Collaboration Agreement cost-share contributions, we determined that our further investment in the development of LUMAKRAS® also known as sotorasib ("AMG 510") was no longer commercially viable for BeiGene. As a result, on February 26, 2023, we entered into an amendment to the Collaboration Agreement to (i) stop sharing costs with Amgen for the further development of AMG 510 during the period starting January 1, 2023 and ending August 31, 2023; and (ii) cooperate in good faith to prepare a transition plan with the anticipated termination of AMG 510 from the Collaboration Agreement. The foregoing description of the terms of the amendment does not purport to be complete and is qualified in its entirety by reference to the full text of the agreement, which the Company intends to file as an exhibit to a subsequent periodic report.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

On March 30, 2022, the SEC added us to its conclusive list of issuers identified under the HFCAA following the filing of our annual report on Form 10-K with the SEC on February 28, 2022, which annual report was audited by Ernst & Young Hua Ming LLP, a registered public accounting firm in mainland China that the PCAOB previously was unable to inspect or investigate completely, because of a position taken by an authority in the foreign jurisdiction. However, as our global business has expanded, we have evaluated, designed and implemented business processes and control changes and built substantial organizational capabilities outside of China. Therefore, on March 23, 2022, following a review process carried out by our audit committee, Ernst & Young Hua Ming LLP resigned as our independent registered public accounting firm for the audit of our financial statements and internal control over financial reporting to be filed with the SEC. On the same day, our audit committee approved the engagement of Ernst & Young LLP, located in Boston, Massachusetts, United States, as the Company's independent registered public accounting firm for the audit of our financial statements and internal control over financial reporting for the fiscal year ending December 31, 2022. Given that Ernst & Young LLP (United States) now serves as the principal accountant to audit our consolidated financial statements, we expect to be able to comply with the HFCAA and AHFCAA and certify that we have retained a registered public accounting firm that the PCAOB has determined it is able to inspect or investigate which would preclude a further finding by the SEC that we are a Commission-Identified Issuer.

Furthermore, in August 2022, the PCAOB signed a Statement of Protocol with the CSRC and the Ministry of Finance of the People's Republic of China, taking the first step toward opening access for the PCAOB to inspect and investigate registered public accounting firms headquartered in mainland China and Hong Kong. PCAOB staff members conducted on-site inspections and investigations from September to November 2022, and in December 2022, the PCAOB announced that it has secured complete access to inspect and investigate registered public accounting firms headquartered in mainland China and Hong Kong and confirmed that until such time as the PCAOB issues any new determination, there are no Commission-Identified Issuers at risk of having their securities subject to a trading prohibition under the HFCAA.

To the extent known by the Company, the Company is not aware of and has no reason to believe that: any governmental entity in the foreign jurisdiction in which the Company is incorporated or otherwise organized owns shares of any capital stock of record of the Company; any official of the Chinese government or Hong Kong SAR is a board member or officer of the Company or its operating subsidiaries; or that the Company's articles of incorporation, as amended, contain any provisions known by the Company to include any charter or charter provisions of the Chinese Communist Party. The Company has determined that no governmental entity in mainland China or Hong Kong, directly or indirectly, possesses the power to direct or cause the direction of the management and policies of the Company or has a controlling financial interest. The Company has made this determination based on the fact that as of the date of this annual report, no such governmental entity has filed a Schedule 13D or 13G, there are no material contracts with such a foreign governmental party, and there is no such foreign government representative on the Company's Board.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

The information required under this item is incorporated herein by reference to our definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the U.S. Securities and Exchange Commission not later than 120 days after the close of our fiscal year ended December 31, 2022.

Item 11. Executive Compensation

The information required under this item is incorporated herein by reference to our definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the U.S. Securities and Exchange Commission not later than 120 days after the close of our fiscal year ended December 31, 2022.

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

The information required under this item is incorporated herein by reference to our definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the U.S. Securities and Exchange Commission not later than 120 days after the close of our fiscal year ended December 31, 2022.

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

The information required under this item is incorporated herein by reference to our definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the U.S. Securities and Exchange Commission not later than 120 days after the close of our fiscal year ended December 31, 2022.

Item 14. Principal Accounting Fees and Services

Our independent public accounting firm is Ernst & Young LLP (PCAOB ID: 0042), located in Boston, Massachusetts, United States. Our independent public accounting firm for the years ended December 31, 2021 and 2020 was Ernst & Young Hua Ming LLP (PCAOB ID: 1408), located in Beijing, People's Republic of China.

The information required under this item is incorporated herein by reference to our definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the U.S. Securities and Exchange Commission not later than 120 days after the close of our fiscal year ended December 31, 2022.

PART IV

Item 15. Exhibits, Financial Statement Schedules

The financial statements listed in the Index to Consolidated Financial Statements beginning on page F-1 are filed as part of this Annual Report.

No financial statement schedules have been filed as part of this Annual Report because they are not applicable, not required or the information required is shown in the financial statements or the notes thereto.

The exhibits filed as part of this Annual Report are set forth on the Exhibit Index immediately following our consolidated financial statements. The Exhibit Index is incorporated herein by reference.

Item 16. Form 10-K Summary

Not applicable.

BEIGENE, LTD.

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Report of Independent Registered Public Accounting Firm

To the Shareholders and the Board of Directors of BeiGene, Ltd.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheet of BeiGene, Ltd. and subsidiaries (the Company) as of December 31, 2022, the related consolidated statements of operations, comprehensive loss, shareholders' equity and cash flows for the year ended December 31, 2022, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2022, and the results of its operations and its cash flows for the year ended December 31, 2022, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2022, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework), and our report dated February 27, 2023 expressed an unqualified opinion thereon.

Basis for Opinion

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

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

Critical Audit Matters

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

Accrued Clinical Trial Expenses

Description of the Matter

As of December 31, 2022, the Company recorded $138 million of accrued external research and development expenses. As discussed in Note 2 to the consolidated financial statements, accrued external research and development expenses consist of various costs including clinical and pre-clinical trials, cost to develop product candidates, research services and other research and development related costs. Expenses related to clinical trials are accrued based on estimates of the actual services performed by third parties for the respective period. As the majority of clinical service providers invoice the Company in arrears for services performed, the Company determines estimates based on reviewing open contracts and purchase orders, assessing services that have been performed on its behalf, and estimating the level of service performed and the associated costs incurred for the services.

Auditing the Company's accrued external clinical trial expenses is especially challenging as the determination of clinical trial activities requires judgment and estimates resulting from delays in reporting from vendors. While the Company's estimates of accrued clinical trial expenses are primarily based on information received related to each study from its vendors, the Company may need to make an estimate for additional costs incurred. These estimates are based on several factors, including management's knowledge of the clinical trial timelines associated with activities, invoicing to date and the provisions in the contracts. Additionally, due to the long duration of clinical trials and the timing of invoicing received from vendors, the actual amounts incurred are not typically known at the time the financial statements are issued.

How We Addressed the Matter in Our Audit

We evaluated and tested the design and operating effectiveness of internal controls over the Company's process used in determining the valuation and completeness of accrued clinical trial expenses. This included testing controls over management's review of the significant assumptions and other inputs used in the estimation of accrued external clinical trial expenses, including contractual terms, estimated expenses incurred, and total invoicing to date.

To test the accrued clinical trial expenses, our audit procedures included, among others, testing the accuracy and completeness of the underlying data used in determining the accrued clinical trial expenses and evaluating the assumptions and estimates used by management. To evaluate the completeness and valuation of the accrual, we corroborated the progress of clinical trials with the Company's research and development personnel that oversee the clinical trials and obtained actual cost information directly from vendors. We also tested subsequent invoices received and evaluated contractual arrangements with vendors, including any pending change orders to assess the impact to the accrual.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2022

Boston, Massachusetts

February 27, 2023

Report of Independent Registered Public Accounting Firm

To the Shareholders and the Board of Directors of BeiGene, Ltd.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheet of BeiGene, Ltd. (the Company) as of December 31, 2021, the related consolidated statements of operations, comprehensive loss, cash flows and shareholders' equity for each of the two years in the period ended December 31, 2021, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2021, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2021, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

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

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

/s/ Ernst & Young Hua Ming LLP

We served as the Company’s auditor from 2014 to 2022.

Beijing, People’s Republic of China

February 28, 2022,

except for the effects on the consolidated financial statements of the correction of an error as described in Notes 2 and 3, as to which the date is

February 27, 2023

Report of Independent Registered Public Accounting Firm

To the Shareholders and the Board of Directors of BeiGene, Ltd.

Opinion on Internal Control Over Financial Reporting

We have audited BeiGene, Ltd.'s internal control over financial reporting as of December 31, 2022, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). In our opinion, BeiGene, Ltd. (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2022, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheet of the Company as of December 31, 2022, the related consolidated statement of operations, comprehensive loss, shareholders' equity and cash flows for the year ended December 31, 2022, and the related notes and our report dated February 27, 2023 expressed an unqualified opinion thereon.

Basis for Opinion

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

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

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

Definition and Limitations of Internal Control Over Financial Reporting

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

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

/s/ Ernst & Young LLP

Boston, Massachusetts

February 27, 2023

BEIGENE, LTD.

CONSOLIDATED BALANCE SHEETS

(Amounts in thousands of U.S. Dollars ("$"), except for number of shares and per share data)

	Note	As of December 31, 2022	As of December 31, 2021
		$	$
Assets			
Current assets:			
Cash and cash equivalents		3,869,564	4,375,678
Short-term restricted cash	5	196	328
Short-term investments	6	665,251	2,241,962
Accounts receivable, net		173,168	483,113
Inventories	7	282,346	242,626
Prepaid expenses and other current assets	13	216,553	270,173
Total current assets		5,207,078	7,613,880
Long-term restricted cash	5	5,277	6,881
Property, plant and equipment, net	10	845,946	587,605
Operating lease right-of-use assets	9	109,960	117,431
Intangible assets, net	11	40,616	46,679
Other non-current assets	13	170,413	163,049
Total non-current assets		1,172,212	921,645
Total assets		6,379,290	8,535,525
Liabilities and shareholders' equity			
Current liabilities:			
Accounts payable		294,781	262,400
Accrued expenses and other payables	13	467,352	558,055
Deferred revenue, current portion	4	213,861	187,414
Tax payable	12	25,189	21,395
Operating lease liabilities, current portion	9	24,041	21,925
Research and development cost share liability, current portion	4	114,335	120,801
Short-term debt	14	328,969	427,565
Total current liabilities		1,468,528	1,599,555
Non-current liabilities:			
Long-term debt	14	209,148	202,113
Deferred revenue, non-current portion	4	42,026	220,289
Operating lease liabilities, non-current portion	9	34,517	43,041
Deferred tax liabilities	12	15,996	14,169
Research and development cost share liability, non-current portion	4	179,625	269,561
Other long-term liabilities	13	46,095	54,234
Total non-current liabilities		527,407	803,407
Total liabilities		1,995,935	2,402,962
Commitments and contingencies	22		
Equity:			
Ordinary shares, 0.0001 par value per share; 9,500,000,000 shares authorized; 1,356,140,180 and 1,334,804,281 shares issued and outstanding as of December 31, 2022 and 2021, respectively		135	133
Additional paid-in capital		11,540,979	11,191,007
Accumulated other comprehensive (loss) income	18	(77,417)	17,950
Accumulated deficit		(7,080,342)	(5,076,527)
Total equity		4,383,355	6,132,563
Total liabilities and equity		6,379,290	8,535,525

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

BEIGENE, LTD.

CONSOLIDATED STATEMENTS OF OPERATIONS

(Amounts in thousands of U.S. Dollars ("$"), except for number of shares and per share data)

	Note	Year Ended December 31, 2022	2021	2020
		$	$	$
Revenues				
Product revenue, net	15	1,254,612	633,987	308,874
Collaboration revenue	4	161,309	542,296	—
Total revenues		1,415,921	1,176,283	308,874
Expenses				
Cost of sales - product		286,475	164,906	70,657
Research and development		1,640,508	1,459,239	1,294,877
Selling, general and administrative		1,277,852	990,123	600,176
Amortization of intangible assets	11	751	750	846
Total expenses		3,205,586	2,615,018	1,966,556
Loss from operations		(1,789,665)	(1,438,735)	(1,657,682)
Interest income (expense), net		52,480	(15,757)	1,998
Other (expense) income, net	6	(223,852)	15,904	37,490
Loss before income taxes		(1,961,037)	(1,438,588)	(1,618,194)
Income tax expense	12	42,778	19,228	10,397
Net loss		(2,003,815)	(1,457,816)	(1,628,591)
Less: net loss attributable to noncontrolling interests		—	—	(3,617)
Net loss attributable to BeiGene, Ltd.		(2,003,815)	(1,457,816)	(1,624,974)
Net loss per share attributable to BeiGene, Ltd., basic and diluted	16	(1.49)	(1.21)	(1.50)
Weighted-average shares outstanding, basic and diluted	16	1,340,729,572	1,206,210,049	1,085,131,783
Net loss per American Depositary Share (ADS), basic and diluted		(19.43)	(15.71)	(19.47)
Weighted-average ADSs outstanding, basic and diluted		103,133,044	92,785,388	83,471,676

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

BEIGENE, LTD.

CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS

(Amounts in thousands of U.S. Dollars ("$"), except for number of shares and per share data)

	Note	Year Ended December 31, 2022	2021	2020
		$	$	$
Net loss		(2,003,815)	(1,457,816)	(1,628,591)
Other comprehensive (loss) income, net of tax of nil:				
Foreign currency translation adjustments	18	(90,421)	13,714	23,603
Pension liability adjustments	21	365	1,865	(8,113)
Unrealized holding loss, net	18	(5,311)	(4,571)	(419)
Comprehensive loss		(2,099,182)	(1,446,808)	(1,613,520)
Less: comprehensive loss attributable to noncontrolling interests		—	—	(3,489)
Comprehensive loss attributable to BeiGene, Ltd.		(2,099,182)	(1,446,808)	(1,610,031)

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

BEIGENE, LTD.

CONSOLIDATED STATEMENTS OF CASH FLOWS

Amounts in thousands of U.S. Dollars ("$"), except for number of shares and per share data)

	Note	Year Ended December 31, 2022	2021	2020
		$	$	$
Cash flows from operating activities:				
Net loss		(2,003,815)	(1,457,816)	(1,628,591)
Adjustments to reconcile net loss to net cash used in operating activities:				
Depreciation and amortization expense		66,278	46,457	31,789
Share-based compensation expense	17	303,162	240,712	183,481
Acquired in-process research and development	4	68,665	83,500	109,500
Amortization of research and development cost share liability	4	(96,402)	(112,486)	(113,986)
Unrealized losses (gains) on equity investments	6	21,996	(7,632)	(11,826)
Deferred income tax expense		2,059	3,377	261
Other items, net		9,047	23,510	(4,673)
Changes in operating assets and liabilities:				
Accounts receivable		304,112	(423,019)	10,363
Inventories		(56,689)	(153,333)	(58,906)
Other assets		(3,282)	(107,128)	(56,217)
Accounts payable		(4,352)	20,008	95,835
Accrued expenses and other payables		45,627	140,044	185,012
Deferred revenue		(151,816)	407,703	—
Other liabilities		(1,209)	(2,620)	(25,503)
Net cash used in operating activities		(1,496,619)	(1,298,723)	(1,283,461)
Cash flows from investing activities:				
Purchases of property and equipment		(325,434)	(262,942)	(117,508)
Purchases of short-term investments		(1,485)	(2,147,881)	(5,663,727)
Proceeds from sale or maturity of short-term investments		1,563,618	3,146,891	2,751,075
Purchase of in-process research and development		(143,665)	(8,500)	(109,500)
Purchase of intangible assets	11	—	(43,409)	—
Purchase of long-term investments	6	(15,911)	(43,500)	(26,681)
Other investing activities		—	—	(2,025)
Net cash provided by (used in) investing activities		1,077,123	640,659	(3,168,366)
Cash flows from financing activities:				
Proceeds from public offering, net of cost	19	—	3,392,616	—
Proceeds from sale of ordinary shares, net of cost	19	—	50,000	4,232,017
Proceeds from research and development cost share liability	4	—	—	616,834
Payment to acquire joint venture (JV) minority interest	8	—	—	(28,723)
Proceeds from long-term loan	14	37,372	16,838	110,208
Repayment of long-term loan	14	—	—	(132,061)
Proceeds from short-term loans	14	313,774	406,449	323,697
Repayment of short-term loans	14	(417,081)	(321,754)	(12,247)
Proceeds from option exercises and employee share purchase plan		46,964	92,762	93,101
Net cash (used in) provided by financing activities		(18,971)	3,636,911	5,202,826
Effect of foreign exchange rate changes, net		(69,383)	14,035	18,231
Net (decrease) increase in cash, cash equivalents, and restricted cash		(507,850)	2,992,882	769,230
Cash, cash equivalents, and restricted cash, beginning of year		4,382,887	1,390,005	620,775
Cash, cash equivalents, and restricted cash, end of year		3,875,037	4,382,887	1,390,005
Supplemental cash flow disclosures:				
Cash and cash equivalents		3,869,564	4,375,678	1,381,950
Short-term restricted cash		196	328	307
Long-term restricted cash		5,277	6,881	7,748
Income taxes paid		29,500	15,695	10,596
Interest paid		25,169	29,967	44,130
Supplemental non-cash activities:				
Accruals for capital expenditures		95,346	53,197	42,762
Purchase of in-process research and development included in accounts payable		—	75,000	—

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

BEIGENE, LTD.

CONSOLIDATED STATEMENTS OF SHAREHOLDERS' EQUITY

(Amounts in thousands of U.S. Dollars ("$"), except for number of shares and per share data)

	Attributable to BeiGene, Ltd.							
	Ordinary Shares		Additional Paid-In Capital	Accumulated Other Comprehensive Income/(Loss)	Accumulated Deficit	Total	Non-Controlling Interests	Total
	Shares	Amount						
		$	$	$	$	$	$	$
Balance at December 31, 2019	801,340,698	79	2,925,970	(8,001)	(1,993,737)	924,311	16,150	940,461
Proceeds from issuance of ordinary shares, net of cost	145,838,979	14	2,069,596	—	—	2,069,610	—	2,069,610
Issuance of ordinary shares in connection with collaboration	206,635,013	21	2,162,386	—	—	2,162,407	—	2,162,407
Exercise of options, ESPP and release of RSUs	38,020,892	3	93,098	—	—	93,101	—	93,101
Use of shares reserved for share option exercises and RSU releases	(1,013,641)	1	—	—	—	1	—	1
Share-based compensation	—	—	183,481	—	—	183,481	—	183,481
Deconsolidation of a subsidiary	—	—	—	—	—	—	(3,545)	(3,545)
Acquisition of joint venture (JV) minority interest	—	—	(19,599)	—	—	(19,599)	(9,116)	(28,715)
Other comprehensive income	—	—	—	14,943	—	14,943	128	15,071
Net loss	—	—	—	—	(1,624,974)	(1,624,974)	(3,617)	(1,628,591)
Balance at December 31, 2020	1,190,821,941	118	7,414,932	6,942	(3,618,711)	3,803,281	—	3,803,281
Issuance of ordinary shares in connection with STAR Offering	115,055,260	12	3,392,604	—	—	3,392,616	—	3,392,616
Proceeds from issuance of ordinary shares, net of cost	2,151,877	—	50,000	—	—	50,000	—	50,000
Exercise of options, ESPP and release of RSUs	28,778,893	3	92,759	—	—	92,762	—	92,762
Use of shares reserved for share option exercises	(2,003,690)	—	—	—	—	—	—	—
Share-based compensation	—	—	240,712	—	—	240,712	—	240,712
Other comprehensive income	—	—	—	11,008	—	11,008		11,008
Net loss	—	—	—	—	(1,457,816)	(1,457,816)	—	(1,457,816)
Balance at December 31, 2021	1,334,804,281	133	11,191,007	17,950	(5,076,527)	6,132,563	—	6,132,563
Cost from issuance of ordinary shares	—	—	(152)	—	—	(152)	—	(152)
Use of shares reserved for share option exercises	1,375,621	—	—	—	—	—	—	—
Exercise of options, ESPP and release of RSUs	19,960,278	2	46,962	—	—	46,964	—	46,964
Share-based compensation	—	—	303,162	—	—	303,162	—	303,162
Other comprehensive loss	—	—	—	(95,367)	—	(95,367)	—	(95,367)
Net loss	—	—	—	—	(2,003,815)	(2,003,815)	—	(2,003,815)
Balance at December 31, 2022	1,356,140,180	135	11,540,979	(77,417)	(7,080,342)	4,383,355	—	4,383,355

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

BEIGENE, LTD.
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS
FOR THE YEARS ENDED DECEMBER 31, 2022, 2021 AND 2020
(Amounts in thousands of U.S. Dollar ("$") and Renminbi ("RMB"),
except for number of shares and per share data)

1. Organization

BeiGene, Ltd. (the "Company", "BeiGene", "it", "its") is a global biotechnology company that is developing and commercializing innovative affordable oncology medicines to improve treatment outcomes and access for patients worldwide.

The Company currently has three approved medicines that were discovered and developed in its own labs, including BRUKINSA®, a small molecule inhibitor of Bruton's Tyrosine Kinase (BTK) for the treatment of various blood cancers; tislelizumab, an anti-PD-1 antibody immunotherapy for the treatment of various solid tumor and blood cancers; and pamiparib, a selective small molecule inhibitor of PARP1 and PARP2. The Company has obtained approvals to market BRUKINSA in the United States, the People's Republic of China (China or the PRC), the European Union (EU), the United Kingdom ("UK"), Canada, Australia and additional international markets, and tislelizumab and pamiparib in China. By leveraging its China commercial capabilities, the Company has in-licensed the rights to distribute 13 approved medicines for the China market. Supported by its global clinical development and commercial capabilities, the Company has entered into collaborations with world-leading biopharmaceutical companies such as Amgen Inc. ("Amgen") and Novartis Pharma AG ("Novartis") to develop and commercialize innovative medicines.

The Company is committed to advancing best and first-in-class clinical candidates internally or with like-minded partners to develop impactful and affordable medicines for patients across the globe. Its internal clinical development capabilities are deep, including a more than 2,700-person global clinical development and medical affairs team that is running close to 80 ongoing or planned clinical trials in over 50 medicines and drug candidates. This includes more than 30 pivotal or potentially registration-enabling trials across its portfolio, including three internally discovered, approved medicines. The Company has enrolled in its clinical trials more than 18,000 subjects, of which approximately one-half have been outside of China.

The Company has built, and is expanding, its internal manufacturing capabilities, through its state-of-the-art biologic and small molecule manufacturing facilities in China to support current and potential future demand of its medicines, and is building a commercial-stage biologics manufacturing and clinical R&D center in New Jersey. The Company also works with high quality contract manufacturing organizations ("CMOs") to manufacture its internally developed clinical and commercial products.

Since its inception in 2010, the Company has become a fully integrated global organization of over 9,000 employees in 29 countries and regions, including the United States, China, Europe and Australia.

2. Summary of Significant Accounting Policies

Basis of Presentation and Principles of Consolidation

The consolidated financial statements of the Company have been prepared in accordance with U.S. generally accepted accounting principles (GAAP). The consolidated financial statements include the financial statements of the Company and its subsidiaries. All significant intercompany transactions and balances between the Company and its wholly-owned subsidiaries are eliminated upon consolidation.

Noncontrolling interests are recognized to reflect the portion of the equity of subsidiaries which are not attributable, directly or indirectly, to the controlling shareholders. Prior to 2020, the Company consolidated its interests in its joint ventures, BeiGene Biologics Co., Ltd. (BeiGene Biologics) and MapKure, LLC (MapKure), under the voting model and recognized the minority shareholders' equity interest as a noncontrolling interest in its consolidated financial statements. In June 2020, the Company deconsolidated MapKure and recorded an equity method investment for its remaining ownership interest in the joint venture (see Note 6). In November 2020, the Company acquired the remaining equity interest in BeiGene Biologics. Subsequent to the share purchase, BeiGene Biologics is a wholly owned subsidiary of the Company (see Note 8).

Use of Estimates

The preparation of the consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, and disclosures of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the period. Areas where management uses subjective judgment include, but are not limited to, estimating the useful lives of long-lived assets, estimating variable consideration in product sales and collaboration revenue arrangements, identifying separate accounting units and the

standalone selling price of each performance obligation in the Company’s revenue arrangements, assessing the impairment of long-lived assets, valuation and recognition of share-based compensation expenses, estimating uncertain tax positions, valuation of inventory, estimating the allowance for credit losses, determining defined benefit pension plan obligations, measurement of right-of-use assets and lease liabilities and the fair value of financial instruments. Management bases the estimates on historical experience, known trends and various other assumptions that are believed to be reasonable, the results of which form the basis for making judgments about the carrying values of assets and liabilities. Actual results could differ from these estimates.

Functional Currency and Foreign Currency Translation

Functional currency

The Company uses the United States dollar ("$" or U.S. dollar) as its reporting currency. Operations in subsidiaries are recorded in the functional currency of the respective subsidiary. The determination of functional currency is based on the criteria of Accounting Standard Codification (ASC) 830, *Foreign Currency Matters*.

Foreign currency translation

For subsidiaries whose functional currencies are not the U.S. dollar, the Company uses the average exchange rate for the year and the exchange rate at the balance sheet date, to translate the operating results and financial position to U.S. dollar, the reporting currency, respectively. Translation differences are recorded in accumulated other comprehensive loss, a component of shareholders’ equity. Transactions denominated in currencies other than the functional currency are translated into the functional currency at the exchange rates prevailing on the transaction dates. Foreign currency denominated financial assets and liabilities are remeasured at the exchange rates prevailing at the balance sheet date. Remeasurement exchange gains and losses are included in the consolidated statements of operations.

Cash, Cash Equivalents and Restricted Cash

Cash and cash equivalents

Cash and cash equivalents consist of cash on hand and bank deposits, which are unrestricted as to withdrawal and use. The Company considers all highly liquid investments with an original maturity date of three months or less at the date of purchase to be cash equivalents. Cash equivalents which consist primarily of money market funds are stated at fair value.

Restricted cash

Restricted cash primarily consists of RMB-denominated cash deposits pledged in designated bank accounts as collateral for bank loans and letters of credit. The Company classifies restricted cash as current or non-current based on the term of the restriction.

In addition to the restricted cash balances above, the Company is required by the PRC securities law to use the proceeds from the STAR offering in strict compliance with the planned uses as disclosed in the PRC prospectus as well as those disclosed in the Company's proceeds management policy approved by the board of directors.

Accounts Receivable and Allowance for Credit Losses

Trade accounts receivable are recorded at their invoiced amounts, net of trade discounts and allowances as well as an allowance for credit losses. The allowance for credit losses reflects the Company's current estimate of credit losses expected to be incurred over the life of the receivables. The Company considers various factors in establishing, monitoring, and adjusting its allowance for credit losses including the aging of receivables and aging trends, customer creditworthiness and specific exposures related to particular customers. The Company also monitors other risk factors and forward-looking information, such as country specific risks and economic factors that may affect a customer's ability to pay in establishing and adjusting its allowance for credit losses. Accounts receivable are written off after all collection efforts have ceased.

Inventory

Prior to the regulatory approval of product candidates, the Company may incur expenses for the manufacture of drug product to support the commercial launch of those products. Until the date at which regulatory approval has been received or is otherwise considered probable, all such costs are recorded as research and development expenses as incurred.

Inventories are stated at the lower of cost and net realizable value, with cost determined in a manner that approximates the first-in, first-out method. The Company periodically analyzes its inventory levels, and writes down inventory that has become obsolete, inventory that has a cost basis in excess of its estimated realizable value and inventory in excess of expected sales requirements as cost of product sales. The determination of whether inventory costs will be realizable requires estimates by management. If actual market conditions are less favorable than projected by management, additional write-downs of inventory may be required, which would be recorded in the consolidated statements of operations.

Investments

The Company's investments consist of available-for-sale debt securities, convertible note instruments, public equity securities with readily determinable fair values, private equity securities without readily determinable fair values, and equity-method investments. The classification of an investment is determined based on the nature of the investment, the Company's ability and intent to hold the investment, and the degree to which the Company may exercise influence over the investee.

- Available-for-sale debt securities are stated at fair value, with the unrealized gains and losses, net of tax, reported in other comprehensive loss. The net carrying value of debt securities classified as available-for-sale is adjusted for amortization of premiums and accretion of discounts to maturity. Such amortization is computed using the effective interest method and included in interest income. Interest and dividends are included in interest income. Available-for-sale debt securities with original maturities greater than three months at the date of purchase and less than one year from the date of the balance sheet are classified as short-term. Available-for-sale debt securities with maturities beyond one year may be classified as short-term marketable securities due to their highly liquid nature and because they represent the Company's investments that are available for current operations.

- Convertible note instruments are recorded using the fair value option method of accounting. Accordingly, convertible note instruments are remeasured at fair value on a recurring basis, with any changes in the fair value option recorded in other (expense) income, net.

- Public equity securities with readily determinable fair values are recorded at fair value. Subsequent changes in fair value are recorded in other (expense) income, net. Derivative financial instruments to purchase public equity securities are recorded at fair value. The estimated fair value of derivative financial instruments is determined based on the Black-Scholes valuation model. Changes in fair value of derivative instruments are recorded in other (expense) income, net.

- Private equity securities without readily determinable fair values and where the Company does not have significant influence are measured at cost minus impairment, if any, plus or minus changes resulting from observable price changes in orderly transactions for the identical or a similar investment of the same issuer. Adjustments to private equity securities are recorded in other (expense) income, net.

- Equity investments in common stock or in-substance common stock where the Company has significant influence over the financial and operating policies of the investee are accounted for as equity-method investments. Equity-method investments are initially recorded at cost and subsequently adjusted based on the Company's percentage ownership in the investee's income and expenses, as well as dividends, if any. The Company records its share of the investee's results of operations in other (expense) income, net. The Company records impairment losses on our equity method investments if it deems the impairment to be other-than-temporary. The Company deems an impairment to be other-than-temporary based on various factors, including but not limited to, the length of time the fair value is below the carrying value and ability to retain the investment to allow for a recovery in fair value.

Realized gains or losses on sales of investments are determined based on the specific identification method.

The Company regularly evaluates its investments in debt and equity for impairment. The Company recognizes an allowance on available-for-sale debt securities when a portion of the unrealized loss is attributable to a credit loss and a corresponding credit loss in net income. No impairment losses or allowance for credit losses on investments were recorded for any periods presented.

Property, Plant and Equipment

Property, plant and equipment are stated at cost, less accumulated depreciation and amortization. Property, plant and equipment, other than land and construction in progress, are depreciated using the straight-line method over the estimated useful lives of the respective assets as follows:

	Useful Lives
Building	20 years
Manufacturing equipment	3 to 10 years
Laboratory Equipment	3 to 5 years
Software, Electronic and Office Equipment	3 to 5 years
Leasehold Improvements	Lesser of useful life or lease term

Leases

The Company applies ASC, Topic 842, *Leases* (ASC 842) to account for its leases. The Company determines if an arrangement is a lease at inception. The Company has lease agreements with lease and non-lease components, which are accounted for as a single lease component based on the Company's policy election to combine lease and non-lease components for its leases. Leases are classified as operating or finance leases in accordance with the recognition criteria in ASC 842-20-25. The Company's lease portfolio consists entirely of operating leases as of December 31, 2022. The Company's leases do not contain any material residual value guarantees or material restrictive covenants.

At the commencement date of a lease, the Company determines the classification of the lease based on the relevant factors present and records a right-of-use (ROU) asset and lease liability. ROU assets represent the right to use an underlying asset for the lease term and lease liabilities represent the obligation to make lease payments arising from the lease. ROU assets and lease liabilities are calculated as the present value of the lease payments not yet paid. Variable lease payments not dependent on an index or rate are excluded from the ROU asset and lease liability calculations and are recognized in expense in the period which the obligation for those payments is incurred. As the rate implicit in the Company's leases is not typically readily available, the Company uses an incremental borrowing rate based on the information available at the lease commencement date in determining the present value of lease payments. This incremental borrowing rate reflects the fixed rate at which the Company could borrow on a collateralized basis the amount of the lease payments in the same currency, for a similar term, in a similar economic environment. ROU assets include any lease prepayments and are reduced by lease incentives. Operating lease expense for lease payments is recognized on a straight-line basis over the lease term. Lease terms are based on the non-cancelable term of the lease and may contain options to extend the lease when it is reasonably certain that the Company will exercise that option.

Operating leases are included in operating lease right-of-use assets and operating lease liabilities on the consolidated balance sheet. Lease liabilities that become due within one year of the balance sheet date are classified as current liabilities.

Leases with an initial lease term of 12 months or less are not recorded on the consolidated balance sheet. Lease expense for these leases is recognized on a straight-line basis over the lease term.

Land Use Right, Net

All land in the PRC is owned by the PRC government. The PRC government may sell land use rights for a specified period of time. Land use rights represent operating leases in accordance with ASC 842. The purchase price of land use rights represents lease prepayments to the PRC government and is recorded as an operating lease ROU asset on the balance sheet. The ROU asset is amortized over the remaining lease term.

In 2017, the Company acquired a land use right from the local Bureau of Land and Resources in Guangzhou for the purpose of constructing and operating the Company's biologics manufacturing facility in Guangzhou. In 2019, the Company acquired a second Guangzhou land use right from the local Bureau of Land and Resources. In 2021, the Company acquired two land use rights from the local Bureau of Land and Resources to expand its biologics manufacturing facility in Guangzhou. Guangzhou land use rights are being amortized over the respective terms of the land use rights, which are each 50 years.

In 2018, the Company acquired a land use right in conjunction with the acquisition of Beijing Innerway Bio-tech Co., Ltd. The land use right is being amortized over the term of the land use right, which is 36 years.

In 2020, the Company acquired a land use right from the local Bureau of Land and Resources in Suzhou to construct its research, development and manufacturing facility in Suzhou. In 2022, the Company acquired a second Suzhou land use right from the local Bureau of Land and Resources. The land use rights are being amortized over the respective terms of the land use rights, which are each 30 years.

Goodwill and Other Intangible Assets

Goodwill is an asset representing the future economic benefits arising from other assets acquired in a business combination that are not individually identified and separately recognized. The Company allocates the cost of an acquired entity to the assets acquired and liabilities assumed based on their estimated fair values at the date of acquisition. The excess of the purchase price for acquisitions over the fair value of the net assets acquired, including other intangible assets, is recorded as goodwill. Goodwill is not amortized, but is tested for impairment at least annually or more frequently if events or changes in circumstances would indicate a potential impairment.

The Company has elected to first assess qualitative factors to determine whether it is more likely than not that the fair value of the Company's reporting unit is less than its carrying amount, including goodwill. The qualitative assessment includes the Company's evaluation of relevant events and circumstances affecting the Company's single reporting unit, including macroeconomic, industry, and market conditions, the Company's overall financial performance, and trends in the market price of the Company's ADSs. If qualitative factors indicate that it is more likely than not that the Company's reporting unit's fair value is less than its carrying amount, then the Company will perform the quantitative impairment test by comparing the reporting unit's carrying amount, including goodwill, to its fair value. If the carrying amount of the reporting unit exceeds its fair value, an impairment loss will be recognized in an amount equal to that excess. For the years ended December 31, 2022, 2021 and 2020 the Company determined that there were no indicators of impairment of goodwill.

Intangible assets acquired through business combinations are recognized as assets separate from goodwill and are measured at fair value upon acquisition. Intangible assets acquired in transactions that are not business combinations are recorded at the allocated portion of total consideration transferred based on their relative fair value in relation to net assets acquired. Intangible assets associated with milestone payments made to third parties subsequent to regulatory approval are recorded at cost. Identifiable intangible assets consist of distribution rights for approved cancer therapies licensed from BMS that are amortized on a straight-line basis over the estimated useful lives of the assets, which is 10 years; post-approval milestone payments under license and commercialization agreements, that are amortized over the remainder of the product patent or the term of the commercialization agreements; and trading licenses that are amortized over the initial license term.

Intangible assets with finite useful lives are tested for impairment when events or circumstances occur that could indicate that the carrying amount of an asset may not be recoverable. When these events occur, the Company evaluates the recoverability of the intangible assets by comparing the carrying amount of the assets to the future undiscounted cash flows expected to result from the use of the assets and their eventual disposition. If the sum of the expected undiscounted cash flows is less than the carrying amount of the assets, the Company recognizes an impairment loss based on the excess of the carrying amount of the assets over their fair value. Fair value is generally determined by discounting the cash flows expected to be generated by the assets, when the market prices are not readily available. For the years ended December 31, 2022, 2021 and 2020, the Company determined that there were no indicators of impairment of its other intangible assets.

Impairment of Long-Lived Assets

Long-lived assets are reviewed for impairment in accordance with authoritative guidance for impairment or disposal of long-lived assets. Long-lived assets are reviewed for events or changes in circumstances, which indicate that their carrying value may not be recoverable. Long-lived assets are reported at the lower of carrying amount or fair value less cost to sell. For the years ended December 31, 2022, 2021 and 2020, there was no impairment of the value of the Company's long-lived assets.

Fair Value Measurements

Fair value of financial instruments

The Company applies ASC topic 820 (ASC 820), *Fair Value Measurements and Disclosures,* in measuring fair value. ASC 820 defines fair value, establishes a framework for measuring fair value and requires disclosures to be provided on fair value measurement. ASC 820 establishes a three-tier fair value hierarchy, which prioritizes the inputs used in measuring fair value as follows:

Level 1 — Observable inputs that reflect quoted prices (unadjusted) for identical assets or liabilities in active markets.

Level 2 — Include other inputs that are directly or indirectly observable in the marketplace.

Level 3 — Unobservable inputs which are supported by little or no market activity.

ASC 820 describes three main approaches to measuring the fair value of assets and liabilities: (1) market approach; (2) income approach; and (3) cost approach. The market approach uses prices and other relevant information generated from market transactions involving identical or comparable assets or liabilities. The income approach uses valuation techniques to convert future amounts to a single present value amount. The measurement is based on the value indicated by current market expectations about those future amounts. The cost approach is based on the amount that would currently be required to replace an asset.

Financial instruments measured at fair value on a recurring basis

The following tables set forth assets measured at fair value on a recurring basis as of December 31, 2022 and 2021:

As of December 31, 2022	Quoted Price in Active Market for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
	$	$	$
Cash equivalents:			
Money market funds	758,114	—	—
Short-term investments (Note 6):			
U.S. treasury securities	665,251	—	—
Other non-current assets (Note 6):			
Equity securities with readily determinable fair values	3,307	706	—
Convertible debt instrument	—	—	3,000
Prepaid expenses and other current assets (Note 6):			
Convertible debt instrument	—	—	5,190
Total	1,426,672	706	8,190

BEIGENE, LTD.
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS
FOR THE YEARS ENDED DECEMBER 31, 2022, 2021 AND 2020
(Amounts in thousands of U.S. Dollar ("$") and Renminbi ("RMB"), except for number of shares and per share data)

As of December 31, 2021	Quoted Price in Active Market for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
	$	$	$
Cash equivalents			
U.S. treasury securities	107,855	—	—
Money market funds	315,564	—	—
Short-term investments (Note 6):			
U.S. treasury securities	2,241,962	—	—
Other non-current assets (Note 6):			
Equity securities with readily determinable fair values	23,809	10,306	—
Total	2,689,190	10,306	—

The Company's cash equivalents are highly liquid investments with original maturities of 3 months or less. Short-term investments represent the Company's investments in available-for-sale debt securities. The Company determines the fair value of cash equivalents and available-for-sale debt securities using a market approach based on quoted prices in active markets.

The Company's equity securities carried at fair value consist of holdings in common stock and warrants to purchase additional shares of common stock of Leap Therapeutics, Inc. (Leap), which were acquired in connection with a collaboration and license agreement entered into in January 2020 and in Leap's underwritten public offering in September 2021. The common stock investment in Leap, a publicly-traded biotechnology company, is measured and carried at fair value and classified as Level 1. The warrants to purchase additional shares of common stock in Leap are classified as a Level 2 investment and are measured using the Black-Scholes option-pricing valuation model, which utilizes a constant maturity risk-free rate and reflects the term of the warrants, dividend yield and stock price volatility, that is based on the historical volatility of similar companies. Refer to Note 6, *Investments* for details of the determination of the carrying amount of private equity investments without readily determinable fair values and equity method investments.

The Company holds convertible notes issued by two private biotech companies. The Company has elected the fair value option method of accounting for the convertible notes. Accordingly, the convertible notes are remeasured at fair value on a recurring basis using Level 3 inputs.

As of December 31, 2022 and 2021, the fair values of cash and cash equivalents, restricted cash, accounts receivable, accounts payable, and short-term debt approximated their carrying values due to their short-term nature. Long-term debt approximates its fair value due to the fact that the related interest rates approximate the rates currently offered by financial institutions for similar debt instrument of comparable maturities.

Revenue Recognition

The Company applies ASC, Topic 606, *Revenue from Contracts with Customers* (ASC 606) to account for its revenue transactions.

Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration that the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the entity performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price, including variable consideration, if any; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation. The Company only applies the five-step model to contracts when it is probable that the entity will collect the consideration to which it is entitled in exchange for the goods or services it transfers to the customer.

Once a contract is determined to be within the scope of ASC 606 at contract inception, the Company reviews the contract to determine which performance obligations it must deliver and which of these performance obligations are distinct. The

Company recognizes as revenue the amount of the transaction price that is allocated to each performance obligation when that performance obligation is satisfied or as it is satisfied.

Product Revenue

The Company generates product revenues in China through the sale of its internally developed drugs tislelizumab, BRUKINSA and pamiparib, and the sale of in-licensed products through its agreements with Amgen, BMS, Bio-Thera and EUSA Pharma. Under the commercial profit share arrangement with Amgen, the Company is the principal for in-licensed product sales to customers in China during the commercialization period and recognizes 100% of net product revenue on these sales. Amounts due to Amgen for its portion of net product sales are recorded as cost of sales. In the United States, the Company generates product revenues from the sale of BRUKINSA.

In China, the Company sells its internally developed products to multiple distributors, who in turn sell the product to hospitals or pharmacies within their authorized territories to be sold ultimately to patients. In-licensed products are sold to a first tier distributor who subsequently resells the products to second tier distributors who ultimately sell the products to health care providers and patients. In the United States, the Company distributes BRUKINSA through specialty pharmacies and specialty distributors. The specialty pharmacies and specialty distributors subsequently resell the product to health care providers and patients.

The Company is the principal under the product sales as the Company controls the products with the ability to direct the use of, and obtain substantially all the remaining benefits from the products before they are sold to the customer. For product sales transactions, the Company has a single performance obligation which is to sell the products to its customer. The Company includes variable consideration in the transaction price to the extent it is probable that a significant reversal will not occur and estimates variable consideration from rebates, chargebacks, trade discounts and allowances, sales returns allowances and other incentives using the expected value method. Revenues for product sales are recognized at a point in time when the single performance obligation is satisfied upon delivery to the customer. The Company's payment terms are approximately 45-90 days. Actual amounts of consideration ultimately received may differ from the Company’s estimates. The Company will reassess estimates for variable consideration periodically. If actual results in the future vary from the Company’s estimates, the Company will adjust these estimates, which would affect net product revenue and earnings in the period such variances become known.

Estimates for variable consideration for which reserves are established at the time of sale include government and commercial rebates, provisions for acceptance of National Reimbursement Drug List pricing in the PRC, chargebacks, trade discounts and allowances, sales returns allowances and other incentives that are offered within contracts between the Company and its customers, health care providers and other indirect customers. Where appropriate, these estimates take into consideration a range of possible outcomes that are probability-weighted for relevant factors such as our historical experience, current contractual and statutory requirements, channel inventory levels, specific known market events and trends, industry data and forecasted customer buying and payment patterns.

The Company bases its sales returns allowance on estimated distributor inventories, customer demand as reported by third-party sources, and actual returns history, as well as other factors, as appropriate. For newly launched products where actual returns history is not yet available, the sales returns allowance is initially calculated based on benchmarking data from similar products and industry experience. If the historical or benchmarking data the Company uses to calculate these estimates do not properly reflect future returns, then a change in the allowance would be made in the period in which such a determination is made and revenues in that period could be materially affected. Any changes from the historical trend rates are considered in determining the current sales return allowance. To date, sales returns have not been significant.

Collaboration Revenue

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

collaboration arrangements that are accounted for pursuant to ASC 808, an appropriate recognition method is determined and applied consistently.

In determining the appropriate amount of revenue to be recognized as it fulfills its obligations under each of its agreements, the Company performs the five-step model under ASC 606 noted above.

The Company’s collaborative arrangements may contain more than one unit of account, or performance obligation, including grants of licenses to intellectual property rights, agreement to provide research and development services and other deliverables. The collaborative arrangements do not include a right of return for any deliverable. As part of the accounting for these arrangements, the Company must develop assumptions that require judgment to determine the stand-alone selling price for each performance obligation identified in the contract. In developing the stand-alone selling price for a performance obligation, the Company considers competitor pricing for a similar or identical product, market awareness of and perception of the product, expected product life and current market trends. In general, the consideration allocated to each performance obligation is recognized when the respective obligation is satisfied either by delivering a good or providing a service, limited to the consideration that is not constrained. Non-refundable payments received before all of the relevant criteria for revenue recognition are satisfied are recorded as advances from customers.

Licenses of Intellectual Property: Upfront non-refundable payments for licensing the Company’s intellectual property are evaluated to determine if the license is distinct from the other performance obligations identified in the arrangement. For licenses determined to be distinct, the Company recognizes revenues from non-refundable up-front fees allocated to the license at a point in time, when the license is transferred to the licensee and the licensee is able to use and benefit from the license.

Options to License Intellectual Property: Upfront non-refundable payments for options to license the Company’s intellectual property are evaluated to determine if the option represents a material right and is distinct from the other performance obligations identified in the arrangement. For options determined to be a material right and distinct, the Company defers the non-refundable up-front fees allocated to the option and recognizes revenues at a point in time, at the earlier of when the option is exercised or the option period expires.

Right to Access Intellectual Property during the Option Period: The portion of a transaction price allocated to the other parties right to access the Company's intellectual property to generate their own data during an option period is deferred and recognized as collaboration revenue over the option period on a straight-line basis as the right to use the intellectual property is provided and the data generated.

Research and Development Services: The portion of a transaction price allocated to research and development services performance obligations is deferred and recognized as collaboration revenue over time as delivery or performance of such services occurs.

Milestone Payments: At the inception of each arrangement that includes development milestone payments, the Company evaluates whether the milestones are considered probable of being reached and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestones related to the Company’s development-based activities may include initiation of various phases of clinical trials. Due to the uncertainty involved in meeting these development-based targets, they are generally fully constrained at contract inception. The Company will assess whether the variable consideration is fully constrained each reporting period based on the facts and circumstances surrounding the clinical trials. Upon changes to constraint associated with the developmental milestones, variable consideration will be included in the transaction price when a significant reversal of revenue recognized is not expected to occur and allocated to the separate performance obligations. Regulatory milestones are fully constrained until the period in which those regulatory approvals are achieved due to the inherent uncertainty with the approval process. Regulatory milestones are included in the transaction price in the period regulatory approval is obtained.

Royalties: For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied).

Research and Development Expenses

Research and development expenses consist of the costs associated with our research and development activities, conducting preclinical studies and clinical trials, and activities related to regulatory filings, which primarily include (i) payroll and related costs (including share-based compensation) associated with research and development personnel, (ii) costs related to clinical trials and preclinical testing of the Company's technologies under development, (iii) costs to develop the product candidates, including raw materials and supplies, product testing, depreciation, and facility related expenses, (iv) expenses for research services provided by universities and contract laboratories, including sponsored research funding, and (v) other research and development expenses. Research and development expenses are charged to expense as incurred when these expenditures relate to the Company's research and development services and have no alternative future uses.

Clinical trial costs are a significant component of the Company's research and development expenses. The Company has a history of contracting with third parties that perform various clinical trial activities on behalf of the Company in the ongoing development of the Company's product candidates. Expenses related to clinical trials are accrued based on the Company's estimates of the actual services performed by the third parties for the respective period. If the contracted amounts are modified (for instance, as a result of changes in the clinical trial protocol or scope of work to be performed), the Company will modify the related accruals accordingly on a prospective basis. Revisions in the scope of a contract are charged to expense in the period in which the facts that give rise to the revision become reasonably certain.

The process of estimating the Company's research and development expenses involves reviewing open contracts and purchase orders, communicating with its personnel to identify services that have been performed on its behalf and estimating the level of service performed and the associated costs incurred for the services when the Company has not yet been invoiced or otherwise notified of the actual costs. The majority of the Company's service providers invoice it in arrears for services performed, on a pre-determined schedule or when contractual milestones are met; however, some require advanced payments. The Company makes estimates of the expenses as of each balance sheet date in its financial statements based on facts and circumstances known to the Company at that time. Although the Company does not expect its estimates to be materially different from amounts actually incurred, the understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in the Company reporting expenses that are too high or too low in any particular period. There were no material adjustments for a change in estimate to research and development expenses in the accompanying consolidated financial statements for the years ended December 31, 2022, 2021 and 2020.

Acquired In-Process Research and Development Expense

The Company has acquired rights to develop and commercialize product candidates. Upfront payments that relate to the acquisition of a new drug compound, as well as pre-commercial milestone payments, are immediately expensed as acquired in-process research and development in the period in which they are incurred, provided that the new drug compound did not also include processes or activities that would constitute a "business" as defined under GAAP, the drug has not achieved regulatory approval for marketing and, absent obtaining such approval, has no established alternative future use. Milestone payments made to third parties subsequent to regulatory approval are capitalized as intangible assets and amortized over the estimated remaining useful life of the related product. Royalties owed on sales of the products licensed pursuant to the agreements are expensed in the period the related revenues are recognized.

Government Grants

Government financial incentives that involve no conditions or continuing performance obligations of the Company are recognized as other (expense) income, net upon receipt. In the event government grants or incentives involve continuing performance obligations, the Company will capitalize the payment as a liability and recognize the same financial statement caption as the performance obligation relates over the performance period.

The Company received government assistance in the form of cash primarily to support the Guangzhou manufacturing facility build-out and research and development programs. Government assistance received related to the Guangzhou manufacturing facility build-out was recognized as other long-term liabilities and is amortized over the same useful lives of the related assets as depreciation expense. As of December 31, 2022 and 2021, other long-term liabilities related to the Guangzhou manufacturing facility build-out totaled $38,118 and $44,593, respectively. For the year ended December 31, 2022, depreciation expense is presented net of amortization of government assistance of $3,169.

Government assistance received to support research and development programs was recorded as other long-term liabilities upon receipt and is recognized as other (expense) income, net when the associated research and development programs are completed. As of December 31, 2022 and 2021, other long-term liabilities related to research and development programs totaled $58 and $1,759, respectively. For the year ended December 31, 2022, the Company recognized other income of $1,664 upon the completion of a designated research and development program.

Comprehensive Loss

Comprehensive loss is defined as the changes in equity of the Company during a period from transactions and other events and circumstances excluding transactions resulting from investments by owners and distributions to owners. Among other disclosures, ASC 220, *Comprehensive Income*, requires that all items that are required to be recognized under current accounting standards as components of comprehensive loss be reported in a financial statement that is displayed with the same prominence as other financial statements. For each of the periods presented, the Company's comprehensive loss includes net loss, foreign currency translation adjustments, pension liability adjustments and unrealized holding gains/losses associated with the available-for-sale debt securities, and is presented in the consolidated statements of comprehensive loss.

Share-Based Compensation

Awards granted to employees

The Company applies ASC 718, *Compensation—Stock Compensation* (ASC 718), to account for its employee share-based payments. In accordance with ASC 718, the Company determines whether an award should be classified and accounted for as a liability award or equity award. All the Company's grants of share-based awards to employees were classified as equity awards and are recognized in the financial statements based on their grant date fair values. Specifically, the grant date fair value of share options is calculated using an option pricing model. The fair value of restricted shares and restricted share units are based on the closing market price of our ADSs on the NASDAQ Global Select Market on the date of grant. The Company has elected to recognize compensation expense using the straight-line method for all employee equity awards granted with graded vesting based on service conditions provided that the amount of compensation cost recognized at any date is at least equal to the portion of the grant-date value of the options that are vested at that date. The Company uses the accelerated method for all awards granted with graded vesting based on performance conditions. To the extent the required vesting conditions are not met resulting in the forfeiture of the share-based awards, previously recognized compensation expense relating to those awards are reversed. ASC 718 requires forfeitures to be estimated at the time of grant and revised, if necessary, in the subsequent period if actual forfeitures differ from initial estimates.

Forfeiture rates are estimated based on historical and future expectations of employee turnover rates and are adjusted to reflect future changes in circumstances and facts, if any. Share-based compensation expense is recorded net of estimated forfeitures such that expense is recorded only for those share-based awards that are expected to vest. To the extent the Company revises these estimates in the future, the share-based payments could be materially impacted in the period of revision, as well as in following periods. The Company, with the assistance of an independent third-party valuation firm, determined the estimated fair value of the stock options granted to employees using the binomial option pricing model.

Awards granted to non-employees

The Company has accounted for equity instruments issued to non-employees in accordance with the provisions of ASC 718 and ASC 505, *Equity*. All transactions in which goods or services are received in exchange for equity instruments are accounted for based on the fair value of the consideration received or the fair value of the equity instrument issued, whichever is more reliably measurable. The grant date is the measurement date of the fair value of the equity instrument issued. The expense is recognized in the same manner as if the Company had paid cash for the services provided by the non-employees in accordance with ASC 505-50, *Equity-based payments to non-employees*. The Company estimated the fair value of share options granted to non-employees using the same method as employees.

Modification of awards

A change in any of the terms or conditions of the awards is accounted for as a modification of the award. Incremental compensation cost is measured as the excess, if any, of the fair value of the modified award over the fair value of the original award immediately before its terms are modified, measured based on the fair value of the awards and other pertinent factors at the modification date. For vested awards, the Company recognizes incremental compensation cost in the period the

modification occurs. For unvested awards, the Company recognizes over the remaining requisite service period, the sum of the incremental compensation cost and the remaining unrecognized compensation cost for the original award on the modification date. If the fair value of the modified award is lower than the fair value of the original award immediately before modification, the minimum compensation cost the Company recognizes is the cost of the original award.

Income Taxes

The Company uses the liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on the differences between the financial reporting and the tax bases of assets and liabilities and are measured using enacted tax rates that will be in effect when the differences are expected to reverse. A valuation allowance is provided when it is more likely than not that some portion or all of a deferred tax asset will not be realized.

The Company evaluates its uncertain tax positions using the provisions of ASC 740, *Income Taxes,* which prescribes a recognition threshold that a tax position is required to meet before being recognized in the financial statements. The Company recognizes in the financial statements the benefit of a tax position which is "more likely than not" to be sustained under examination based solely on the technical merits of the position assuming a review by tax authorities having all relevant information. Tax positions that meet the recognition threshold are measured using a cumulative probability approach, at the largest amount of tax benefit that has a greater than fifty percent likelihood of being realized upon settlement. It is the Company's policy to recognize interest and penalties related to unrecognized tax benefits, if any, as a component of income tax expense.

Loss Per Share

Loss per share is calculated in accordance with ASC 260, *Earnings per Share*. Basic loss per ordinary share is computed by dividing net loss attributable to ordinary shareholders by the weighted average number of ordinary shares outstanding during the period using the two-class method. Under the two-class method, net income is allocated between ordinary shares and participating securities based on dividends declared (or accumulated) and participating rights in undistributed earnings as if all the earnings for the reporting period had been distributed. The Company's restricted shares are participating securities because they have contractual rights to share in the profits of the Company.

However, the restricted shares do not have contractual rights and obligations to share in the losses of the Company. For the periods presented herein, the computation of basic loss per share using the two-class method is not applicable as the Company is in a net loss position.

Diluted loss per share is calculated by dividing net loss attributable to ordinary shareholders as adjusted for the effect of dilutive ordinary equivalent shares, if any, by the weighted average number of ordinary and dilutive ordinary equivalent shares outstanding during the period. Ordinary equivalent shares consist of the ordinary shares issuable upon the conversion of the Company's convertible preferred shares, if any, using the if-converted method, and ordinary shares issuable upon the conversion of the share options and unvested restricted shares, using the treasury stock method.

Ordinary share equivalents are excluded from the computation of diluted loss per share if their effects would be anti-dilutive. Basic and diluted loss per ordinary share is presented in the Company's consolidated statements of operations.

Segment Information

In accordance with ASC 280, *Segment Reporting*, the Company's chief operating decision maker, the Chief Executive Officer, reviews the consolidated results when making decisions about allocating resources and assessing performance of the Company as a whole and hence, the Company has only one reportable segment: pharmaceutical products.

Concentration of Risks

Concentration of credit risk

Financial instruments that are potentially subject to credit risk consist of cash and cash equivalents, short-term investments, and accounts receivable.

As of December 31, 2022 and 2021, $3,869,564 and $4,375,678 were deposited with various major reputable financial institutions located in the PRC and international financial institutions outside of the PRC, respectively. The deposits placed with

financial institutions are not protected by statutory or commercial insurance. In the event of bankruptcy of one of these financial institutions, the Company may be unable to claim its deposits back in full. Management believes that these financial institutions are of high credit quality and continually monitors the credit worthiness of these financial institutions. As of December 31, 2022 and 2021, the Company had short-term investments amounting to $665,251 and $2,241,962, respectively.

At December 31, 2022 and 2021, the Company’s short-term investments were comprised of U.S. treasury securities. The Company believes that U.S. treasury securities are of high credit quality and continually monitors the credit worthiness of these institutions.

As of December 31, 2022 and 2021, the Company had accounts receivable, net of $173,168 and $483,113, respectively. Accounts receivable, net represent amounts arising from product sales and amounts due from its collaboration partners. The Company monitors economic conditions to identify facts or circumstances that may indicate receivables are at risk of collection.

Customer concentration risk

For the year ended December 31, 2022, sales to the Company's four largest product distributors, Sinopharm, Shanghai Pharmaceutical, ASD Specialty Healthcare and China Resources represented approximately 18.1%, 15.5%, 14.2% and 12.1% of product revenue, respectively, and collectively, represented approximately 57.0% of trade accounts receivable as of December 31, 2022. For the year ended December 31, 2022, the Company's collaboration revenue consisted entirely of revenue recognized under its out-licensing collaboration agreements with Novartis.

For the year ended December 31, 2021, sales to the Company's three largest product distributors, Sinopharm, China Resources, and Shanghai Pharmaceutical represented approximately 26.0%, 19.9% and 16.7% of product revenue, respectively, and collectively, represented approximately 23.4% of trade accounts receivable as of December 31, 2021. For the year ended December 31, 2021, the Company's collaboration revenue consisted entirely of revenue recognized under its out-licensing collaboration agreements with Novartis. Receivables from Novartis represented approximately 66.4% of trade accounts receivable as of December 31, 2021, primarily due to the invoicing of the $300,000 upfront fee related to the Ociperlimab option, collaboration and license agreement.

For the year ended December 31, 2020, sales to the Company's two largest product distributors, China Resources and Sinopharm, represented approximately 38.7% and 25.4% of product revenue, respectively, and collectively, represented approximately 59.6% of trade accounts receivable as of December 31, 2020.

Business, customer, political, social and economic risks

The Company participates in a dynamic biopharmaceutical industry and believes that changes in any of the following areas could have a material adverse effect on the Company’s future financial position, results of operations, or cash flows: changes in the overall demand for services and products; competitive pressures due to existing competitors and new entrants; advances and new trends in new drugs and industry standards; changes in clinical research organizations, contract manufacturers and other key vendors; changes in certain strategic relationships or customer relationships; regulatory considerations; intellectual property considerations; and risks associated with the Company’s ability to attract and retain employees necessary to support its growth. The Company’s operations could be also adversely affected by significant political, economic and social uncertainties in the PRC and in relations between the PRC and United States.

Currency convertibility risk

A significant portion of the Company’s expenses, assets and liabilities are denominated in RMB. In 1994, the PRC government abolished the dual rate system and introduced a single rate of exchange as quoted daily by the People’s Bank of China (the PBOC). However, the unification of the exchange rates does not imply that the RMB may be readily convertible into U.S. dollar or other foreign currencies. All foreign exchange transactions continue to take place either through the PBOC or other banks authorized to buy and sell foreign currencies at the exchange rates quoted by the PBOC. Approvals of foreign currency payments by the PBOC or other institutions require submitting a payment application form together with suppliers’ invoices, shipping documents and signed contracts.

Additionally, the value of the RMB is subject to changes in central government policies and international economic and political developments affecting supply and demand in the PRC foreign exchange trading system market.

Foreign currency exchange rate risk

The Company is exposed to foreign exchange risk arising from various currency exposures. The Company's reporting currency is the U.S. dollar, but a portion of its operating transactions and assets and liabilities are in other currencies, such as RMB, Euro, and Australian dollar. While the Company holds significant amounts of RMB, and is subject to foreign currency exchange risk upon revaluation or translation into the Company's reporting currency, the Company expects to utilize its existing RMB cash deposits in the operation of its China business over the next several years, and as a result, has not used derivative financial instruments to hedge exposure to such risk.

RMB is not freely convertible into foreign currencies for capital account transactions. The value of RMB against the U.S. dollar and other currencies is affected by, among other things, changes in China’s political and economic conditions and China’s foreign exchange prices. Since July 21, 2005, the RMB is permitted to fluctuate within a narrow and managed band against a basket of certain foreign currencies. For RMB against U.S. dollar, there was depreciation of approximately 8.2%, appreciation of approximately 2.3% and appreciation of approximately 6.3%, in the years ended December 31, 2022, 2021 and 2020. It is difficult to predict how market forces or PRC or U.S. government policy may impact the exchange rate between the RMB and the U.S. dollar in the future.

To the extent that the Company needs to convert U.S. dollar into RMB for capital expenditures and working capital and other business purposes, appreciation of RMB against U.S. dollar would have an adverse effect on the RMB amount the Company would receive from the conversion. Conversely, if the Company decides to convert RMB into U.S. dollar for the purpose of making payments for dividends on ordinary shares, strategic acquisitions or investments or other business purposes, appreciation of U.S. dollar against RMB would have a negative effect on the U.S. dollar amount available to the Company.

In addition, a significant depreciation of the RMB against the U.S. dollar may significantly reduce the U.S. dollar equivalent of the Company's foreign cash balances and trade receivables. Further, volatility in exchange rate fluctuations may have a significant impact on the foreign currency translation adjustments recorded in other comprehensive income (loss). The revaluation impact of foreign currencies held in U.S. functional currency subsidiaries may result in significant foreign exchange gains (losses) in the consolidated statement of operations. The Company has not used derivative financial instruments to hedge exposure to foreign exchange risk.

Revision of prior period financial statements

The Company evaluates the recoverability of its deferred tax assets on a jurisdiction-by-jurisdiction basis by assessing the adequacy of future expected taxable income from all sources, including reversal of temporary differences, forecasted operating earnings and available tax planning strategies in accordance with ASC 740. This assessment is subject to a high degree of subjectivity, as the sources of income rely heavily on estimates that are based on a number of factors, including historical experience and short-range and long-range business forecasts. A valuation allowance is provided when the Company determines that it is more-likely-than-not that some portion or all of a deferred tax asset will not be realized.

Prior to the third quarter of 2022, the Company determined that the majority of its net deferred tax assets (primarily in the U.S.) were realizable on a more-likely-than-not basis, primarily due to cumulative pre-tax income at the taxpaying entity and the weighting of available positive and negative evidence. Accordingly, no valuation allowance was previously recorded related to those deferred tax assets. In October 2022, in connection with the preparation of its condensed consolidated financial statements for the three and nine months ended September 30, 2022, the Company reassessed its position on the realizability of its net deferred tax assets and determined that the negative evidence associated with cumulative losses at the consolidated financial statement level are not able to be overcome by other positive evidence, and therefore, a valuation allowance should be applied to its net deferred tax asset balance. The Company determined the previous conclusion to not apply a valuation allowance to certain net deferred tax assets was an error.

In accordance with Staff Accounting Bulletin (SAB) No. 99, “Materiality,” and SAB No. 108, “Considering the Effects of Prior Year Misstatements when Quantifying Misstatements in Current Year Financial Statements,” the Company evaluated the error and determined that the related impact was not material to any of its previously issued financial statements, but that correcting the cumulative impact of the error would be significant to its statements of operations for the twelve months ended December 31, 2022. Accordingly, the Company has revised the annual periods of fiscal year 2021 and 2020 consolidated financial statements and related notes included herein to record a valuation allowance against the Company’s net deferred tax asset balance for all periods presented. A summary of revisions to previously reported financial statements is presented in Note 3, *Revision of Prior Period Financial Statements.* Note 12, *Income Taxes* and Note 16, *Loss Per Share* have been updated to

reflect the revision. The Company will also correct previously reported financial information for this error in its future filings, as applicable.

Recent Accounting Pronouncements

New accounting standards which have been adopted

In November 2021, the FASB issued ASU 2021-10, Government Assistance (Topic 832): Disclosures by Business Entities about Government Assistance. This update requires certain annual disclosures about transactions with a government that are accounted for by applying a grant or contribution accounting model by analogy. This update is effective for annual periods beginning after December 15, 2021, and early application is permitted. This guidance should be applied either prospectively to all transactions that are reflected in financial statements at the date of initial application and new transactions that are entered into after the date of initial application or retrospectively to those transactions. The Company adopted this standard on January 1, 2022. The adoption of this standard has been applied to existing government assistance transactions.

3. Revision of Prior Period Financial Statements

As discussed in Note 2, the Company revised certain prior period financial statements to correct an error related to the valuation of net deferred tax assets, the impact of which was immaterial to our previously filed financial statements in the annual periods of fiscal 2021 and 2020 (See Note 2). Specifically, a valuation allowance should have been recorded on all net deferred tax assets and such a valuation allowance was not previously recorded. A summary of revisions to the Company's previously reported financial statements for the comparative periods presented within this Annual Report on Form 10-K is presented below.

Consolidated Balance Sheet

	As of December 31, 2021		
	As Reported	Adjustments	As Revised
	$	$	$
Deferred tax assets	110,424	(110,424)	—
Total non-current assets	1,032,069	(110,424)	921,645
Total assets	8,645,949	(110,424)	8,535,525
Accumulated deficit	(4,966,103)	(110,424)	(5,076,527)
Total equity	6,242,987	(110,424)	6,132,563
Total liabilities and equity	8,645,949	(110,424)	8,535,525

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Consolidated Statements of Operations

	Year Ended December 31, 2021			Year Ended December 31, 2020		
	As Reported	Adjustments	As Revised	As Reported	Adjustments	As Revised
	$	$	$	$	$	$
Income tax expense (benefit)	(25,234)	44,462	19,228	(17,671)	28,068	10,397
Net loss	(1,413,354)	(44,462)	(1,457,816)	(1,600,523)	(28,068)	(1,628,591)
Net loss attributable to BeiGene, Ltd.	(1,413,354)	(44,462)	(1,457,816)	(1,596,906)	(28,068)	(1,624,974)
Net loss per share attributable to BeiGene, Ltd., basic and diluted	(1.17)	(0.04)	(1.21)	(1.47)	(0.03)	(1.50)
Net loss per American Depositary Share ("ADS")	(15.23)	(0.48)	(15.71)	(19.13)	(0.34)	(19.47)

Consolidated Statements of Comprehensive Loss

	Year Ended December 31, 2021			Year Ended December 31, 2020		
	As Reported	Adjustments	As Revised	As Reported	Adjustments	As Revised
	$	$	$	$	$	$
Net loss	(1,413,354)	(44,462)	(1,457,816)	(1,600,523)	(28,068)	(1,628,591)
Comprehensive loss	(1,402,346)	(44,462)	(1,446,808)	(1,585,452)	(28,068)	(1,613,520)
Comprehensive loss attributable to BeiGene, Ltd.	(1,402,346)	(44,462)	(1,446,808)	(1,581,963)	(28,068)	(1,610,031)

Consolidated Statement of Cash Flows

	Year Ended December 31, 2021			Year Ended December 31, 2020		
	As Reported	Adjustments	As Revised	As Reported	Adjustments	As Revised
	$	$	$	$	$	$
Operating activities:						
Net loss	(1,413,354)	(44,462)	(1,457,816)	(1,600,523)	(28,068)	(1,628,591)
Adjustments to reconcile net loss to net cash used in operating activities:						
Deferred income tax expense	(41,085)	44,462	3,377	(27,807)	28,068	261
Net cash used in operating activities	(1,298,723)	—	(1,298,723)	(1,283,461)	—	(1,283,461)

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Consolidated Statement of Stockholders' Equity

	Accumulated Deficit			Total Equity		
	As Reported	Adjustments	As Revised	As Reported	Adjustments	As Revised
	$	$	$	$	$	$
Balance at December 31, 2019	(1,955,843)	(37,894)	(1,993,737)	978,355	(37,894)	940,461
Net loss	(1,596,906)	(28,068)	(1,624,974)	(1,600,523)	(28,068)	(1,628,591)
Balance at December 31, 2020	(3,552,749)	(65,962)	(3,618,711)	3,869,243	(65,962)	3,803,281
Net loss	(1,413,354)	(44,462)	(1,457,816)	(1,413,354)	(44,462)	(1,457,816)
Balance at December 31, 2021	(4,966,103)	(110,424)	(5,076,527)	6,242,987	(110,424)	6,132,563

4. Collaborative and Licensing Arrangements

The Company enters into collaborative arrangements for the research and development, manufacture and/or commercialization of drug products and drug candidates. To date, these collaborative arrangements have included out-licenses of and options to out-license internally developed products and drug candidates to other parties, in-licenses of products and drug candidates from other parties, and profit- and cost-sharing arrangements. These arrangements may include non-refundable upfront payments, contingent obligations for potential development, regulatory and commercial performance milestone payments, cost-sharing and reimbursement arrangements, royalty payments, and profit sharing.

Out-Licensing Arrangements

During the three years ended December 31, 2022, the Company's collaboration revenue related to its out-licensing collaborative agreements has consisted of upfront license fees, research and development services revenue and right to access intellectual property revenue from its collaboration agreements with Novartis for tislelizumab and ociperlimab.

The following table summarizes total collaboration revenue recognized for the years ended December 31, 2022, 2021 and 2020:

	Year Ended December 31,		
	2022	2021	2020
Revenue from Collaborators	$	$	$
License revenue	—	484,646	—
Research and development service revenue	46,822	53,671	—
Right to access intellectual property revenue	104,994	3,979	—
Other	9,493	—	—
Total	161,309	542,296	—

Novartis

Tislelizumab Collaboration and License

In January 2021, the Company entered into a collaboration and license agreement with Novartis, granting Novartis rights to develop, manufacture and commercialize tislelizumab in North America, Europe, and Japan (the "Novartis Territory"). The Company and Novartis have agreed to jointly develop tislelizumab in these licensed countries, with Novartis responsible for regulatory submissions after a transition period and for commercialization upon regulatory approvals. In addition, both companies may conduct clinical trials globally to explore combinations of tislelizumab with other cancer treatments, and the Company has an option to co-detail the product in North America, funded in part by Novartis.

Under the agreement the Company received an upfront cash payment of $650,000 from Novartis. The Company is eligible to receive up to $1,300,000 upon the achievement of regulatory milestones, $250,000 upon the achievement of sales milestones, and royalties on future sales of tislelizumab in the licensed territory. Under the terms of the agreement, the Company is responsible for funding ongoing clinical trials of tislelizumab, Novartis has agreed to fund new registrational, bridging, or post-marketing studies in its territory, and each party will be responsible for funding clinical trials evaluating tislelizumab in

combination with its own or third party products. Each party retains the worldwide right to commercialize its propriety products in combination with tislelizumab.

The Company evaluated the Novartis agreement under ASC 606 as all the material units of account within the agreement represented transactions with a customer. The Company identified the following material components under the agreement: (1) exclusive license for Novartis to develop, manufacture, and commercialize tislelizumab in the Novartis Territory, transfer of know-how and use of the tislelizumab trademark; (2) conducting and completing ongoing trials of tislelizumab (R&D services); and (3) supplying Novartis with required quantities of the tislelizumab drug product, or drug substance, upon receipt of an order from Novartis.

The Company determined that the license, transfer of know-how and use of trademarks are not distinct from each other and represent a single performance obligation. The R&D services represent a material promise and were determined to be a separate performance obligation at the outset of the agreement as the promise is distinct and has standalone value to Novartis. The Company evaluated the supply component of the contract and noted the supply will not be provided at a significant incremental discount to Novartis. The Company concluded that, for the purpose of ASC 606, the provision related to providing clinical and commercial supply of tislelizumab in the Novartis Territory was an option but not a performance obligation of the Company at the outset of the Novartis collaboration agreement. A performance obligation for the clinical and commercial supply will be established as quantities of drug product or drug substance are ordered by Novartis.

The Company determined that the transaction price as of the outset of the arrangement was the upfront payment of $650,000. The potential milestone payments that the Company is eligible to receive were excluded from the transaction price, as all milestone amounts were fully constrained due to uncertainty of achievement. The transaction price was allocated to the two identified performance obligations based on a relative fair value basis. The standalone selling price of the license, transfer of know-how and use of trademarks performance obligation was determined using the adjusted market assessment approach based on the probability-weighted present value of forecasted cash flows associated with out-licensing tislelizumab in the Novartis Territory. The standalone selling price of the R&D services was valued using a cost plus margin valuation approach based on the present value of estimated tislelizumab clinical trial costs plus a reasonable margin. Based on the relative standalone selling prices of the two performance obligations, $484,646 of the total transaction price was allocated to the license and $165,354 was allocated to the R&D services. The estimates of the standalone selling prices involved management's key assumptions such as revenue growth rate, estimated clinical trial costs, mark-up rate, probability of technical and regulatory success, and discount rates. These significant assumptions are forward looking and could be affected by future economic, regulatory and market conditions.

The Company satisfied the license performance obligation at a point in time when the license was delivered and the transfer of know-how completed which occurred during the year ended December 31, 2021. As such, the Company recognized the entire amount of the transaction price allocated to the license as collaboration revenue during the year ended December 31, 2021. The portion of the transaction price allocated to the R&D services was deferred and is being recognized as collaboration revenue as the R&D services are performed using a percentage-of-completion method. Estimated costs to complete are reassessed on a periodic basis and any updates to the revenue earned are recognized on a prospective basis. The Company recognized R&D service revenue of $39,655 and $53,421 during the years ended December 31, 2022 and 2021, respectively. The Company also recognized other collaboration revenue of $9,493 related to the sale of tislelizumab clinical supply to Novartis in conjunction with the collaboration during the years ended December 31, 2022.

Ociperlimab Option, Collaboration and License Agreement and China Broad Market Development Agreement

In December 2021, the Company expanded its collaboration with Novartis by entering into an option, collaboration and license agreement with Novartis to develop, manufacture and commercialize the Company's investigational TIGIT inhibitor ociperlimab in the Novartis Territory. In addition, the Company and Novartis entered into an agreement granting the Company rights to market, promote and detail five approved Novartis oncology products, TAFINLAR® (dabrafenib), MEKINIST® (trametinib), VOTRIENT® (pazopanib), AFINITOR® (everolimus), and ZYKADIA® (ceritinib), across designated regions of China referred to as "broad markets." In the first quarter of 2022, the Company initiated marketing and promotion of these five products.

Under the terms of the option, collaboration and license agreement, the Company received an upfront cash payment of $300,000 in January 2022 from Novartis and will receive an additional payment of $600,000 or $700,000 in the event Novartis exercises its exclusive time-based option prior to mid-2023 or between then and late-2023, respectively. Following option

exercise, the Company is eligible to receive up to $745,000 upon the achievement of regulatory approval milestones, $1,150,000 upon the achievement of sales milestones, and royalties on future sales of ociperlimab in the Novartis Territory. Subject to the terms of the option, collaboration and license agreement, during the option period, Novartis has agreed to initiate and fund additional global clinical trials with ociperlimab and the Company has agreed to expand enrollment in two ongoing trials. Following the option exercise, Novartis has agreed to share development costs of global trials. Following approval, the Company has agreed to provide 50 percent of the co-detailing and co-field medical efforts in the United States, and has an option to co-detail up to 25 percent in Canada and Mexico, funded in part by Novartis. Each party retains the worldwide right to commercialize its propriety products in combination with ociperlimab, as is the case with tislelizumab under the tislelizumab collaboration and license agreement. The existing tislelizumab collaboration and license agreement was not modified as a result of the ociperlimab option, collaboration and license agreement.

The Company evaluated the Novartis agreements under ASC 606 as the units of account within the agreement represented transactions with a customer. The Company identified the following material promises under the agreement: (1) exclusive option for Novartis to license the rights develop, manufacture, and commercialize ociperlimab in the Novartis Territory; (2) Novartis' right to access ociperlimab in its own clinical trials during the option period; (3) initial transfer of BeiGene know-how; and (4) conducting and completing ongoing trials of ociperlimab during the option period (R&D Services). The market development activities are considered immaterial in the context of the contracts.

The Company concluded that, at the inception of the agreement, the option for the exclusive product license constitutes a material right as it represents a significant and incremental discount to the fair value of the exclusive product license that Novartis would not have received without entering into the agreement and is therefore considered a distinct performance obligation. The Company determined that Novartis' right to access ociperlimab in its own trials over the option period and the initial transfer of know-how were not distinct from each other, as the right to access ociperlimab has limited value without the corresponding know-how transfer, and therefore should be combined into one distinct performance obligation. The R&D Services represent a material promise and were determined to be a separate performance obligation at the outset of the agreement as the promise is distinct and has standalone value to Novartis.

The Company determined the transaction price as of the outset of the arrangement was the upfront payment of $300,000. The option exercise fee is contingent upon Novartis exercising its right and is considered fully constrained until the option is exercised. Additionally, the milestone and royalty payments are not applicable until after the option is exercised, at which point the likelihood of meeting milestones, regulatory approval and meeting certain sales thresholds will be assessed. The transaction price was allocated to the three identified performance obligations based on a relative fair value basis. The standalone selling price of the material right for the option to the exclusive product license was calculated as the incremental discount between (i) the value of the license determined using a discounted cash flow method adjusted for probability of the option being exercised and (ii) the expected option exercise fee using the most-likely-amount method at option exercise. The standalone selling price of the combined performance obligation for Novartis' right to access ociperlimab for its own clinical trials during the option period and the initial transfer of BeiGene know-how was determined using a discounted cash flow method. The standalone selling price of the R&D Services was determined using an expected cost plus margin approach. Based on the relative standalone selling prices of the three performance obligations, $71,980 of the total transaction price was allocated to the material right, $213,450 was allocated to Novartis' right to use ociperlimab in its own clinical trials during the option period and the transfer of BeiGene know-how, and $14,570 was allocated to the R&D Services.

The Company will satisfy the material right performance obligation at a point in time at the earlier of when Novartis exercises the option and the license is delivered or the expiration of the option period. As such, the entire amount of the transaction price allocated to the material right was deferred. The portion of the transaction price allocated to Novartis' right to access ociperlimab in its own clinical trials during the option period and the initial transfer of BeiGene know-how was deferred and is being recognized over the expected option period. The portion of the transaction price allocated to the R&D Services was deferred and is being recognized as collaboration revenue as the R&D Services are performed over the expected option period. The Company recognized collaboration revenue of $104,994 and $3,979 related to Novartis right to access ociperlimab in clinical trials and the transfer of know how performance obligation during the years ended December 31, 2022 and 2021, respectively, and R&D service revenue of $7,167 and $250 during the years ended December 31, 2022 and 2021, respectively.

In-Licensing Arrangements - Commercial

Amgen

In October 2019, the Company entered into a global strategic oncology collaboration with Amgen ("Amgen Collaboration Agreement") for the commercialization and development in China, excluding Hong Kong, Taiwan and Macau, of Amgen’s XGEVA®, KYPROLIS®, and BLINCYTO®, and the joint global development of a portfolio of oncology assets in Amgen’s pipeline, with BeiGene responsible for development and commercialization in China. The agreement became effective on January 2, 2020, following approval by the Company's shareholders and satisfaction of other closing conditions.

Under the agreement, the Company is responsible for the commercialization of XGEVA, KYPROLIS and BLINCYTO in China for five or seven years. Amgen is responsible for manufacturing the products globally and will supply the products to the Company at an agreed upon price. The Company and Amgen will share equally in the China commercial profits and losses during the commercialization period. Following the commercialization period, the Company has the right to retain one product and is entitled to receive royalties on sales in China for an additional five years on the products not retained. XGEVA was approved in China in 2019 for patients with giant cell tumor of the bone and in November 2020 for the prevention of skeletal-related events in cancer patients with bone metastases. In July 2020, the Company began commercializing XGEVA in China. In December 2020, BLINCYTO was approved in China for injection for the treatment of adult patients with relapsed or refractory (R/R) B-cell precursor acute lymphoblastic leukemia (ALL). In July 2021, KYPROLIS was conditionally approved in China for injection in combination with dexamethasone for the treatment of adult patients with R/R multiple myeloma. In April 2022, BLINCYTO was conditionally approved for injection for the treatment of pediatric patients with R/R CD19-positive B-cell precursor ALL.

Amgen and the Company are also jointly developing a portfolio of Amgen oncology pipeline assets under the collaboration. The Company is responsible for conducting clinical development activities in China and co-funding global development costs by contributing cash and development services up to a total cap of $1,250,000. Amgen is responsible for all development, regulatory and commercial activities outside of China. For each pipeline asset that is approved in China, the Company will receive commercial rights for seven years from approval. The Company has the right to retain approximately one out of every three approved pipeline assets, other than LUMAKRAS (sotorasib) ("AMG 510"), Amgen's KRAS G12C inhibitor, for commercialization in China. The Company and Amgen will share equally in the China commercial profits and losses during the commercialization period. The Company is entitled to receive royalties from sales in China for pipeline assets returned to Amgen for five years after the seven-year commercialization period. The Company is also entitled to receive royalties from global sales of each product outside of China (with the exception of AMG 510). Amgen advised the Company that its applications to the Human Genetic Resources Administration of China ("HGRAC") to obtain approval to conduct clinical studies in China for the pipeline assets, including its application for AMG 510, were delayed between 2020 and 2022. In connection with our ongoing assessment of the Collaboration Agreement cost-share contributions, we determined that our further investment in the development of AMG 510 was no longer commercially viable for BeiGene. As a result, in February 2023, we entered into an amendment to the Collaboration Agreement to (i) stop sharing costs with Amgen for the further development of AMG 510 during the period starting January 1, 2023 and ending August 31, 2023; and (ii) cooperate in good faith to prepare a transition plan with the anticipated termination of AMG 510 from the Collaboration Agreement.

The Amgen Collaboration Agreement is within the scope of ASC 808, as both parties are active participants and are exposed to the risks and rewards dependent on the commercial success of the activities performed under the agreement. The Company is the principal for product sales to customers in China during the commercialization period and will recognize 100% of net product revenue on these sales. Amounts due to Amgen for its portion of net product sales will be recorded as cost of sales. Cost reimbursements due to or from Amgen under the profit share will be recognized as incurred and recorded to cost of sales; selling, general and administrative expense; or research and development expense, based on the underlying nature of the related activity subject to reimbursement. Costs incurred for the Company's portion of the global co-development funding are recorded to research and development expense as incurred.

In connection with the Amgen Collaboration Agreement, a Share Purchase Agreement (SPA) was entered into by the parties on October 31, 2019. On January 2, 2020, the closing date of the transaction, Amgen purchased 15,895,001 of the Company's ADSs for $174.85 per ADS, representing a 20.5% ownership stake in the Company. Per the SPA, the cash proceeds shall be used as necessary to fund the Company's development obligations under the Amgen Collaboration Agreement. Pursuant to the SPA, Amgen also received the right to designate one member of the Company's board of directors, and Anthony

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Hooper joined the Company's board of directors as the Amgen designee in January 2020. Amgen relinquished its right to appoint a designated director to the Company's board of directors in January 2023.

On April 20, 2022, the parties entered into the First Amendment to Amgen Collaboration Agreement, which amends certain terms and conditions relating to the financial responsibilities of the parties in connections with the development and commercialization of certain Amgen proprietary products for the treatment of oncology-related diseases and conditions.

In determining the fair value of the common stock at closing, the Company considered the closing price of the common stock on the closing date of the transaction and included a lack of marketability discount because the shares are subject to certain restrictions. The fair value of the shares on the closing date was determined to be $132.74 per ADS, or $2,109,902 in the aggregate. The Company determined that the premium paid by Amgen on the share purchase represents a cost share liability due to the Company's co-development obligations. The fair value of the cost share liability on the closing date was determined to be $601,857 based on the Company's discounted estimated future cash flows related to the pipeline assets. The estimation of future cash flows involved management assumptions of revenue growth rates and probability of technical and regulatory success of the pipeline assets. The total cash proceeds of $2,779,241 were allocated based on the relative fair value method, with $2,162,407 recorded to equity and $616,834 recorded as a research and development cost share liability. The cost share liability is being amortized proportionately as the Company contributes cash and development services to its total co-development funding cap.

Amounts recorded related to the cash proceeds received from the Amgen collaboration for the year ended December 31, 2020 were as follows:

	Year Ended December 31, 2020
	$
Fair value of equity issued to Amgen	2,162,407
Fair value of research and development cost share liability	616,834
Total cash proceeds	2,779,241

Amounts recorded related to the Company's portion of the co-development funding on the pipeline assets for the years ended December 31, 2022, 2021 and 2020 were as follows:

	Year Ended December 31,		
	2022	2021	2020
	$	$	$
Research and development expense	98,955	115,464	117,005
Amortization of research and development cost share liability	96,402	112,486	113,986
Total amount due to Amgen for BeiGene's portion of the development funding	195,357	227,950	230,991

	As of December 31, 2022
Remaining portion of development funding cap	595,702

As of December 31, 2022 and 2021, the research and development cost share liability recorded in the Company's balance sheet was as follows:

	As of December 31,	
	2022	2021
	$	$
Research and development cost share liability, current portion	114,335	120,801
Research and development cost share liability, non-current portion	179,625	269,561
Total research and development cost share liability	293,960	390,362

The net reimbursement due under the commercial profit-sharing agreement for in-line product sales is classified in the consolidated statements of operations for the three years ended December 31, 2022 as follows:

	Year Ended December 31,		
	2022	2021	2020
	$	$	$
Cost of sales - product	5,898	1,893	(1,210)
Selling, general and administrative	(54,865)	(45,152)	(9,750)
Research and development	(1,216)	423	(660)
Total	(50,183)	(42,836)	(11,620)

The Company purchases commercial inventory from Amgen to distribute in China. Total inventory purchases amounted to $71,720, $110,303 and 38,392, respectively, during the year ended December 31, 2022, 2021 and 2020. Net amounts payable to Amgen as of December 31, 2022 and 2021 were $54,064 and $106,790, respectively.

In-Licensing Arrangements - Development

The Company has in-licensed the rights to develop, manufacture and, if approved, commercialize multiple development stage drug candidates globally or in specific territories. These arrangements typically include non-refundable upfront payments, contingent obligations for potential development, regulatory and commercial performance milestone payments, cost-sharing arrangements, royalty payments, and profit sharing.

Upfront and milestone payments made under these arrangements for the years ended December 31, 2022, 2021 and 2020 are set forth below. All upfront and development milestones were expensed to research and development expense. All regulatory and commercial milestones were capitalized as intangible assets and are being amortized over the remainder of the respective product patent or the term of the commercialization agreements.

		Year Ended December 31,		
		2022	2021	2020
Payments due to collaboration partners	**Classification**	$	$	$
Upfront payments	Research and development expense	68,665	83,500	109,500
Development milestone payments	Research and development expense	5,500	15,000	15,800
Regulatory and commercial milestone payments	Intangible asset	—	43,394	—
Total		74,165	141,894	125,300

Our significant license agreements are described below:

Shandong Luye Pharmaceutical Co., Ltd.

In December 2022, the Company entered into an exclusive license agreement with Shandong Luye Pharmaceutical Co., Ltd. ("Luye") to develop (exclusive of indications for which Luye has submitted the drug marketing authorization application to the China National Medical Products Administration) and commercialize Luye's proprietary goserelin acetate extended-release microspheres for intramuscular injection known as LY01005 in mainland China. Under the terms of the agreement, the Company paid Luye an upfront license payment of $48,665, exclusive of VAT, which was recognized as in-process research and development expense, and a prepayment of $30,000 to be applied toward future supply purchases in December 2022. Luye is also eligible to receive future milestone payments upon achievement of certain regulatory milestones. Luye is also eligible to receive tiered royalties on net sales. Luye is considered a related party due to a significant common shareholder. That shareholder has different representatives serving on each companies' respective board of directors.

Shoreline Biosciences, Inc.

In June 2021, the Company entered into an exclusive worldwide strategic collaboration with Shoreline Biosciences, Inc. (Shoreline) to develop and commercialize a portfolio of natural killer (NK)-based cell therapeutics with Shoreline's induced pluripotent stem cells (iPSC) NK cell technology and the Company's research and clinical development capabilities for different malignancies. Under the collaboration, the Company and Shoreline are working jointly to develop cell therapies for four

designated therapeutic targets, with an option to expand the collaboration at a future date. Clinical development is being led by the Company globally, with Shoreline responsible for clinical manufacturing. The Company has commercial rights globally, with Shoreline having an option to retain commercialization rights in the United States and Canada for two targets. Under the terms of the agreement, Shoreline received a $45,000 upfront payment in January 2022 and is eligible to receive additional R&D funding, milestone payments and royalties based upon the achievement of certain development, regulatory, and commercial milestones. The upfront payment was expensed to research and development expense during the year ended December 31, 2021 in accordance with the Company's acquired in-process research and development expense policy.

Nanjing Leads Biolabs, Inc.

In December 2021, the Company entered into a license and collaboration agreement with Nanjing Leads Biolabs, Inc. (Leads Biolabs) for worldwide research, development and manufacturing rights and exclusive commercialization rights outside of China to LBL-007, a novel investigational antibody targeting the LAG-3 pathway. Under the terms of the agreement, Leads Biolabs received an upfront payment of $30,000 in January 2022 and is eligible to receive up to $742,000 in clinical development, regulatory approval and sales milestones. Leads Biolabs is also eligible to receive tiered royalties on future sales in the licensed territory. The upfront payment was expensed to research and development expense during the year ended December 31, 2021 in accordance with the Company's acquired in-process research and development expense policy.

EUSA Pharma

In January 2020, the Company entered into an exclusive development and commercialization agreement with EUSA Pharma (EUSA) for the orphan biologic products SYLVANT® (siltuximab) and QARZIBA® (dinutuximab beta) in China. Under the terms of the agreement, EUSA granted the Company exclusive rights to SYLVANT in greater China and to QARZIBA in mainland China. Under the agreement, the Company is funding and undertaking all clinical development and regulatory submissions in the territories, and commercializing both products once approved. EUSA received a $40,000 upfront payment upon contract execution and is eligible to receive additional payments upon the achievement of regulatory and commercial milestones up to a total of $120,000. The upfront payment was expensed to research and development expense during the year ended December 31, 2020 in accordance with the Company's acquired in-process research and development expense policy. In 2021, QARZIBA and SYLVANT were approved and launched in mainland China and greater China, respectively. The approvals triggered regulatory milestone payments that were capitalized as intangible assets and are being amortized over the remaining term of the license agreement. EUSA is receiving tiered royalties on SYLVANT product sales, which the Company records as cost of sales in the period the respective sales are generated.

Assembly Biosciences, Inc.

In July 2020, the Company entered into a collaboration agreement with Assembly Biosciences, Inc. (Assembly) for Assembly's portfolio of three clinical-stage core inhibitor candidates for the treatment of patients with chronic hepatitis B virus (HBV) infection in China. Under the terms of the agreement, Assembly granted BeiGene exclusive rights to develop and commercialize ABI-H0731, ABI-H2158 and ABI-H3733 in China, including Hong Kong, Macau, and Taiwan. BeiGene is responsible for development, regulatory submissions, and commercialization in China. Assembly retains full worldwide rights outside of the partnered territory for its HBV portfolio. Assembly received an upfront payment of $40,000 and is eligible to receive payments upon achievement of development, regulatory and commercial milestones up to a total of $503,750. Assembly is also eligible to receive tiered royalties on net sales. The upfront payment was expensed to research and development expense during the year ended December 31, 2020 in accordance with the Company's acquired in-process research and development expense policy.

Bio-Thera Solutions, Ltd.

In August 2020, the Company entered into a license, distribution and supply agreement with Bio-Thera Solutions, Ltd. (Bio-Thera) for Bio-Thera's POBEVCY® (BAT1706), a biosimilar to Avastin® (bevacizumab) in China. The agreement became effective on September 10, 2020 upon approval of Bio-Thera's shareholders, and was subsequently assigned by the Company to its affiliate BeiGene (Guangzhou) Co., Ltd. (BeiGene Guangzhou) on September 18, 2020, as permitted by the agreement. Under the terms of the agreement, Bio-Thera agreed to grant BeiGene the right to develop, manufacture, and commercialize POBEVCY in China, including Hong Kong, Macau, and Taiwan. Bio-Thera retained rights outside of the partnered territory. Bio-Thera received an upfront payment of $20,000 in October 2020 and is eligible to receive payments upon the achievement of regulatory and commercial milestones up to a total of $145,000. The upfront payment was expensed to research and

development expense during the year ended December 31, 2020 in accordance with the Company's acquired in-process research and development expense policy. In November 2021, POBEVCY obtained regulatory approval, and was subsequently launched, in China, triggering a milestone payment that was capitalized as an intangible asset that is being amortized over the remaining term of the license agreement. Bio-Thera is also receiving tiered royalties on product sales, which the Company records as cost of sales in the period the respective sales are generated.

Other

In addition to the collaborations discussed above, the Company has entered into additional collaborative arrangements during the years ended December 31, 2022, 2021 and 2020. The Company may be required to pay additional amounts upon the achievement of various development and commercial milestones under these agreements. The Company may also incur significant research and development costs if the related product candidate were to advance to late-stage clinical trials. In addition, if any products related to these collaborations are approved for sale, the Company may be required to pay significant milestones upon approval and milestones and/or royalties on future sales. The payment of these amounts, however, is contingent upon the occurrence of various future events, which have a high degree of uncertainty of occurrence.

5. Restricted Cash

The Company's restricted cash balance of $5,473 and $7,209 as of December 31, 2022 and 2021, respectively, primarily consist of RMB-denominated cash deposits held in designated bank accounts for collateral for letters of credit. The Company classifies restricted cash as current or non-current based on term of restriction.

In addition to the restricted cash balances above, the Company is required by the PRC securities law to use the proceeds from the STAR offering in strict compliance with the planned uses as disclosed in the PRC prospectus as well as those disclosed in the Company's proceeds management policy approved by the board of directors.

6. Investments

Short-Term Investments

Short-term investments as of December 31, 2022 consisted of the following available-for-sale debt securities:

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value (Net Carrying Amount)
	$	$	$	$
U.S. treasury securities	674,262	—	9,011	665,251
Total	674,262	—	9,011	665,251

Short-term investments as of December 31, 2021 consisted of the following available-for-sale debt securities:

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value (Net Carrying Amount)
	$	$	$	$
U.S. treasury securities	2,245,662	—	3,700	2,241,962
Total	2,245,662	—	3,700	2,241,962

The Company does not consider the investments in U.S. treasury securities to be other-than-temporarily impaired at December 31, 2022. As of December 31, 2022, the Company's available-for-sale debt securities consisted entirely of short-term U.S. treasury securities, which were determined to have zero risk of expected credit loss. Accordingly, no allowance for credit loss was recorded as of December 31, 2022.

Equity Securities with Readily Determinable Fair Values

Leap Therapeutics, Inc. (Leap)

In January 2020, the Company purchased $5,000 of Series B mandatorily convertible, non-voting preferred stock of Leap in connection with a strategic collaboration and license agreement the Company entered into with Leap. The Series B shares were subsequently converted into shares of Leap common stock and warrants to purchase additional shares of common stock upon approval of Leap's shareholders in March 2020. In September 2021, the Company purchased $7,250 of common stock in Leap's underwritten public offering. As of December 31, 2022, the Company's ownership interest in the outstanding common stock of Leap was 7.4% based on information from Leap. Inclusive of the shares of common stock issuable upon the exercise of the currently exercisable warrants, the Company's interest is approximately 11.7%. The Company measures the investment in the common stock and warrants at fair value, with changes in fair value recorded to other (expense) income, net. During the years ended December 31, 2022, 2021 and 2020, the Company recorded unrealized (losses) gains of $(30,102), $9,386 and $12,479, respectively, in the consolidated statement of operations, respectively.

As of December 31, 2022 and 2021, the fair value of the common stock and warrants was as follows:

	As of December 31,	
	2022	2021
	$	$
Fair value of Leap common stock	3,307	23,809
Fair value of Leap warrants	706	10,306

Private Equity Securities without Readily Determinable Fair Values

The Company invests in equity securities of certain companies whose securities are not publicly traded and fair value is not readily determinable and where the Company has concluded it does not have significant influence based on its ownership percentage and other factors. These investments are recorded at cost minus impairment, if any, plus or minus changes resulting from observable price changes in orderly transactions for the identical or a similar investment of the same issuer. The Company held investments of $57,054 and $43,722 in equity securities without readily determinable fair values as of December 31, 2022 and 2021, respectively. The Company recorded gains of $5,065 related to observable price changes in orderly transactions for similar investments of the same issuer for the year ended December 31, 2022 to other (expense) income, net in the consolidated statements of operations. There were no adjustments to the carrying values of these securities for the years ended December 31, 2021 and 2020.

Equity-Method Investments

The Company records equity-method investments at cost and subsequently adjusts the basis based on the Company's ownership percentage in the investees' income and expenses, as well as dividends, if any. The Company holds equity-method investments totaling $27,710 and $22,955 as of December 31, 2022 and 2021, respectively, that it does not consider to be individually significant to its financial statements. The Company recorded unrealized losses of $3,682, $1,796 and $491 for the years ended December 31, 2022, 2021 and 2020, respectively, to other (expense) income, net in the consolidated statements of operations.

7. Inventories

The Company's inventory balance consisted of the following:

	As of December 31,	
	2022	2021
	$	$
Raw materials	88,957	78,140
Work in process	20,886	9,397
Finished goods	172,503	155,089
Total inventories	282,346	242,626

8. Manufacturing Facility in Guangzhou, China

Manufacturing legal entity structure

BeiGene Shanghai, originally established as a wholly-owned subsidiary of BeiGene (Hong Kong) Co., Ltd. (BeiGene HK), and currently a wholly-owned subsidiary of BeiGene Biologics, as described below, provides clinical development services for BeiGene affiliates and is the clinical trial authorization (CTA) holder and marketing authorization application (MAA) holder for tislelizumab in China.

In March 2017, BeiGene HK, a wholly owned subsidiary of the Company, and Guangzhou GET Technology Development Co., Ltd. (now Guangzhou High-tech Zone Technology Holding Group Co., Ltd.) (GET), entered into a definitive agreement to establish a commercial scale biologics manufacturing facility in Guangzhou, Guangdong Province, PRC. BeiGene HK and GET entered into an Equity Joint Venture Contract (the “JV Agreement”).

Under the terms of the JV Agreement, BeiGene HK made an initial cash capital contribution of RMB200,000 and a subsequent contribution of one or more biologics assets in exchange for a 95% equity interest in BeiGene Biologics. GET made a cash capital contribution of RMB100,000 to BeiGene Biologics, representing a 5% equity interest in BeiGene Biologics. In addition, on March 7, 2017, BeiGene Biologics entered into a contract with GET, under which GET agreed to provide a RMB900,000 loan (the "Shareholder Loan”) to BeiGene Biologics. In September 2019, BeiGene Biologics completed the first phase of construction of a biologics manufacturing facility in Guangzhou, through a wholly owned subsidiary, the BeiGene Guangzhou Biologics Manufacturing Co., Ltd. (BeiGene Guangzhou Factory), to manufacture biologics for the Company and its subsidiaries.

BeiGene HK and BeiGene Biologics subsequently entered into an Equity Transfer Agreement to transfer 100% of the equity interest of BeiGene Shanghai to BeiGene Biologics, as required by the JV agreement, such that the CTA holder and MAA holder for tislelizumab in China was controlled by BeiGene Biologics. Upon the transfer of equity in BeiGene Shanghai, BeiGene HK's equity interest in BeiGene Shanghai became 95%.

In September 2020, BeiGene HK entered into a share purchase agreement (the "JV Share Purchase Agreement") with GET to acquire GET’s 5% equity interest in BeiGene Biologics for a total purchase price of $28,723 (RMB195,262). The transaction was finalized in November 2020 upon completion of the business registration filing. The share purchase was recorded as an equity transaction. The carrying amount of the noncontrolling interest balance of $9,116 was adjusted to nil to reflect the increase in BeiGene HK’s ownership interest to 100%, and the difference in the fair value of the consideration paid and the carrying amount of the noncontrolling interest of $19,599 was recorded to additional paid in capital. In connection with the JV Share Purchase Agreement, BeiGene Biologics repaid the outstanding principal of the Shareholder Loan of $132,061 (RMB900,000) and accrued interest of $36,558 (RMB249,140).

In connection with the JV share purchase, the Company entered into a loan agreement with China Minsheng Bank for a total loan facility of up to $200,000 (the "Senior Loan"), of which $120,000 was used to fund the JV share repurchase and repayment of the shareholder loan and $80,000 could be used for general working capital purposes. The Company may extend the original maturity date for up to two additional twelve month periods. In October 2020, the Company drew down $80,000 of the working capital facility and $118,320 of the acquisition facility to be used for the JV share repurchase. On October 9, 2021, the Company repaid $198,320 and drew down $200,000 from the Senior Loan. In addition, the Company entered into a loan agreement with Zhuhai Hillhouse Zhaohui Equity Investment Partnership (Zhuhai Hillhouse) for a total loan facility of $73,640 (RMB500,000) (the "Related Party Loan"), of which $14,728 (RMB100,000) can be used for general corporate purposes and $58,912 (RMB400,000) can only be applied towards the repayment of the Senior Loan facility, including principal, interest and fees. The Company drew down $15,693 (RMB100,000) of the Related Party Loan as of December 31, 2021 and repaid the loan in full in November of 2022. See Note 14 for further discussion of the loans.

9. Leases

The Company has operating leases for office and manufacturing facilities in the United States, Switzerland, and China. The leases have remaining lease terms of up to five years, some of which include options to extend the leases that have not been included in the calculation of the Company’s lease liabilities and ROU assets. The Company has land use rights, which represent land acquired for the biologics manufacturing facility in Guangzhou, the land acquired for the Company's research, development and office facility in Changping, Beijing, and the land acquired for the Company's research, development and manufacturing facility in Suzhou. The land use rights represent lease prepayments and are expensed over the remaining term of

the rights, which is 50 years for the Guangzhou land use rights, 36 years for the Changping land use right, and 30 years for the Suzhou land use rights. The Company also has certain leases with terms of 12 months or less for certain equipment, office and lab space, which are expensed and not recorded on the balance sheet.

The components of lease expense were as follows:

	Year Ended December 31,		
	2022	2021	2020
	$	$	$
Operating lease cost	25,938	22,536	18,271
Variable lease cost	6,834	4,892	2,465
Short-term lease cost	1,299	1,823	1,018
Total lease cost	34,071	29,251	21,754

Supplemental balance sheet information related to leases was as follows:

	As of December 31,	
	2022	2021
	$	$
Operating lease right-of-use assets	56,008	60,762
Land use rights, net	53,952	56,669
Total operating lease right-of-use assets	109,960	117,431
Current portion of operating lease liabilities	24,041	21,925
Operating lease liabilities, non-current portion	34,517	43,041
Total lease liabilities	58,558	64,966

Maturities of operating lease liabilities are as follows:

	$
Year ending December 31, 2023	26,278
Year ending December 31, 2024	21,647
Year ending December 31, 2025	11,312
Year ending December 31, 2026	2,821
Year ending December 31, 2027	966
Total lease payments	63,024
Less imputed interest	(4,466)
Present value of lease liabilities	58,558

Other supplemental information related to leases is summarized below:

	Year ended December 31,		
	2022	2021	2020
	$	$	$
Operating cash flows used in operating leases	28,064	19,962	17,571
ROU assets obtained in exchange for new operating lease liabilities	22,278	37,454	17,634

	As of December 31,	
	2022	2021
Weighted-average remaining lease term (years)	3	3
Weighted-average discount rate	5.76 %	5.15 %

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10. Property, Plant and Equipment, Net

Property, plant and equipment, net are recorded at cost less accumulated depreciation and consisted of the following:

	As of December 31,	
	2022	2021
	$	$
Land	65,485	65,485
Laboratory equipment	158,908	118,203
Leasehold improvements	53,786	50,288
Building	222,448	144,083
Manufacturing equipment	175,679	119,585
Software, electronics and office equipment	47,483	27,404
Property and equipment, at cost	723,789	525,048
Less: Accumulated depreciation	(171,470)	(124,286)
Construction in progress	293,627	186,843
Property, plant and equipment, net	845,946	587,605

In November 2021, the Company purchased a 42-acre site located in Hopewell, NJ for $75,197. The total purchase price was allocated between the land and an existing building on the property based on their relative fair values. The Company is constructing a biologics manufacturing facility and research and development center on the land.

Construction in progress (CIP) as of December 31, 2022 and 2021 primarily related to the construction of the manufacturing and clinical R&D campus in Hopewell, a new building for Beijing Innerway Bio-tech Co., Ltd., and additional capacity at the Guangzhou and Suzhou manufacturing facilities. CIP by fixed asset class are summarized as follows:

	As of December 31,	
	2022	2021
	$	$
Building	224,392	90,229
Manufacturing equipment	33,332	63,361
Laboratory equipment	12,256	17,178
Other	23,647	16,075
Total	293,627	186,843

Depreciation expense for the years ended December 31, 2022, 2021 and 2020 were $62,302, $44,742 and $30,943, respectively.

11. Intangible Assets

Intangible assets as of December 31, 2022 and December 31, 2021 are summarized as follows:

	December 31, 2022			December 31, 2021		
	Gross carrying amount	Accumulated amortization	Intangible assets, net	Gross carrying amount	Accumulated amortization	Intangible assets, net
	$	$	$	$	$	$
Finite-lived intangible assets:						
Product distribution rights	7,500	(4,000)	3,500	7,500	(3,250)	4,250
Developed products	41,235	(4,119)	37,116	43,394	(965)	42,429
Trading license	816	(816)	—	816	(816)	—
Total finite-lived intangible assets	49,551	(8,935)	40,616	51,710	(5,031)	46,679

Product distribution rights consist of distribution rights for the approved cancer therapies licensed from BMS as part of the BMS collaboration. The Company is amortizing the product distribution rights, as a single identified asset, over the term of the license agreement of 10 years from the date of acquisition. Developed products represent the post-approval milestone payments under license and commercialization agreements. The Company is amortizing the developed products over the remainder of the respective product patent or the term of the commercialization agreements. Trading license represents the Guangzhou drug distribution license acquired in September 2018. The Company amortized the drug distribution trading license over the remainder of the initial license term through February 2020. The trading license has been renewed through February 2024.

Amortization expense for developed products is included in cost of sales - product in the accompanying consolidated statements of operations. Amortization expense for product distribution rights and trading licenses is included in operating expenses in the accompanying consolidated statements of operations. The weighted-average life for each finite-lived intangible assets is approximately 12 years. Amortization expense is as follows:

	Year Ended December 31,		
	2022	2021	2020
	$	$	$
Amortization expense - Cost of sales - product	3,225	965	—
Amortization expense - Operating expense	751	750	846
Total	3,976	1,715	846

Estimated amortization expense for each of the five succeeding years and thereafter, as of December 31, 2022 is as follows:

Year Ending December 31,	Cost of Sales - Product	Operating Expenses	Total
	$	$	$
2023	3,170	750	3,920
2024	3,170	750	3,920
2025	3,170	750	3,920
2026	3,170	750	3,920
2027	3,170	500	3,670
2028 and thereafter	21,266	—	21,266
Total	37,116	3,500	40,616

12. Income Taxes

The components of income (loss) before income taxes are as follows:

	Year Ended December 31,		
	2022	2021	2020
	$	$	$
PRC	(583,610)	(606,752)	(369,066)
U.S.	67,744	34,923	33,608
Other	(1,445,171)	(866,759)	(1,282,736)
Total	(1,961,037)	(1,438,588)	(1,618,194)

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The current and deferred components of the income tax expense (benefit) from continuing operations are as follows:

	Year Ended December 31,		
	2022	2021	2020
	$	$	$
Current Tax Expense (Benefit):			
PRC	27,905	15,252	16,121
U.S.	4,844	(9)	(5,678)
Other	6,547	805	68
Total	39,296	16,048	10,511
Deferred Tax Expense (Benefit):			
PRC	3,480	4,919	(114)
U.S.	—	(35)	—
Other	2	(1,704)	—
Total	3,482	3,180	(114)
Income Tax (Benefit) Expense	42,778	19,228	10,397

The reconciliation of the statutory tax rate to our effective income tax rate is as follow:

	Year Ended December 31,		
	2022	2021	2020
	$	$	$
Loss before tax	(1,961,037)	(1,438,588)	(1,618,194)
China statutory tax rate	25 %	25 %	25 %
Expected taxation at China statutory tax rate	(490,259)	(359,647)	(404,549)
Foreign and preferential tax rate differential	288,133	185,874	218,473
Non-deductible expenses	30,598	(2,826)	8,436
Stock compensation expenses	33,872	(27,411)	(22,032)
Effect of tax rate change	—	—	(3,827)
Change in valuation allowance	229,550	254,768	237,153
Research tax credits and incentives	(49,116)	(31,530)	(23,257)
Taxation for the year	42,778	19,228	10,397
Effective tax rate	(2.2)%	(1.3)%	(0.6)%

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Significant components of deferred tax assets (liabilities) are as follows:

	Year Ended December 31,		
	2022	2021	2020
	$	$	$
Deferred tax assets (liabilities):			
Accruals and reserves	97,896	84,766	33,512
Net operating losses carryforward	862,214	625,114	358,425
Stock-based compensation	19,700	14,982	13,981
Research tax credits	86,000	82,060	58,835
Depreciable and amortizable assets	798,563	937,069	724,779
Lease liability obligation	10,348	11,571	9,066
R&D and other capitalized costs	63,156	—	—
Right of use asset	(10,098)	(11,322)	(8,843)
Gross deferred tax assets	1,927,779	1,744,240	1,189,755
Less valuation allowance	(1,943,775)	(1,758,409)	(1,200,547)
Net deferred tax liabilities	(15,996)	(14,169)	(10,792)

Valuation allowances have been provided on deferred tax assets where, based on all available evidence, it was considered more likely than not that some portion or all of the recorded deferred tax assets will not be realized in future periods. After consideration of all positive and negative evidence, the Company believes that as of December 31, 2022, it is more likely than not that certain deferred tax assets will not be realized for our subsidiaries in Australia, Switzerland, the United States, and for certain subsidiaries in China. For the years ended December 31, 2022 and 2021, there were increases in the valuation allowance of $229,550 and $254,768, respectively. Adjustments may be required in the future if the Company estimates that the amount of deferred tax assets to be realized is more or less than the net amount recorded.

As of December 31, 2022 and 2021, the Company had net operating losses of approximately $5,077,247 and $3,644,981, respectively. As of December 31, 2022, net operating losses were primarily comprised of: $1,633,101 from entities in the PRC which expire in years 2024 through 2032; $3,397,529 derived from Switzerland which expires in years 2025 through 2029; and, $26,079 derived from entities in the United States that have an indefinite carryforward. The Company has approximately $108,861 of U.S. research tax credits which will expire between 2036 and 2042, if not utilized.

The gross unrecognized tax benefits for the years ended December 31, 2022, 2021 and 2020 were as follows:

	Year Ended December 31,		
	2022	2021	2020
	$	$	$
Beginning balance, as of January 1	9,925	7,123	4,633
Additions based on tax positions related to prior tax years	—	—	—
Reductions based on tax positions related to prior tax years	—	—	—
Additions based on tax positions related to the current tax year	1,630	2,802	2,497
Reductions based on lapse of statute of limitations	—	—	(7)
Ending balance, as of December 31	11,555	9,925	7,123

Current and prior year additions include an assessment of U.S. federal and state tax credits and incentives. None of the unrecognized tax benefits as of December 31, 2022 would impact the consolidated income tax rate if ultimately recognized due to valuation allowances. The Company does not anticipate that the amount of existing unrecognized tax benefits will significantly change within the next 12 months.

The Company has elected to record interest and penalties related to income taxes as a component of income tax expense. For the years ended December 31, 2022, 2021 and 2020, the Company's accrued interest and penalties, where applicable, related to uncertain tax positions were not material.

The Company conducts business in a number of tax jurisdictions and, as such, is required to file income tax returns in multiple jurisdictions globally. As of December 31, 2022, Australia tax matters are open to examination for the years 2013 through 2022, China tax matters are open to examination for the years 2012 through 2022, Switzerland tax matters are open to examination for the years 2018 through 2022, and U.S. federal tax matters are open to examination for years 2015 through 2022. Various U.S. states and other non-US tax jurisdictions in which the Company files tax returns remain open to examination for 2012 through 2022.

The Company qualifies for the Technology Advanced Service Enterprises (TASE) and High and New Technology Enterprise (HNTE) status for certain subsidiaries in China, which expire at the end of 2025. The income tax benefits attributable to this status for the year ended December 31, 2022 is approximately $3,894, or less than $0.01 per share outstanding.

As of December 31, 2022, the Company asserts indefinite reinvestment on the excess of the financial reporting bases over tax bases in the Company's investments in foreign subsidiaries to the extent reversal would incur a significant tax liability. A deferred tax liability has not been established for the approximately $2,379 of cumulative undistributed foreign earnings. Determination of the unrecognized deferred tax liability is not practicable due to the uncertainty and overall complexity of the hypothetical calculation.

13. Supplemental Balance Sheet Information

Changes in the allowance for credit losses related to trade accounts receivable consist of the following:

	Year Ended December 31,		
	2022	2021	2020
	$	$	
Beginning balance, as of January 1	415	112	—
Provision charged to selling, general and administrative expenses	(219)	309	109
Amounts written-off, net of recoveries of amounts previously reserved	1	—	—
Exchange rate changes	14	(6)	3
Ending balance, as of December 31	211	415	112

Prepaid expenses and other current assets consist of the following:

	As of December 31,	
	2022	2021
	$	$
Prepaid research and development costs	71,488	87,239
Prepaid taxes	20,478	58,579
Other receivables	22,777	12,010
Interest receivable	3,039	5,052
Prepaid insurance	3,664	1,695
Prepaid manufacturing cost	58,950	78,538
Short-term deposit	1,510	2,982
Other current assets	34,647	24,078
Total	216,553	270,173

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Other non-current assets consist of the following:

	As of December 31,	
	2022	2021
	$	$
Goodwill	109	109
Prepayment of property and equipment	22,025	14,140
Prepaid supply cost (1)	48,642	24,237
Prepaid VAT	804	17,162
Rental deposits and other	7,054	6,609
Long-term investments	91,779	100,792
Total	170,413	163,049

(1) Represents payments for future supply purchases under the license agreement with Luye and facility expansion under commercial supply agreements. The payments are providing future benefit to the Company through credits on commercial supply purchases.

Accrued expenses and other payables consisted of the following:

	As of December 31,	
	2022	2021
	$	$
Compensation related	184,775	139,966
External research and development activities related	139,168	213,922
Commercial activities	51,806	71,560
Individual income tax and other taxes	18,815	45,661
Sales rebates and returns related	41,817	59,639
Other	30,971	27,307
Total accrued expenses and other payables	467,352	558,055

Other long-term liabilities consist of the following:

	As of December 31,	
	2022	2021
	$	$
Deferred government grant income	38,176	46,352
Pension liability	7,760	7,814
Other	159	68
Total other long-term liabilities	46,095	54,234

14. Debt

The following table summarizes the Company's short-term and long-term debt obligations as of December 31, 2022 and 2021:

Lender	Agreement Date	Line of Credit	Term	Maturity Date	Interest Rate	As of December 31,			
						2022		2021	
						$	RMB	$	RMB
China Construction Bank	April 4, 2018	RMB580,000	9-year	April 4, 2027	(1)	7,250	50,000	1,255	8,000
China Merchants Bank	January 22, 2020	(2)	9-year	January 20, 2029	(2)	1,450	10,000	1,569	10,000
China Merchants Bank	November 9, 2020	RMB378,000	9-year	November 8, 2029	(3)	5,437	37,500	—	—

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China Minsheng Bank (the "Senior Loan")	September 24, 2020	$200,000		(4)	4.3%	150,000	1,034,554	200,000	1,274,535
Zhuhai Hillhouse (the "Related Party Loan")	September 24, 2020	RMB500,000		(5)	4.5%	—	—	15,693	100,000
Shanghai Pudong Development Bank	February 25, 2022	$50,000	1-year	February 25, 2023	2.2 %	50,000	344,851	—	—
Other short-term debt (6)						114,832	792,000	209,048	1,332,197
Total short-term debt						328,969	2,268,905	427,565	2,724,732
China Construction Bank	April 4, 2018	RMB580,000	9-year	April 4, 2027	(1)	75,395	520,000	89,444	570,000
China Merchants Bank	January 22, 2020	(2)	9-year	January 20, 2029	(2)	49,369	340,500	53,353	340,000
China Merchants Bank	November 9, 2020	RMB378,000	9-year	November 8, 2029	(3)	47,847	330,000	59,316	378,000
China CITIC Bank	July 29, 2022	RMB480,000	10-year	July 28, 2032	(7)	36,537	252,000	—	—
Total long-term debt						209,148	1,442,500	202,113	1,288,000

1. The outstanding borrowings bear floating interest rates benchmarking RMB loan interest rates of financial institutions in the PRC. The loan interest rate was 4.7% as of December 31, 2022. The Company repaid $1,171 (or RMB8,000) during the year ended December 31, 2022. The loan is secured by BeiGene Guangzhou Factory's land use right and certain Guangzhou Factory fixed assets in the first phase of the Guangzhou manufacturing facility's build out.

2. On January 22, 2020, BeiGene Guangzhou Biologics Manufacturing Co., Ltd.("BeiGene Guangzhou Factory") entered into a nine-year bank loan with China Merchants Bank to borrow up to RMB1,100,000 at a floating interest rate benchmarked against prevailing interest rates of certain PRC financial institutions. The loan is secured by Guangzhou Factory's second land use right and fixed assets that will be placed into service upon completion of the second phase of the Guangzhou manufacturing facility's build out. In connection with the Company's short-term loan agreements with China Merchants Bank entered into during the year ended December 31, 2020, the borrowing capacity was reduced from RMB1,100,000 to RMB350,000. The loan interest rate was 4.4% as of December 31, 2022. The Company repaid $1,484 (RMB10,000) during the year ended December 31, 2022. BeiGene Guangzhou Biologics Manufacturing Co., Ltd. is a company incorporated under the laws of the PRC on March 3, 2017 and a wholly owned subsidiary of BeiGene Biologics.

3. The outstanding borrowings bear floating interest rates benchmarking RMB loan interest rates of financial institutions in the PRC. The loan interest rate was 4.0% as of December 31, 2022. The loan is secured by fixed assets that will be placed into service upon completion of the third phase of the Guangzhou manufacturing facility's build out.

4. In September 2020, the Company entered into a loan agreement with China Minsheng Bank for a total loan facility of up to $200,000, of which $120,000 was designated to fund the JV share purchase and repayment of the Shareholder Loan and $80,000 was designated for general working capital purposes. The Senior Loan had an original maturity date of October 8, 2021, which was the first anniversary of the first date of utilization of the loan. The Company may extend the original maturity date for up to two additional twelve month periods. On October 8, 2021, the Company extended the maturity date for twelve months to October 8, 2022 and repurposed the Senior Loan for general working capital purposes. On September 30, 2022, the Company entered into an amendment and restatement agreement with China Minsheng Bank to extend the maturity date. On October 10, 2022, the Company repaid $200,000 and drew down $150,000 from the Senior Loan.

5. In September 2020, the Company entered into a loan agreement with Zhuhai Hillhouse Zhaohui Equity Investment Partnership (Zhuhai Hillhouse) for a total loan facility of $73,640 (RMB500,000), of which $14,728 (RMB100,000) can be used for general corporate purposes and $58,912 (RMB400,000) can only be applied towards the repayment of the Senior Loan facility, including principal, interest and fees. The loan originally matured at the earlier of: (i) November 9, 2021, which is one month after the Senior Loan maturity date, if not extended, or (ii) 10 business days after the Senior Loan is fully repaid. On October 8, 2021, the Company extended the maturity date of the Related Party Loan to the earlier of: (i) November 9, 2022, which is one month after the Senior Loan maturity date, if not extended, or (ii) 10 business days after the Senior Loan is fully repaid. On October 10, 2022, the Company repaid in full the outstanding borrowing in the amount of $13,980 (RMB100,000). Zhuhai Hillhouse is a related party of the Company, as it is an affiliate of Hillhouse Capital. Hillhouse Capital is a shareholder of the Company, and a Hillhouse Capital employee is a member of the Company's board of directors.

6. During the three years ended December 31, 2022, the Company entered into additional short-term working capital loans with China Industrial Bank and China Merchants Bank to borrow up to RMB2,435,000 in aggregate, with maturity dates ranging from January 19, 2021 to September 18, 2023. The Company drew down $113,774 (RMB792,000) during the year ended December 31, 2022. The Company repaid $200,446 (RMB1,332,197) of the short-term loans during the year ended. December 31, 2022. The weighted average interest rate for the short-term working capital loans was approximately 2.6% as of December 31, 2022.

7. In July 2022, the Company entered into a 10-year bank loan agreement with China CITIC Bank to borrow up to RMB480,000 at a floating interest rate benchmarked against prevailing interest rates of certain PRC financial institutions. The loan interest rate was 4.2% as of December 31, 2022. The loan is secured by BeiGene Suzhou Co., Ltd.'s land use right. The Company drew down $37,372 (RMB252,000) during the year ended December 31, 2022.

Contractual Maturities of Debt Obligations

The aggregate contractual maturities of all borrowings due subsequent to December 31, 2022 are as follows:

Maturity dates	Amounts
	$
Year ending December 31, 2023	328,969
Year ending December 31, 2024	29,412
Year ending December 31, 2025	35,136
Year ending December 31, 2026	44,697
Year ending December 31, 2027	44,697
Thereafter	55,206
Total	538,117

Interest Expense

Interest on bank loans and the Related Party Loan is paid quarterly until the respective loans are fully settled. Interest expense recognized for the years ended December 31, 2022, 2021 and 2020 amounted to $21,699, $29,263 and $18,309, respectively, among which, $2,594, $1,054 and $338 was capitalized, respectively.

15. Product Revenue

The Company's product revenue is primarily derived from the sale of its internally developed products BRUKINSA in the United States and China, and tislelizumab and pamiparib in China; REVLIMID® and VIDAZA® in China under a license from BMS; XGEVA, BLINCYTO and KYPROLIS in China under a license from Amgen; and POBEVCY in China under a license from Bio-Thera.

The table below presents the Company's net product sales for the years ended December 31, 2022, 2021 and 2020.

	Year Ended December 31,		
	2022	2021	2020
	$	$	$
Product revenue - gross	1,438,440	748,824	324,672
Less: Rebates and sales returns	(183,828)	(114,837)	(15,798)
Product revenue - net	1,254,612	633,987	308,874

The following table disaggregates net product revenue by product for the years ended December 31, 2022, 2021 and 2020.

	Year Ended December 31,		
	2022	2021	2020
	$	$	$
BRUKINSA®	564,651	217,987	41,702
Tislelizumab	422,885	255,119	163,358
REVLIMID®	79,049	70,065	47,372
XGEVA®	63,398	45,956	8,496
POBEVCY®	38,124	1,353	—
BLINCYTO®	36,107	12,515	—
KYPROLIS®	13,696	—	—
VIDAZA®	15,213	19,591	29,975
Pamiparib	5,460	3,661	—
ABRAXANE®	—	—	17,770
Other	16,029	7,740	201
Total product revenue - net	1,254,612	633,987	308,874

The following table presents the roll-forward of accrued sales rebates and returns for the years ended December 31, 2022 and December 31, 2021.

	Year Ended December 31,	
	2022	2021
	$	$
Beginning balance, as of January 1	59,639	11,874
Accrual	183,828	114,837
Payment	(201,650)	(67,072)
Ending balance, as of December 31	41,817	59,639

16. Loss Per Share

Loss per share was calculated as follows:

	Year Ended December 31,		
	2022	2021	2020
	$	$	$
Numerator:			
Net loss	(2,003,815)	(1,457,816)	(1,628,591)
Less: Net loss attributable to noncontrolling interest	—	—	(3,617)
Net loss attributable to BeiGene, Ltd.	(2,003,815)	(1,457,816)	(1,624,974)
Denominator:			
Weighted average shares outstanding for computing basic and diluted loss per share	1,340,729,572	1,206,210,049	1,085,131,783
Net loss per share attributable to BeiGene, Ltd., basic and diluted	(1.49)	(1.21)	(1.50)

For the years ended December 31, 2022, 2021 and 2020, the computation of basic loss per share using the two-class method was not applicable, as the Company was in a net loss position.

The effects of all share options and restricted share units were excluded from the calculation of diluted loss per share as their effect would have been anti-dilutive during the years ended December 31, 2022, 2021 and 2020.

17. Share-Based Compensation

2016 Share Option and Incentive Plan

In January 2016, in connection with its U.S. IPO, the board of directors and shareholders of the Company approved the 2016 Share Option and Incentive Plan (the “2016 Plan”), which became effective in February 2016. The Company initially reserved 65,029,595 ordinary shares for the issuance of awards under the 2016 Plan, plus any shares available under the 2011 Option Plan (the “2011 Plan”), and not subject to any outstanding options as of the effective date of the 2016 Plan, along with underlying share awards under the 2011 Plan that are cancelled or forfeited without issuance of ordinary shares. As of December 31, 2022, ordinary shares cancelled or forfeited under the 2011 Plan that were carried over to the 2016 Plan totaled 5,166,653. The 2016 Plan provided for an annual increase in the shares available for issuance, to be added on the first day of each fiscal year, beginning on January 1, 2017, equal to the lesser of (i) five percent (5)% of the outstanding shares of the Company's ordinary shares on the last day of the immediately preceding fiscal year or (ii) such number of shares determined by the Company’s board of directors or the compensation committee. On January 1, 2018, 29,603,616 ordinary shares were added to the 2016 Plan under this provision. However, in August 2018, in connection with the Hong Kong IPO, the board of directors of the Company approved an amended and restated 2016 Plan to remove this "evergreen" provision and implement other changes required by the Hong Kong Stock Exchange (HKEx) rules. In December 2018, the shareholders of the Company approved a second amended and restated 2016 Plan to increase the number of shares authorized for issuance by 38,553,159 ordinary shares, as well as amend the cap on annual compensation to independent directors and make other changes. In June 2020, the shareholders approved an Amendment No. 1 to the 2016 Plan to increase the number of shares authorized for issuance by 57,200,000 ordinary shares and to extend the term of the plan through April 13, 2030. The number of shares available for issuance under the 2016 Plan is subject to adjustment in the event of a share split, share dividend or other change in the Company’s capitalization.

As of December 31, 2022, share-based awards to acquire 75,034,504 ordinary shares were available for future grant under the 2016 Plan.

In order to continue to provide incentive opportunities under the 2016 Plan, the Board of Directors and shareholders of the Company approved an amendment to the 2016 Plan (the "Amendment No. 2"), which became effective as of June 22, 2022, to increase the number of authorized shares available for issuance under the 2016 Plan by 66,300,000 ordinary shares, or 5%, of the Company's outstanding shares as of March 31, 2022.

2018 Inducement Equity Plan

In June 2018, the board of directors of the Company approved the 2018 Inducement Equity Plan (the “2018 Plan”) and reserved 12,000,000 ordinary shares to be used exclusively for grants of awards to individuals who were not previously employees of the Company or its subsidiaries, as a material inducement to the individual’s entry into employment with the Company or its subsidiaries, within the meaning of Rule 5635(c)(4) of the NASDAQ Listing Rules. The 2018 Plan was approved by the board of directors upon recommendation of the compensation committee, without shareholder approval pursuant to Rule 5635(c)(4) of the NASDAQ Listing Rules. The terms and conditions of the 2018 Plan, and the forms of award agreements to be used thereunder, are substantially similar to the 2016 Plan and the forms of award agreements thereunder. In August 2018, in connection with the listing of the Company’s ordinary shares on the HKEx, the board of directors of the Company approved an amended and restated 2018 Plan to implement changes required by the HKEx rules.

Upon the effectiveness of Amendment No. 2 to the 2016 Plan, on June 22, 2022, the 2018 Plan was terminated to the effect that no new equity awards shall be granted under the plan but the outstanding equity awards under the plan shall continue to vest and/or be exercisable in accordance with their terms.

2018 Employee Share Purchase Plan

In June 2018, the shareholders of the Company approved the 2018 Employee Share Purchase Plan (the ESPP). Initially, 3,500,000 ordinary shares of the Company were reserved for issuance under the ESPP. In August 2018, in connection with the Hong Kong IPO, the board of directors of the Company approved an amended and restated ESPP to remove an “evergreen” share replenishment provision originally included in the plan and implement other changes required by

the HKEx rules. In December 2018, the shareholders of the Company approved a second amended and restated ESPP to increase the number of shares authorized for issuance by 3,855,315 ordinary shares to 7,355,315 ordinary shares. The ESPP allows eligible employees to purchase the Company's ordinary shares (including in the form of ADSs) at the end of each offering period, which will generally be six months, at a 15% discount to the market price of the Company's ADSs at the beginning or the end of each offering period, whichever is lower, using funds deducted from their payroll during the offering period. Eligible employees are able to authorize payroll deductions of up to 10% of their eligible earnings, subject to applicable limitations.

The following tables summarizes the shares issued under the ESPP:

		Market Price[1]		Purchase Price[2]		
Issuance Date	Number of Ordinary Shares Issued	ADS	Ordinary	ADS	Ordinary	Proceeds
August 31, 2022	861,315	$ 171.66	$ 13.20	$ 145.91	$ 11.22	$ 9,667
February 28, 2022	667,160	$ 210.52	$ 16.19	$ 178.94	$ 13.76	$ 9,183
August 31, 2021	425,386	$ 308.30	$ 23.72	$ 262.06	$ 20.16	$ 8,575
February 26, 2021	436,124	$ 236.30	$ 18.18	$ 200.86	$ 15.45	$ 6,738
August 31, 2020	485,069	$ 164.06	$ 12.62	$ 139.45	$ 10.73	$ 5,203
February 28, 2020	425,425	$ 145.54	$ 11.20	$ 123.71	$ 9.52	$ 4,048

[1] The market price is the lower of the closing price on the NASDAQ Stock Market on the issuance date or the offering date, in accordance with the terms of the ESPP.

[2] The purchase price is the price which was discounted from the applicable market price, in accordance with the terms of the ESPP.

As of December 31, 2022, 3,666,071 ordinary shares were available for future issuance under the ESPP.

Share options

Generally, share options have a contractual term of 10 years and vest over a three- to five-year period, with the first tranche vesting one calendar year after the grant date or the service relationship start date and the remainder of the awards vesting on a monthly basis thereafter. Restricted shares and restricted share units generally vest over a four-year period, with the first tranche vesting one calendar year after the grant date or the service relationship start date and the remainder of the awards vesting on a yearly basis thereafter, or sometimes vest upon the achievement of pre-specified performance conditions.

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The following table summarizes the Company's share option activities under the 2011, 2016 and 2018 Plans:

	Number of Options	Weighted Average Exercise Price	Weighted Average Grant Date Fair Value	Weighted Average Remaining Contractual Term	Aggregate Intrinsic Value
		$	$	Years	$
Outstanding at December 31, 2019	108,417,254	3.96			
Granted	8,999,536	13.54	7.15		
Exercised	(29,707,587)	2.82			416,509
Forfeited	(2,717,488)	7.22			
Outstanding at December 31, 2020	84,991,715	5.27			
Granted	6,244,524	26.46	12.40		
Exercised	(17,233,853)	4.52			367,110
Forfeited	(1,797,498)	13.27			
Outstanding at December 31, 2021	72,204,888	7.08			
Granted	12,516,816	12.34	6.40		
Exercised	(5,898,217)	4.63			52,258
Forfeited	(2,296,634)	16.46			
Outstanding at December 31, 2022	76,526,853	7.85		5.33	745,340,712
Exercisable as of December 31, 2022	58,017,219	5.67		4.2	673,364,735
Vested and expected to vest at December 31, 2022	73,842,956	7.60		5.2	734,904,195

As of December 31, 2022, the unrecognized compensation cost related to 15,825,737 unvested share options expected to vest was $88,859. This unrecognized compensation will be recognized over an estimated weighted-average amortization period of 2.4 years.

The total fair value of employee share option awards vested during the years ended December 31, 2022, 2021 and 2020 was $62,548, $53,571 and $55,127, respectively.

Fair value of options

The Company uses the binomial option-pricing model in determining the estimated fair value of the options granted. The model requires the input of highly subjective assumptions including the estimated expected stock price volatility and, the exercise multiple for which employees are likely to exercise share options. For expected volatilities, the trading history and observation period of the Company's own share price is used in conjunction with historical price volatilities of ordinary shares of several comparable companies in the same industry as the Company. For the exercise multiple, the Company was not able to develop an exercise pattern as reference, thus the exercise multiple is based on management's estimation, which the Company believes is representative of the future exercise pattern of the options. The risk-free rate for periods within the contractual life of the option is based on the U.S. Treasury Bills yield curve in effect at the time of grant.

The following table presents the range of fair values and the assumptions used to estimate those fair values of the share options granted in the years presented:

	Year Ended December 31,		
	2022	2021	2020
Fair value of ordinary share	$5.51 ~ $9.04	$9.94 ~ $14.97	$4.95 ~ $11.89
Risk-free interest rate	1.8% ~ 3.9%	1.1% ~ 1.7%	0.6% ~ 1.1%
Expected exercise multiple	2.8	2.8	2.8
Expected volatility	51% ~ 60%	51% ~ 59%	58% ~ 59%
Expected dividend yield	0%	0%	0%
Contractual life	10 years	10 years	10 years

Restricted shares

The following table summarizes the Company's restricted share activities under the 2016 Plan:

	Numbers of Shares	Weighted-Average Grant Date Fair Value
		$
Outstanding at December 31, 2019	75,000	2.27
Granted	—	—
Vested	(75,000)	2.27
Forfeited	—	—
Outstanding at December 31, 2020	—	—

The Company had no restricted share activities during the year ended December 31, 2022 and 2021.

As of December 31, 2022, all compensation cost related to restricted shares was fully recognized.

Restricted share units

The following table summarizes the Company's restricted share unit activities under the 2016 and 2018 Plans:

	Numbers of Shares	Weighted-Average Grant Date Fair Value
		$
Outstanding at December 31, 2019	26,852,267	10.72
Granted	18,820,581	14.20
Vested	(7,302,828)	10.88
Forfeited	(3,493,048)	11.36
Outstanding at December 31, 2020	34,876,972	12.50
Granted	17,173,767	25.58
Vested	(10,703,381)	12.23
Forfeited	(5,264,376)	15.82
Outstanding at December 31, 2021	36,082,982	18.33
Granted	38,707,669	12.46
Vested	(12,533,586)	16.37
Forfeited	(6,859,892)	16.72
Outstanding at December 31, 2022	55,397,173	14.87
Expected to vest at December 31, 2022	47,392,282	14.87

As of December 31, 2022, the unrecognized compensation cost related to unvested restricted share units expected to vest was $580,815. This unrecognized compensation will be recognized over an estimated weighted-average amortization period of 2.9 years.

Share-based compensation expense

The following table summarizes total share-based compensation cost recognized for the years ended December 31, 2022, 2021 and 2020:

	Year Ended December 31,		
	2022	2021	2020
	$	$	$
Research and development	139,348	114,357	92,999
Selling, general and administrative	163,814	126,355	90,482
Total	303,162	240,712	183,481

18. Accumulated Other Comprehensive (Loss) Income

The movement of accumulated other comprehensive (loss) income was as follows:

	Foreign Currency Translation Adjustments	Unrealized Gains/Losses on Available-for-Sale Securities	Pension Liability Adjustments	Total
	$	$	$	$
December 31, 2020	14,184	871	(8,113)	6,942
Other comprehensive income (loss) before reclassifications	13,714	(4,504)	309	9,519
Amounts reclassified from accumulated other comprehensive (loss) income (1)	—	(67)	1,556	1,489
Net-current period other comprehensive (loss) income	13,714	(4,571)	1,865	11,008
December 31, 2021	27,898	(3,700)	(6,248)	17,950
Other comprehensive income (loss) before reclassifications	(90,421)	(5,311)	(446)	(96,178)
Amounts reclassified from accumulated other comprehensive (loss) income (1)	—	—	811	811
Net-current period other comprehensive (loss) income	(90,421)	(5,311)	365	(95,367)
December 31, 2022	(62,523)	(9,011)	(5,883)	(77,417)

(1) The amounts reclassified from accumulated other comprehensive (loss) income were included in other (expense) income, net in the consolidated statements of operations.

19. Shareholders' Equity

During the years ended December 31, 2022, 2021 and 2020, the Company completed the following equity offerings:

In January 2020, the Company sold 15,895,001 ADSs, representing a 20.5% ownership stake in the Company, to Amgen for aggregate cash proceeds of $2,779,241, or $174.85 per ADS, pursuant to the Share Purchase Agreement executed in connection with the Amgen Collaboration Agreement. On March 17, 2020, BeiGene, Ltd. and Amgen entered into an Amendment No. 2 (the "Second Amendment") to the Share Purchase Agreement in order to account for periodic dilution from the issuance of shares by the Company, which was restated in its entirety on September 24, 2020 (the "Restated Second Amendment"). Pursuant to the Restated Second Amendment, Amgen has an option (the "Direct Purchase Option") to subscribe for additional ordinary shares of the Company in the form of ADSs (the "Additional Shares") in an amount necessary to enable it to increase (and subsequently maintain) its ownership at approximately 20.6% of the Company's outstanding shares. The Direct Purchase Option is exercisable on a monthly basis, but only if Amgen's interest in the outstanding shares of the Company at the monthly reference date is less than 20.4%. The Direct Purchase Option (i) will be exercisable by Amgen solely as a result of dilution arising from issuance of new shares under the Company's equity incentive plans from time to time, and (ii) is subject to annual approval by the Company's independent shareholders each year during the term of the Restated Second Amendment. The exercise period of the Direct Purchase Option commenced on December 1, 2020 and will terminate on the earliest of: (a) the date on which Amgen and its affiliates collectively own less than 20% of the outstanding share capital of the Company as a result of Amgen's sale of shares; (b) at least 60-day advance written notice from either Amgen or the Company that such party wishes to terminate the Direct Purchase Option; or (c) December 1, 2023. The Direct Purchase Option has no vesting period.

In July 2020, the Company issued 145,838,979 ordinary shares, par value $0.0001, to eight existing investors, including entities associated with Hillhouse Capital and Baker Bros. Advisors LP, as well as Amgen, in a registered direct offering under the Company's effective Registration Statement on Form S-3 (File No. 333-238181). Each ordinary share was sold for a purchase price of $14.2308 per share ($185.00 per ADS), resulting in net proceeds, after offering expenses, of $2,069,610. Amgen purchased 29,614,832 ordinary shares for $421,443 as part of this offering. The offering was made without an underwriter or a placement agent, and as a result the Company did not pay any underwriting discounts or commissions in connection with the offering.

In September 2021, upon Amgen's exercise of its Direct Purchase Option, the Company issued an aggregate of 165,529 ADSs, representing 2,151,877 ordinary shares, to Amgen Inc. for a total consideration of $50,000, in a private placement pursuant to a Share Purchase Agreement dated October 31, 2019, as amended on December 6, 2019 and September 24, 2020 by and between Amgen and Company.

In December 2021, the Company completed an initial public offering of (STAR Offering) on the Science and Technology Innovation Board (STAR Market) of the Shanghai Stock Exchange (SSE). The shares offered in the STAR Offering were issued to and subscribed for by permitted investors in the People’s Republic of China (PRC) in Renminbi (RMB Shares). The public offering price of the RMB Shares was RMB192.60 per ordinary share, or $391.68 per ADS. In this offering, the Company sold 115,055,260 ordinary shares. Net proceeds after deducting underwriting commission and offering expenses were $3,392,616. As required by the PRC securities laws, the net proceeds from the STAR Offering must be used in strict compliance with the planned uses as disclosed in the PRC prospectus as well as the Company's proceeds management policy for the STAR Offering approved by the board of directors.

20. Restricted Net Assets

The Company’s ability to pay dividends may depend on the Company receiving distributions of funds from its PRC subsidiaries. Relevant PRC laws and regulations permit payments of dividends by the Company’s PRC subsidiaries only out of its retained earnings, if any, as determined in accordance with PRC accounting standards and regulations. The results of operations reflected in the consolidated financial statements prepared in accordance with GAAP differ from those reflected in the statutory financial statements of the Company’s PRC subsidiaries.

In accordance with the company law of the PRC, a domestic enterprise is required to provide statutory reserves of at least 10% of its annual after-tax profit until such reserve has reached 50% of its respective registered capital based on the enterprise’s PRC statutory accounts. A domestic enterprise is also required to provide discretionary surplus reserve, at the discretion of the Board of Directors, from the profits determined in accordance with the enterprise’s PRC statutory accounts. The aforementioned reserves can only be used for specific purposes and are not distributable as cash dividends. The Company’s PRC subsidiaries were established as domestic invested enterprises and therefore were subject to the above-mentioned restrictions on distributable profits.

During the years ended December 31, 2022, 2021 and 2020, no appropriation to statutory reserves was made, because the PRC subsidiaries had an accumulated deficit as of the end of such periods.

As a result of these PRC laws and regulations, including the requirement to make annual appropriations of at least 10% of after-tax income and set aside as general reserve fund prior to payment of dividends, the Company’s PRC subsidiaries are restricted in their ability to transfer a portion of their net assets to the Company.

Foreign exchange and other regulations in the PRC may further restrict the Company’s PRC subsidiaries from transferring funds to the Company in the form of dividends, loans, and advances. As of December 31, 2022 and 2021, amounts restricted were the net assets of the Company’s PRC subsidiaries, which amounted to 3,548,881 and $760,476, respectively.

21. Employee Benefit Plans

Defined Contribution Plans

Full-time employees of the Company in the PRC participate in a government mandated defined contribution plan, pursuant to which certain pension benefits, medical care, employee housing fund and other welfare benefits are provided to employees. Chinese labor regulations require that the Company’s PRC subsidiaries make contributions to the government for these benefits based on certain percentages of the employees’ salaries. The Company has no legal obligation for the benefits beyond the contributions made. The total amounts for such employee benefits, which were expensed as incurred, were $83,860, $63,772 and $23,717 for the years ended December 31, 2022, 2021 and 2020, respectively.

The Company maintains a defined contribution 401(k) savings plan (the "401(k) Plan") for U.S. employees. The 401(k) Plan covers all U.S. employees, and allows participants to defer a portion of their annual compensation on a pretax basis. In addition, the Company has a matching contribution to the 401(k) Plan, which, in the 2021 plan year, matched dollar for dollar of eligible contributions up to 4%. Company contributions to the 401(k) plan totaled $10,298, $7,483 and $4,840 in the years ended December 31, 2022, 2021 and 2020, respectively.

The Company maintains a government mandated program to cover its employees in Switzerland for pension, death, or disability. The program is considered a defined contribution plan. Employer and employee contributions are made based on various percentages of salaries and wages that vary based on employee age and other factors. Company contributions into the program amounted to $3,887, $2,986, and $2,960 in the years ended December 31, 2022, 2021 and 2020, respectively.

Employee benefit expenses for the remaining subsidiaries were immaterial.

Defined Benefit Plan

The Company maintains a defined benefit pension plan covering its employees in Switzerland (the "Swiss Plan"). This plan is a government mandated fund that provides benefits to employees upon retirement, death, or disability. Contributions are made based on various percentages of participants' salaries and wages determined based on participants' age and other factors. As of December 31, 2022 and 2021, the projected benefit obligations under the Swiss Plan were approximately $45,835 and $34,517, respectively, and plan assets were approximately $38,075 and $26,703, respectively. The funded status of the Swiss Plan is included in other long-term liabilities in the accompanying consolidated balance sheets. The initial determination of the pension liability was recorded as other comprehensive loss during the year ended December 31, 2020 and subsequently amortized as a component of net periodic pension cost (see Note 18).

The Company's annual contribution to the Swiss Plan is estimated to be approximately $2,553 in 2023 and is expected to evolve thereafter proportionally with changes in staffing and compensation levels, actuarial assumptions and actual investment returns on plan assets.

The following table reflects the total expected benefit payments to Swiss Plan participants and have been estimated based on the same assumptions used to measure the Company's benefit obligations as of December 31, 2022:

Year(s)	Amounts $
2023	68
2024	545
2025	442
2026	260
2027	755
2028 – 2032	7,185
Total	9,255

22. Commitments and Contingencies

Purchase Commitments

As of December 31, 2022, the Company had purchase commitments amounting to $117,293, of which $55,346 related to minimum purchase requirements for supply purchased from contract manufacturing organizations and $61,947 related to binding purchase order obligations of inventory from BMS and Amgen. The Company does not have any minimum purchase requirements for inventory from BMS or Amgen.

Capital commitments

The Company had capital commitments amounting to $404,914 for the acquisition of property, plant and equipment as of December 31, 2022, which were mainly for the Company's manufacturing and clinical R&D campus in Hopewell, NJ, additional capacity at the Guangzhou and Suzhou manufacturing facilities, and a new building for Beijing Innerway Bio-tech Co., Ltd.

Co-development funding commitment

Under the Amgen Collaboration Agreement, the Company is responsible for co-funding global clinical development costs for the Amgen oncology pipeline assets up to a total cap of $1,250,000. The Company is funding its portion of the co-

development costs by contributing cash and/or development services. As of December 31, 2022, the Company's remaining co-development funding commitment was $595,702.

Research and Development Commitment

The Company entered into long-term research and development agreements, which include obligations to make upfront payments and fixed quarterly payments over the next four years. As of December 31, 2022, the total research and development commitment amounted to $22,327.

Funding Commitment

The Company had committed capital related to two equity method investments in the amount of $19,000. As of December 31, 2022, the remaining capital commitment was $16,000 and is expected to be paid from time to time over the investment period.

Other Business Agreements

The Company enters into agreements in the ordinary course of business with contract research organizations (CROs) to provide research and development services. These contracts are generally cancellable at any time by the Company with prior written notice.

The Company also enters into collaboration agreements with institutions and companies to license intellectual property. The Company may be obligated to make future development, regulatory and commercial milestone payments and royalty payments on future sales of specified products associated with its collaboration agreements. Payments under these agreements generally become due and payable upon achievement of such milestones or sales. These commitments are not recorded on the consolidated balance sheet because the achievement and timing of these milestones are not fixed and determinable. When the achievement of these milestones or sales have occurred, the corresponding amounts are recognized in the consolidated financial statements.

23. Segment and Geographic Information

The Company operates in one segment: pharmaceutical products. Its chief operating decision maker is the Chief Executive Officer, who makes operating decisions, assesses performance, and allocates resources on a consolidated basis.

The Company's long-lived assets are primarily located in the PRC and the U.S.

Net product revenues by geographic area are based upon the location of the customer, and net collaboration revenue is recorded in the jurisdiction in which the related income is expected to be sourced from. Total net revenues by geographic area are presented as follows:

	Year Ended December 31,		
	2022	2021	2020
	$	$	$
PRC	840,032	517,173	290,646
U.S.	502,626	495,265	18,228
ROW	73,263	163,845	—
Total	1,415,921	1,176,283	308,874

PRC revenues for each of the three years in the period ended December 31, 2022 consisted entirely of product sales. U.S. revenues for the year ended December 31, 2022 consisted of collaboration revenues of $112,916 and BRUKINSA product sales of $389,710, respectively. U.S. revenues for the year ended December 31, 2021 consisted of collaboration revenue of $379,607 and BRUKINSA product sales of $115,658, respectively. U.S. revenues for the year ended December 31, 2020 consisted entirely of BRUKINSA product sales. Rest of world revenues for each of the year ended December 31, 2022 consisted of collaboration revenues of $48,393 and product sales of $24,870, respectively. Rest of world revenues for each of the year ended December 31, 2021 consisted primarily of collaboration revenues.

Supplementary Information

The Company's unaudited quarterly information has been prepared on a basis consistent with the audited financial statements and includes all adjustments that the Company considers necessary for a fair presentation of the information shown. The operating results for any fiscal quarter are not necessarily indicative of the operating results for a full fiscal year or for any future period and there can be no assurances that any trend reflected in such results will continue in the future.

As discussed in Note 2, the Company revised certain prior period financial statements to correct an error related to the valuation of net deferred tax assets, the impact of which was immaterial to its previously filed financial statements in the annual periods of fiscal 2021 and 2020. The following table summarizes the unaudited statements of operations for each quarter of 2022 and 2021 (in thousands except share and per share amounts).

	Quarter Ended			
	March 31,	June 30,	September 30,	December 31,
2022	$	$	$	$
Total revenues	306,626	341,572	387,628	380,095
Loss from operations	(443,287)	(439,399)	(438,357)	(468,622)
Net loss	(435,198)	(565,726)	(557,556)	(445,335)
Net loss attributable to BeiGene, Ltd.	(435,198)	(565,726)	(557,556)	(445,335)
Net loss per share attributable to BeiGene, Ltd., basic and diluted	(0.33)	(0.42)	(0.41)	(0.33)

	Quarter Ended			
	March 31,	June 30,	September 30,	December 31,
2021	$	$	$	$
Total revenues	605,872	149,992	206,440	213,979
Income (loss) from operations	70,167	(474,838)	(462,325)	(571,739)
Net income (loss)	55,580	(484,604)	(438,114)	(590,678)
Net income (loss) attributable to BeiGene, Ltd.	55,580	(484,604)	(438,114)	(590,678)
Net income (loss) per share attributable to BeiGene, Ltd., basic	0.05	(0.41)	(0.36)	(0.48)
Net income (loss) per share attributable to BeiGene, Ltd., diluted	0.04	(0.41)	(0.36)	(0.48)

Exhibit Index

Exhibit No.		Exhibit Description	Filed/ Furnished Herewith	Incorporated by Reference Herein from Form or Schedule	Filing Date	SEC File/ Reg. Number
3.1		Sixth Amended and Restated Memorandum and Articles of Association of the Registrant, as currently in effect		8-K (Exhibit 3.1)	12/17/2021	001-37686
4.1	.1	Deposit Agreement dated February 5, 2016 by and among the Company, the Depositary and holders of the American Depositary Receipts		8-K (Exhibit 4.1)	2/11/2016	001-37686
	.2	Amendment No. 1 to Deposit Agreement, dated April 11, 2016, by and among the Registrant, Citibank, N.A. and holders of the American Depositary Receipts		8-K (Exhibit 4.1)	4/11/2016	001-37686
	.3	Letter Agreement, dated as of July 11, 2016, between the Registrant and Citibank, N.A.		10-Q (Exhibit 4.7)	8/10/2016	001-37686
	.4	Form of Letter Agreement between the Registrant and Citibank, N.A.		10-Q (Exhibit 4.9)	5/10/2017	001-37686
4.2		Form of American Depositary Receipt (included in Exhibit 4.1.1)				
4.3		Specimen Certificate for Ordinary Shares		S-1 (Exhibit 4.3)	12/9/2015	333-207459
4.4	.1	Second Amended and Restated Investors' Rights Agreement, dated as of April 21, 2015, by and among the Registrant and certain shareholders named therein		S-1 (Exhibit 4.4)	10/16/2015	333-207459
	.2	Amendment No. 1 to Second Amended and Restated Investors' Rights Agreement, dated January 26, 2016, by and among the Registrant and certain shareholders named therein		S-1 (Exhibit 10.21)	1/27/2016	333-207459
4.5	.1	Registration Rights Agreement, dated as of November 16, 2016, by and among the Registrant and the investors named therein		8-K (Exhibit 4.1)	11/17/2016	001-37686
	.2	Amendment No. 1 to Registration Rights Agreement, dated December 1, 2020, between the Company and the Investors		8-K (Exhibit 10.1)	12/2/2020	001-37686
4.6		Description of the Registrant's Securities Registered Pursuant to Section 12 of the Securities Exchange Act of 1934	X			
Collaboration, License and Commercial Agreements						
10.1#	.1#	License and Supply Agreement, dated July 5, 2017, by and between the Registrant and Celgene Logistics Sàrl		10-Q (Exhibit 10.3)	11/13/2017	001-37686

Exhibit No.		Exhibit Description	Filed/ Furnished Herewith	Incorporated by Reference Herein from Form or Schedule	Filing Date	SEC File/ Reg. Number
	.2	Assignment and Assumption Agreement, dated December 29, 2017, by and between the Registrant and BeiGene Switzerland GmbH		10-K (Exhibit 10.6.1)	3/2/2020	001-37686
10.2		Share Subscription Agreement, dated July 5, 2017, by and between Celgene Switzerland LLC and the Registrant		8-K (Exhibit 10.1)	7/6/2017	001-37686
10.3##		Letter Agreement, dated June 14, 2019, by and among the Registrant, BeiGene Switzerland GmbH, Celgene Corporation and Celgene Switzerland LLC, to terminate the Amended and Restated Exclusive License and Collaboration Agreement, dated August 31, 2017		10-Q (Exhibit 10.1)	8/8/2019	001-37686
10.4##	.1##	Share Purchase Agreement, dated October 31, 2019, by and between the Registrant and Amgen Inc.		10-K (Exhibit 10.9)	3/2/2020	001-37686
	.2	Amendment No. 1 to Share Purchase Agreement, dated December 6, 2019, by and between the Registrant and Amgen Inc.		10-K (Exhibit 10.10)	3/2/2020	001-37686
	.3	Restated Amendment No. 2 to Share Purchase Agreement, dated September 24, 2020, by and between the Registrant and Amgen Inc.		8-K (Exhibit 10.1)	9/24/2020	001-37686
	.4	Amendment No. 3 to Share Purchase Agreement, dated January 30, 2023, by and between the Registrant and Amgen Inc.	X			

Exhibit No.		Exhibit Description	Filed/ Furnished Herewith	Incorporated by Reference Herein from Form or Schedule	Filing Date	SEC File/ Reg. Number
10.5##	.1##	Collaboration Agreement, dated October 31, 2019, by and among the Registrant, BeiGene Switzerland GmbH and Amgen Inc.		10-K (Exhibit 10.11)	3/2/2020	001-37686
	.2##	First Amendment to Collaboration Agreement, dated April 20, 2022, by and among the Registrant, BeiGene Switzerland GmbH and Amgen Inc.		10-Q (Exhibit 10.1)	8/8/2022	001-37686
10.6		Guarantee, dated October 31, 2019, by and between the Registrant and Amgen Inc.		10-K (Exhibit 10.12)	3/2/2020	001-37686
10.7##	.1##	Collaboration and License Agreement, dated January 11, 2021, by and between BeiGene Switzerland GmbH and Novartis Pharma AG		10-Q (Exhibit 10.1)	5/6/2021	001-37686
	.2##	Option, Collaboration and License Agreement, dated December 19, 2021, by and between BeiGene Switzerland GmbH and Novartis Pharma AG		10-K (Exhibit 10.7.2)	2/28/2022	001-37686
Equity and Other Compensation Plans						
10.8†		2011 Option Plan, as amended and form of option agreements thereunder		S-1 (Exhibit 10.1)	10/16/2015	333-207459
10.9†	.1†	Second Amended and Restated 2016 Share Option and Incentive Plan		8-K (Exhibit 10.1)	12/12/2018	001-37686
	.2†	Amendment No. 1 to the Second Amended and Restated 2016 Share Option and Equity Plan		8-K (Exhibit 10.1)	6/17/2020	001-37686
	.3†	Amendment No. 2 to the Second Amended and Restated 2016 Share Option and Equity Plan		8-K (Exhibit 10.1)	6/22/2022	001-37686
	.4†	Form of Global Restricted Share Unit Award Agreement for Non-Employee Directors under the Second Amended and Restated 2016 Share Option and Incentive Plan		10-Q (Exhibit 10.4)	8/8/2022	001-37686
	.5†	Form of Global Restricted Share Unit Award Agreement for Employees under the Second Amended and Restated 2016 Share Option and Incentive Plan		10-Q (Exhibit 10.2)	11/9/2022	001-37686
	.6†	Form of Global Restricted Share Unit Award Agreement for Consultants under the Second Amended and Restated 2016 Share Option and Incentive Plan		10-Q (Exhibit 10.3)	11/9/2022	001-37686
	.7†	Form of Global Non-Qualified Share Option Agreement for Employees under the Second Amended and Restated 2016 Share Option and Incentive Plan		10-Q (Exhibit 10.1)	11/9/2022	001-37686
	.8†	Form of Global Non-Qualified Share Option Agreement for Non-Employee Directors under the Second Amended and Restated 2016 Share Option and Incentive Plan		10-Q (Exhibit 10.7)	8/8/2022	001-37686
	.9†	Form of Global Non-Qualified Share Option Agreement for Non-Employee Consultants under the Second Amended and Restated 2016 Share Option and Incentive Plan		10-Q (Exhibit 10.8)	8/8/2022	001-37686
10.10†	.1†	Third Amended and Restated 2018 Employee Share Purchase Plan		10-Q (Exhibit 10.7)	8/5/2021	001-37686

Exhibit No.		Exhibit Description	Filed/ Furnished Herewith	Incorporated by Reference Herein from Form or Schedule	Filing Date	SEC File/ Reg. Number
10.11†		Senior Executive Cash Incentive Bonus Plan		S-1 (Exhibit 10.19)	1/19/2016	333-207459
10.12†		Independent Director Compensation Policy, as amended		8-K (Exhibit 10.1)	2/22/2022	001-37686
Agreements with Executive Officers and Directors						
10.14†		Form of Indemnification Agreement, entered into between the Registrant and its directors and officers		S-1 (Exhibit 10.3)	1/19/2016	333-207459
10.15†		Employment Agreement, dated April 25, 2017, by and between the Registrant and John V. Oyler		8-K (Exhibit 10.1)	4/26/2017	001-37686
10.16†	.1†	Executive Employment Agreement, dated April 28, 2018, by and between BeiGene (Beijing) Co., Ltd. and Xiaobin Wu		10-Q (Exhibit 10.1)	8/9/2018	001-37686
	.2†	Employment Apportionment Agreement, dated March 1, 2020, by and between BeiGene (Beijing) Co., Ltd., BeiGene Guangzhou Biologics Manufacturing Co., Ltd. and Xiaobin Wu		10-Q (Exhibit 10.2)	5/11/2020	001-37686
10.17†		Offer letter, dated May 29, 2020, by and between the Registrant and Julia Wang		10-Q (Exhibit 10.9)	8/5/2021	001-37686
10.18†		Consulting Agreement, dated February 24, 2021, by and between the Registrant and Xiaodong Wang		10-K (Exhibit 10.20)	2/25/2021	001-37686
10.19†		Employment Agreement, dated December 30, 2021, by and between BeiGene (Shanghai) Co., Ltd. and Lai Wang		10-K (Exhibit 10.20)	2/28/2022	001-37686
16.1		Letter from Ernst & Young Hua Ming LLP addressed to the U.S. Securities and Exchange Commission dated March 25, 2022		8-K (Exhibit 16.1)	3/25/2022	001-37686
21.1		List of Subsidiaries of the Registrant	X			

Exhibit No.	Exhibit Description	Filed/ Furnished Herewith	Incorporated by Reference Herein from Form or Schedule	Filing Date	SEC File/ Reg. Number
23.1	Consent of Ernst & Young LLP	X			
23.2	Consent of Ernst & Young Hua Ming LLP	X			
31.1	Certification of Principal Executive Officer pursuant to Rule 13a-14(a) and Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002	X			
31.2	Certification of Principal Financial Officer pursuant to Rule 13a-14(a) and Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002	X			
32.1*	Certification of Principal Executive Officer and Principle Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002	X			
99.1	Disclosure Regarding Foreign Jurisdictions that Prevent Inspections	X			
101.INS	Inline XBRL Instance Document - the instance document does not appear in the interactive data file because its XBRL tags are embedded within the Inline XBRL document				
101.SCH	Inline XBRL Taxonomy Extension Schema Document	X			
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document	X			
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document	X			
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document	X			
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document	X			
104	Cover Page Interactive Data File (formatted as inline XBRL with applicable taxonomy extension information contained in Exhibits 101.*)	X			

† Indicates a management contract or any compensatory plan, contract or arrangement.

Confidential treatment has been granted by the U.S. Securities and Exchange Commission as to certain portions of this exhibit omitted and filed separately.

Certain portions of the exhibit have been omitted by means of redacting a portion of the text and replacing it with "[*]", because they are both (i) not material and (ii) the type of information that the Registrant treats as private or confidential.

* Furnished herewith.

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SIGNATURES

Pursuant to the requirements of the Section 13 or 15(d) of the Securities Exchange Act of 1934, the Registrant has duly caused this Form 10-K to be signed on its behalf by the undersigned, thereunto duly authorized.

BEIGENE, LTD.

Date: February 27, 2023

By: /s/ JOHN V. OYLER

John V. Oyler
Chief Executive Officer and Chairman
(Principal Executive Officer)

POWER OF ATTORNEY

Each person whose individual signature appears below hereby authorizes and appoints John V. Oyler, Julia Wang, and Chan Lee, and each of them, with full power of substitution and resubstitution and full power to act without the other, as his or her true and lawful attorney-in-fact and agent to act in his or her name, place and stead and to execute in the name and on behalf of each person, individually and in each capacity stated below, and to file any and all amendments to this Annual Report on Form 10-K and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing, ratifying and confirming all that said attorneys-in-fact and agents or any of them or their or his substitute or substitutes may lawfully do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this Annual Report on Form 10-K has been signed by the following persons in the capacities indicated below and on the dates indicated:

Signature	Title	Date
/s/ JOHN V. OYLER John V. Oyler	Chief Executive Officer and Chairman *(Principal Executive Officer)*	February 27, 2023
/s/ JULIA WANG Julia Wang	Chief Financial Officer *(Principal Financial and Accounting Officer)*	February 27, 2023
/s/ MARGARET DUGAN Margaret Dugan	Director	February 27, 2023
/s/ DONALD W. GLAZER Donald W. Glazer	Director	February 27, 2023
/s/ MICHAEL GOLLER Michael Goller	Director	February 27, 2023
/s/ ANTHONY C. HOOPER Anthony C. Hooper	Director	February 27, 2023
/s/ RANJEEV KRISHANA Ranjeev Krishana	Director	February 27, 2023
/s/ THOMAS MALLEY Thomas Malley	Director	February 27, 2023
/s/ ALESSANDRO RIVA Alessandro Riva	Director	February 27, 2023
/s/ CORAZON (CORSEE) D. SANDERS Corazon (Corsee) D. Sanders	Director	February 27, 2023
/s/ XIAODONG WANG Xiaodong Wang	Director	February 27, 2023
/s/ QINGQING YI Qingqing Yi	Director	February 27, 2023

DESCRIPTION OF SECURITIES REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934

The following description of our share capital is a summary and does not purport to be complete. It is subject to and qualified in its entirety by reference to our sixth amended and restated memorandum and articles of association (as amended or amended and restated, "our articles"), which is incorporated by reference as an exhibit to the Annual Report on Form 10-K. The terms "we," "our," and "us" refer solely to BeiGene, Ltd. and not its subsidiaries.

Ordinary Shares

We are an exempted company incorporated in the Cayman Islands with limited liability and our affairs are governed by our articles, the Companies Act (as amended) of the Cayman Islands (the "Cayman Companies Act") and the common law of the Cayman Islands.

As of February 25, 2023, our authorized share capital was $1,000,000 divided into (i) 9,500,000,000 ordinary shares of a par value of $0.0001 each and (ii) 500,000,000 shares of a par value of $0.0001 each of such class or classes (howsoever designated) as the board of directors may determine.

Our articles were adopted by special resolution passed on June 16, 2021 with effect from the listing of our ordinary shares traded in Renminbi (the "RMB Shares") on the Science and Technology Innovation Board (the "STAR Market") of the Shanghai Stock Exchange (the "SSE") on December 15, 2021. The following are summaries of material provisions of our articles and the Cayman Companies Act insofar as they relate to the material terms of our ordinary shares. Under our articles, our name is BeiGene, Ltd.

The following discussion primarily concerns ordinary shares and the rights of holders of ordinary shares. The holders of American Depositary Shares ("ADSs") are not treated as our shareholders and will be required to surrender their ADSs for cancellation and withdrawal from the depositary facility in which the ordinary shares are held in accordance with the provisions of the deposit agreement, as amended, in order to exercise directly shareholders' rights in respect of the ordinary shares. The depositary has agreed, so far as it is practical, to vote or cause to be voted the amount of ordinary shares represented by ADSs in accordance with the written instructions of the holders of such ADSs. See "Description of American Depositary Shares—Voting Rights."

Our ordinary shares are listed on The Stock Exchange of Hong Kong Limited (the "HKEx") under the stock code "06160". Our ADSs representing our ordinary shares are listed on the NASDAQ Global Select Market (the "NASDAQ") under the symbol "BGNE". Our RMB Shares are listed on the STAR Market of the SSE under the stock code "688235".

General

All of our issued and outstanding ordinary shares are fully paid and non-assessable. Our ordinary shares are issued in registered form and are issued when registered in our registers of members. Each holder of our ordinary shares will be entitled to receive a certificate in respect of such ordinary shares if our directors resolve that share certificate shall be issued. Our shareholders who are non-residents of the Cayman Islands may freely hold and vote their ordinary shares. We may not issue shares to bearer.

Our registers of members holding ordinary shares (other than the RMB Shares) are maintained by our principal share registrar, Mourant Governance Services (Cayman) Limited, in the Cayman Islands, and by our Hong Kong share registrar, Computershare Hong Kong Investor Services Limited, in Hong Kong, respectively. Our register of members holding RMB Shares are maintained by China Securities Depository and Clearing Corporation Limited in China.

Although the RMB Shares are of the same class and have the same rights as our ordinary shares listed on the HKEx, the RMB Shares are not fungible with our ordinary shares listed on the HKEx or our ADSs representing our ordinary shares listed on the NASDAQ, and in no event will any RMB Shares be able to be converted into our ordinary shares listed on the HKEx or our ADSs listed on NASDAQ, or vice versa.

Dividends

The holders of our ordinary shares are entitled to such dividends as may be declared by our board of directors. In addition, our shareholders may by ordinary resolution declare a dividend, but no dividend may exceed the amount recommended by our directors. Under Cayman Companies Act, a Cayman Islands company may pay a dividend out of either profit or share premium account, provided that in no circumstances may a dividend be paid if this would result in the company being unable to pay its debts as they fall due in the ordinary course of business.

Voting Rights

Each ordinary share is entitled to one vote on all matters upon which the ordinary shares are entitled to vote.

Voting at any meeting of shareholders is by poll.

An ordinary resolution to be passed by the shareholders requires the affirmative vote of a simple majority of the votes cast by the shareholders entitled to vote who are present in person or by proxy at a general meeting, while a special resolution requires the affirmative vote of at least two-thirds of the votes cast by the shareholders entitled to vote who are present in person or by proxy at a general meeting (except for certain types of winding up of the company, in which case the required majority to pass a special resolution shall be 100%). Both ordinary resolutions and special resolutions may also be passed by a unanimous written resolution signed by all the shareholders of our company, as permitted by the Cayman Companies Act and our articles. A special resolution is required for important matters such as a change of name and amendments to our articles. Our shareholders may effect certain changes by ordinary resolution, including increasing the amount of our authorized share capital, consolidating and dividing all or any of our share capital into shares of larger amounts than our existing shares and cancelling any authorized but unissued shares.

Transfer of Ordinary Shares

Subject to the restrictions contained in our articles, any of our shareholders may transfer all or any of his or her ordinary shares by an instrument of transfer in any usual or common form or any other form approved by our board of directors, executed by or on behalf of the transferor (and, if in respect of a nil or partly paid-up share, or if so required by our directors, by or on behalf of the transferee).

Our board of directors may, in its absolute discretion, decline to register any transfer of any ordinary share that has not been fully paid up or is subject to a company lien. Our board of directors may also decline to register any transfer of any ordinary share unless:

- the instrument of transfer is lodged with us, accompanied by the certificate (if any) for the ordinary shares to which it relates and such other evidence as our board of directors may reasonably require to show the right of the transferor to make the transfer;
- the instrument of transfer is in respect of only one class of shares;
- the instrument of transfer is properly stamped, if required;
- the ordinary share transferred is fully paid and free of any lien in favor of us;
- any fee related to the transfer has been paid to us; and
- the transfer is not to more than four joint holders.

If our directors refuse to register a transfer, they are required, within three months after the date on which the instrument of transfer was lodged, to send to each of the transferor and the transferee notice of such refusal.

Liquidation

On a winding up of our company, if the assets available for distribution among the holders of our ordinary shares shall be more than sufficient to repay the whole of the share capital at the commencement of the winding up, the surplus will be distributed among the holders of our ordinary shares on a pro rata basis in proportion to the par value of the ordinary shares held by them. If our assets available for distribution are insufficient to repay all of the paid-up capital, the assets will be distributed so that the losses are borne by the holders of our ordinary shares in proportion to the par value of the ordinary shares held by them.

The liquidator may, with the sanction of a special resolution of our shareholders and any other sanction required by the Cayman Companies Act, divide amongst the shareholders in specie or in kind the whole or any part of the assets of our company, and may for that purpose value any assets and determine how the division shall be carried out as between our shareholders or different classes of shareholders.

Because we are a "limited liability" company registered under the Cayman Companies Act, the liability of our shareholders is limited to the amount, if any, unpaid on the shares respectively held by them. Our articles contain a declaration that the liability of our shareholders is so limited.

Calls on Ordinary Shares and Forfeiture of Ordinary Shares

Our board of directors may from time to time make calls upon shareholders for any amounts unpaid on their ordinary shares. The ordinary shares that have been called upon and remain unpaid are subject to forfeiture by the company. In addition, the holders of partly paid ordinary shares will have no right pursuant to the Cayman Companies Act to dividends nor will they be able to redeem their shares.

Redemption, Repurchase and Surrender of Ordinary Shares

We may issue shares on terms that such shares are subject to redemption, at our option or at the option of the holders thereof, on such terms and in such manner as may be determined by our board of directors. We may also repurchase any of our shares provided that the manner and terms of such purchase have been approved by our board of directors or by ordinary resolution of our shareholders (but no repurchase may be made contrary to the terms or manner recommended by our directors), or as otherwise authorized by our articles. Under the Cayman Companies Act, the redemption or repurchase of any share may be paid out of our company's profits or out of the proceeds of a new issue of shares made for the purpose of such redemption or repurchase, or out of capital (including share premium account and capital redemption reserve) if our company can, immediately following such payment, pay its debts as they fall due in the ordinary course of business. In addition, under the Cayman Companies Act no such share may be redeemed or repurchased (1) unless it is fully paid up, (2) if such redemption or repurchase would result in there being no shares outstanding or (3) if the company has commenced liquidation. In addition, our company may accept the surrender of any fully paid share for no consideration.

Variations of Rights of Shares

If at any time our share capital is divided into different classes of shares, all or any of the rights attached to any class of shares may be varied with the consent in writing of the holders of two-thirds of the issued shares of that class or with the sanction of a special resolution passed at a general meeting of the holders of the shares of that class. The rights conferred upon the holders of the shares of any class issued with preferred or other rights will not, unless otherwise expressly provided by the terms of issue of the shares of that class, be deemed to be varied by the creation or issue of further shares ranking *pari passu* with such existing class of shares.

Notwithstanding the foregoing, our board of directors may issue preferred shares, without further action by the shareholders. See "— Differences in Corporate Law—Directors' Power to Issue Shares".

General Meetings of Shareholders

Shareholders' meetings may be convened by a majority of our board of directors or our chairman. As a Cayman Islands exempted company, we are not obligated by the Cayman Companies Act to call shareholders' annual general meetings;

however, our corporate governance guidelines provide that we will hold an annual general meeting of shareholders every year to the extent required by the applicable listing rules. The annual general meeting shall be held at such time and place as may be determined by our board of directors.

The Cayman Companies Act provides shareholders with only limited rights to requisition a general meeting, and does not provide shareholders with any right to put any proposal before a general meeting. However, these rights may be provided in a company's articles of association. Our articles provide that upon the requisition of shareholders representing not less than one-tenth of the voting rights entitled to vote at general meetings, our board will convene an extraordinary general meeting and put the resolutions so requisitioned to a vote at such meeting. However, shareholders may propose only ordinary resolutions to be put to a vote at such meeting. Our articles provide no other right for our shareholders to put any proposals before annual general meetings or extraordinary general meetings.

Advance notice of at least 21 calendar days is required for the convening of any annual general meeting of our shareholders and advance notice of at least 14 calendar days is required for the convening of any other general meeting of our shareholders (including any extraordinary general meeting). All general meetings of shareholders shall occur at such time and place as determined by our directors and set forth in the notice for such meeting.

The quorum required for a general meeting of shareholders at which an ordinary resolution has been proposed consists of such shareholders present in person or by proxy who together hold shares which carry the right to at least a simple majority of all votes capable of being exercised on a poll. The quorum required for a general meeting at which a special resolution has been proposed consists of such shareholders present in person or by proxy who together hold shares which carry the right to at least two-thirds of all votes capable of being exercised on a poll.

Nomination, Election and Removal of Directors

Our articles provide that persons standing for election as directors at a duly constituted general meeting with requisite quorum shall be elected by an ordinary resolution of our shareholders, which requires the affirmative vote of a simple majority of the votes cast on the resolution by the shareholders entitled to vote who are present in person or by proxy at the meeting. Our articles further provide that our board of directors will be divided into three groups designated as Class I, Class II and Class III with as nearly equal a number of directors in each group as possible, with each director serving a three-year term and until his or her successor is duly elected and qualified, subject to his or her earlier resignation or removal.

Upon the expiration of the term of each class, each director in that class, if nominated by the board of directors, shall be eligible for re-election at the annual general meeting to hold office for another three-year term and until such director's successor has been duly elected. Our articles provide that, unless otherwise determined by shareholders in a general meeting, our board of directors will consist of not less than three directors. We have no provisions relating to retirement of directors upon reaching any age limit.

In the event of a vacancy arising from the resignation of a director or as an addition to the existing board of directors, our board may, by the affirmative vote of a simple majority of the remaining directors present and voting at a board meeting, appoint any person to be a director, unless the board resolves to follow any available exceptions or exemptions.

For so long as our ordinary shares or ADSs are listed on the NASDAQ and/or the HKEx, our directors are required to comply with the director nomination procedures required under the NASDAQ Stock Market rules and the HK Listing Rules, and our board of directors is required to include at least such number of independent directors as required by the NASDAQ Stock Market rules and the HK Listing Rules.

Our board shall have a chairman who has been elected and appointed by a majority of the directors then in office. The period for which our chairman holds office shall also be determined by a majority of all of our directors then in office. Our chairman shall preside as chairman at every meeting of our board. To the extent that our chairman is not present at a meeting of our board within 15 minutes after the time appointed for holding the same, the remaining attending directors may choose one of their number to be the chairman of that meeting.

Our directors shall be elected by an ordinary resolution of the holders of ordinary shares at each annual general meeting of the company to fill the seats of those directors whose terms expire at such annual general meeting.

Each of our directors shall hold office until his or her successor is duly elected or appointed or his or her earlier resignation or removal, notwithstanding any agreement between the company and the director. Our directors may be removed at any time by an affirmative vote of a simple majority of the issued shares as of the applicable record date, with or without cause.

Our board of directors may, from time to time, and except as required by applicable law or applicable listing rules, adopt, institute, amend, modify or revoke any of our corporate governance policies or initiatives of the company, which shall be intended to set forth the guiding principles and policies of the company and our board on various corporate governance related matters as the board shall determine by resolution from time to time.

Proceedings of Board of Directors

Our articles provide that our business is to be managed and conducted by our board of directors. The quorum necessary for a board meeting may be fixed by the board and, unless so fixed at another number, will be a majority of the directors.

Our articles provide that the board may from time to time at its discretion exercise all powers of our company to raise capital or borrow money, to mortgage or charge all or any part of the undertaking, property and assets (present and future) and uncalled capital of our company and, subject to the Cayman Companies Act, issue debentures, bonds and other securities of our company, whether outright or as collateral security for any debt, liability or obligation of our company or of any third party.

Inspection of Books and Records

Holders of our ordinary shares will have no general right under Cayman Companies Act to inspect or obtain copies of our list of shareholders or our corporate records provided that they are entitled to a copy of our articles.

Changes in Capital

Our shareholders may from time to time by ordinary resolution:

- increase the share capital by such sum, to be divided into shares of such classes and amount, as the resolution shall prescribe;
- consolidate and divide all or any of our share capital into shares of a larger amount than our existing shares;
- sub-divide our existing shares, or any of them into shares of a smaller amount, provided that in the subdivision the proportion between the amount paid and the amount, if any, unpaid on each reduced share shall be the same as it was in case of the share from which the reduced share is derived; or
- cancel any shares which, at the date of the passing of the resolution, have not been taken or agreed to be taken by any person and diminish the amount of our share capital by the amount of the shares so cancelled.

Our shareholders may by special resolution, subject to any confirmation or consent required by the Cayman Companies Act, reduce our share capital or any capital redemption reserve in any manner permitted by law.

Restrictive Provisions

Under our articles, in connection with any change of control, merger or sale of our company, the holders of our ordinary shares shall receive the same consideration with respect to their ordinary shares in connection with any such transaction.

Claims Against the Company

Our articles provide that, unless otherwise determined by a simple majority of our board of directors in its sole discretion, consistent with the directors' fiduciary duties to act in the best interests of the company, in the event that (1) any shareholder (the claiming party) initiates or asserts any claim or counterclaim or joins, offers substantial assistance to or has a direct financial interest in any claim against our company and (2) the claiming party (or the third party that received substantial

assistance from the claiming party or in whose claim the claiming party had a direct financial interest) does not obtain a judgment on the merits in which the claiming party prevails, then each claiming party shall, to the fullest extent permissible by law, be obligated jointly and severally to reimburse us for all fees, costs and expenses (including, but not limited to, all reasonable attorneys' fees and other litigation expenses) that we may incur in connection with such claim.

Exclusive Forum

Our articles provide that, subject to limited exceptions, the courts of Cayman Islands will be the sole and exclusive forum for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our shareholders, (3) any action asserting a claim against us arising pursuant to any provision of the Cayman Companies Act or our articles, or (4) any other action asserting a claim against us that is governed by the internal affairs doctrine (as such concept is recognized under the laws of the United States). Any person or entity purchasing or otherwise acquiring any interest in our share capital shall be deemed to have notice of and to have consented to the provisions of our articles described above. Although we believe these provisions benefit us by providing increased consistency in the application of Cayman Islands law for the specified types of actions and proceedings, the provisions may have the effect of discouraging lawsuits against our directors and officers. It is possible that, in connection with one or more actions or proceedings described above, a court could find the choice of forum provisions contained in our articles to be inapplicable or unenforceable.

Our articles also provide that, unless our company consents in writing to the selection of an alternative forum, the federal district courts of the United States shall be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act of 1933, as amended (the "Securities Act"). Any person or entity purchasing or otherwise acquiring any share, ADS or other types of securities of our company shall be deemed to have notice of and consented to the provisions of our articles described above.

In connection with our initial public offering of the RMB Shares on the STAR Market (the “STAR Offering”) and the listing of the RMB Shares on the STAR Market, we and each of our directors and executive officers have signed letters of undertaking to (i) confirm and acknowledge that any legal suits, actions or proceedings against us and/or our directors and officers arising from the STAR Offering and the listing of the RMB Shares on the STAR Market during the period when our RMB Shares are listed on the STAR Market (collectively, the “RMB Share Disputes”) shall be governed by the laws of China and subject to the jurisdiction of competent courts in China if such RMB Share Disputes are instituted in competent courts in China, and (ii) undertake that we and our directors and officers waive any objections that we may have to the jurisdiction of such courts over the RMB Share Disputes or the application of Chinese laws by such courts to the RMB Share Disputes.

Exempted Company

We are an exempted company with limited liability incorporated under the Cayman Companies Act. The Cayman Companies Act distinguishes between ordinary resident companies and exempted companies. 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 requirements for an exempted company are essentially the same as for an ordinary company except for the exemptions and privileges listed below:

- an exempted company does not have to file an annual return of its shareholders with the Registrar of Companies;
- an exempted company's register of members is not open to inspection;
- an exempted company does not have to hold an annual general meeting;
- an exempted company may issue no par value, negotiable or bearer shares;
- an exempted company may obtain an undertaking against the imposition of any future taxation (such undertakings are usually given for 20 years in the first instance);
- an exempted company may register by way of continuation in another jurisdiction and be deregistered in the Cayman Islands;

- an exempted company may register as a limited duration company; and
- an exempted company may register as a segregated portfolio company.

"Limited liability" means that the liability of each shareholder is limited to the amount unpaid by the shareholder on the shares of the company.

We are subject to reporting and other informational requirements of the Securities Exchange Act of 1934, as amended, as applicable to U.S. domestic issuers. The applicable listing rules require that every company listed on the applicable stock exchange hold an annual general meeting of shareholders. In addition, our articles allow directors to call an extraordinary general meeting of shareholders pursuant to the procedures set forth in our articles.

Register of Members

Under the Cayman Companies Act, we must keep a register of members and there should be entered therein:

- the names and addresses of our members and a statement of the shares held by each member that distinguishes each share by its number (if applicable), confirms the amount paid or agreed to be considered as paid on the shares of each member, confirms the number and category of shares held by each member and confirms whether each relevant category of shares held by a member carries voting rights under the articles and, if so, whether such voting rights are conditional
- the date on which the name of any person was entered on the register as a member; and
- the date on which any person ceased to be a member.

Under Cayman Companies Act, the register of members of our company is prima facie evidence of the matters set out in the register (that is, the register of members will raise a presumption of fact on the matters referred to above unless rebutted) and a member registered in the register of members is deemed as a matter of Cayman Companies Act to have legal title to the shares as set against its name in the register of members. Once our register of members has been updated, the shareholders recorded in the register of members will be deemed to have legal title to the shares set against their names.

If the name of any person is incorrectly entered in or omitted from our register of members, or if there is any default or unnecessary delay in entering on the register the fact of any person having ceased to be a member of our company, the person or member aggrieved (or any member of our company or our company itself) may apply to the Grand Court of the Cayman Islands for an order that the register be rectified, and the Court may either refuse such application or it may, if satisfied of the justice of the case, make an order for the rectification of the register.

Differences in Corporate Law

The Cayman Companies Act is derived, to a large extent, from the older Companies Acts of England and Wales but does not follow recent United Kingdom statutory enactments, and accordingly there are significant differences between the Cayman Companies Act and the current Companies Act of England. In addition, the Cayman Companies Act differs from laws applicable to United States corporations and their shareholders. Set forth below is a summary of certain significant differences between the provisions of the Cayman Companies Act applicable to us and the comparable laws applicable to companies incorporated in the State of Delaware in the United States.

Mergers and Similar Arrangements

The Cayman Companies Act permits mergers and consolidations between Cayman Islands companies and between Cayman Islands companies and non-Cayman Islands companies. For these purposes, (1) "merger" means the merging of two or more constituent companies and the vesting of their undertaking, property and liabilities in one of such companies as the surviving company, and (2) a "consolidation" means the combination of two or more constituent companies into a consolidated company and the vesting of the undertaking, property and liabilities of such companies to the consolidated company. In order to effect such a merger or consolidation, the directors of each constituent company must approve a written plan of merger or

consolidation, which must then be authorized by (1) a special resolution of the shareholders of each constituent company, and (2) such other authorization, if any, as may be specified in such constituent company's articles of association.

The plan must be filed with the Registrar of Companies together with a declaration as to the solvency of the consolidated or surviving company, a list of the assets and liabilities of each constituent company and an undertaking that a copy of the certificate of merger or consolidation will be given to the members and creditors of each constituent company and that notification of the merger or consolidation will be published in the Cayman Islands Gazette. Court approval is not required for a merger or consolidation effected in compliance with these statutory procedures.

A merger between a Cayman parent company and its Cayman subsidiary or subsidiaries does not require authorization by a resolution of shareholders. For this purpose a subsidiary is a company of which at least 90% of the issued shares entitled to vote are owned by the parent company.

The consent of each holder of a fixed or floating security interest of a constituent company is required unless this requirement is waived by a court in the Cayman Islands.

Except in certain limited circumstances, a dissenting shareholder of a Cayman Islands constituent company is entitled to payment of the fair value of his or her shares upon dissenting from a merger or consolidation. The exercise of such dissenter rights will preclude the exercise by the dissenting shareholder of any other rights to which he or she might otherwise be entitled by virtue of holding shares, except for the right to seek relief on the grounds that the merger or consolidation is void or unlawful.

In addition, there are statutory provisions that facilitate the reconstruction and amalgamation of companies, provided that the arrangement is approved by a majority in number of each class of shareholders and creditors with whom the arrangement is to be made, and who must, in addition, represent three-fourths in value of each such class of shareholders or creditors, as the case may be, that are present and voting either in person or by proxy at a meeting, or meetings, convened for that purpose. The convening of the meetings and subsequently the arrangement must be sanctioned by the Grand Court of the Cayman Islands. While a dissenting shareholder has the right to express to the court the view that the transaction ought not to be approved, the court can be expected to approve the arrangement if it determines that:

- the statutory provisions as to the required majority vote have been met;
- the shareholders have been fairly represented at the meeting in question and the statutory majority are acting bona fide without coercion of the minority to promote interests adverse to those of the class;
- the arrangement is such that may be reasonably approved by an intelligent and honest man of that class acting in respect of his interest; and
- the arrangement is not one that would more properly be sanctioned under some other provision of the Cayman Companies Act.

When a takeover offer is made and accepted by holders of 90% of the shares affected within four months the offeror may, within a two-month period commencing on the expiration of such four-month period, require the holders of the remaining shares to transfer such shares on the terms of the offer. An objection can be made to the Grand Court of the Cayman Islands but this is unlikely to succeed in the case of an offer which has been so approved unless there is evidence of fraud, bad faith or collusion.

If an arrangement and reconstruction is thus approved, or if a takeover offer is made and accepted, a dissenting shareholder would have no rights comparable to appraisal rights, which would otherwise ordinarily be available to dissenting shareholders of Delaware corporations, providing rights to receive payment in cash for the judicially determined value of the shares.

Shareholders' Suits

In principle, we will normally be the proper plaintiff to sue for a wrong done to us as a company, and as a general rule, a derivative action may not be brought by a minority shareholder. However, based on English law authorities, which would in all

likelihood be of persuasive authority in the Cayman Islands, the Cayman Islands courts can be expected to follow and apply the common law principles (namely the rule in *Foss v. Harbottle* and the exceptions thereto) so that a non-controlling shareholder may be permitted to commence a class action against or derivative actions in the name of the company to challenge:

- an act that is illegal or ultra vires with respect to the company and is therefore incapable of ratification by the shareholders;
- an act that, although not ultra vires, requires authorization by a qualified (or special) majority (that is, more than a simple majority) that has not been obtained; and
- an act that constitutes a "fraud on the minority" where the wrongdoers are themselves in control of the company.

Indemnification of Directors and Executive Officers and Limitation of Liability

The Cayman Companies Act does not limit the extent to which a company's articles of association may provide for indemnification of officers and directors, except to the extent any such provision may be held by the Cayman Islands courts to be contrary to public policy, such as to provide indemnification against civil fraud or the consequences of committing a crime. Our articles provide that we shall indemnify our officers and directors against all actions, proceedings, costs, charges, expenses, losses, damages or liabilities incurred or sustained by such directors or officer, other than by reason of such person's dishonesty, willful default or fraud, in or about the conduct of our company's business or affairs (including as a result of any mistake of judgment) or in the execution or discharge of his duties, powers, authorities or discretions, including without prejudice to the generality of the foregoing, any costs, expenses, losses or liabilities incurred by such director or officer in defending (whether successfully or otherwise) any civil proceedings concerning our company or its affairs in any court whether in the Cayman Islands or elsewhere. This standard of conduct is generally the same as permitted under the Delaware General Corporation Law for a Delaware corporation. In addition, we intend to enter into indemnification agreements with our directors and executive officers that will provide such persons with additional indemnification beyond that provided in our articles.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to our directors, officers or persons controlling us under the foregoing provisions, we have been informed that, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

Anti-Takeover Provisions in Our Articles

Some provisions of our articles may discourage, delay or prevent a change in control of our company or management that shareholders may consider favorable, including limitations on shareholder rights to nominate or remove directors, as well as provisions that authorize our board of directors to issue preferred shares in one or more series and to designate the price, rights, preferences, privileges and restrictions of such preferred shares without any further vote or action by our shareholders.

Under the Cayman Companies Act, our directors may only exercise the rights and powers granted to them under our articles, as amended and restated from time to time, for what they believe in good faith to be in the best interests of our company and for a proper purpose.

Directors' Fiduciary Duties

Under Delaware corporate law, a director of a Delaware corporation has a fiduciary duty to the corporation and its shareholders. This duty has two components: the duty of care and the duty of loyalty. The duty of care requires that a director act in good faith, with the care that an ordinarily prudent person would exercise under similar circumstances. Under this duty, a director must inform himself of, and disclose to shareholders, all material information reasonably available regarding a significant transaction. The duty of loyalty requires that a director act in a manner he or she reasonably believes to be in the best interests of the corporation. He or she must not use his or her corporate position for personal gain or advantage. This duty prohibits self-dealing by a director and mandates that the best interests of the corporation and its shareholders take precedence over any interest possessed by a director, officer or controlling shareholder and not shared by the shareholders generally. In general, actions of a director are presumed to have been made on an informed basis, in good faith and in the honest belief that the action taken was in the best interests of the corporation. However, this presumption may be rebutted by evidence of a breach

of one of the fiduciary duties. Should such evidence be presented concerning a transaction by a director, a director must prove the transaction was procedurally fair and provided fair value to the corporation.

As a matter of Cayman law, a director of a Cayman Islands company is in the position of a fiduciary with respect to the company and therefore owes the following duties to the company—a duty to act bona fide in the best interests of the company, a duty not to make a profit based on his or her position as director (unless the company permits him or her to do so), a duty not to put himself or herself in a position where the interests of the company conflict with his or her personal interest or his or her duty to a third party, and a duty to exercise powers for the purpose for which such powers were intended. A director of a Cayman Islands company owes to the company a duty to act with skill and care. It was previously considered that a director need not exhibit in the performance of his or her duties a greater degree of skill than may reasonably be expected from a person of his or her knowledge and experience. However, English and Commonwealth courts have moved towards an objective standard with regard to the required skill and care, and these authorities are likely to be followed in the Cayman Islands.

Shareholder Proposals

Under the Delaware General Corporation Law, a shareholder has the right to put any proposal before the annual meeting of shareholders, provided it complies with the notice provisions in the governing documents. The Delaware General Corporation Law does not provide shareholders an express right to put any proposal before the annual meeting of shareholders, but in keeping with common law, Delaware corporations generally afford shareholders an opportunity to make proposals and nominations provided that they comply with the notice provisions in the certificate of incorporation or bylaws. A special meeting may be called by the board of directors or any other person authorized to do so in the governing documents, but shareholders may be precluded from calling special meetings.

The Cayman Companies Act provides shareholders with only limited rights to requisition a general meeting, and does not provide shareholders with any right to put any proposal before a general meeting. However, these rights may be provided in a company's articles of association. Our articles allow our shareholders holding not less than one-tenth of the voting rights entitled to vote at general meetings to requisition an extraordinary general meeting of our shareholders, in which case our board is obliged to convene an extraordinary general meeting and to put the resolutions so requisitioned to a vote at such meeting. However, our shareholders may propose only ordinary resolutions to be put to a vote at such meetings. Our articles provide no other right to put any proposals before annual general meetings or extraordinary general meetings. As a Cayman Islands exempted company, we are not obligated by law to call shareholders' annual general meetings.

However, our corporate governance guidelines require us to call such meetings every year to the extent required by the applicable listing rules.

Cumulative Voting

Under the Delaware General Corporation Law, cumulative voting for elections of directors is not permitted unless the corporation's certificate of incorporation specifically provides for it. Cumulative voting potentially facilitates the representation of minority shareholders on a board of directors since it permits the minority shareholder to cast all the votes to which the shareholder is entitled on a single director, which increases the shareholder's voting power with respect to electing such director. As permitted under the Cayman Companies Act, our articles do not provide for cumulative voting. As a result, our shareholders are not afforded any less protections or rights on this issue than shareholders of a Delaware corporation.

Removal of Directors

Under the Delaware General Corporation Law, a director of a corporation with a classified board may be removed only for cause with the approval of a majority of the outstanding shares entitled to vote, unless the certificate of incorporation provides otherwise. Under our articles, any director may be removed by an affirmative vote of a simple majority of the issued shares as of the applicable record date, with or without cause.

Transactions with Interested Shareholders

The Delaware General Corporation Law contains a business combination statute applicable to Delaware public corporations whereby, unless the corporation has specifically elected not to be governed by such statute by amendment to its certificate of incorporation or bylaws that is approved by its shareholders, it is prohibited from engaging in certain business combinations with an "interested shareholder" for three years following the date that such person becomes an interested shareholder. An interested shareholder generally is a person or a group who or which owns or owned 15% or more of the target's outstanding voting stock or who or which is an affiliate or associate of the corporation and owned 15% or more of the corporation's outstanding voting stock within the past three years. This has the effect of limiting the ability of a potential acquirer to make a two-tiered bid for the target in which all shareholders would not be treated equally. The statute does not apply if, among other things, prior to the date on which such shareholder becomes an interested shareholder, the board of directors approves either the business combination or the transaction which resulted in the person becoming an interested shareholder. This encourages any potential acquirer of a Delaware corporation to negotiate the terms of any acquisition transaction with the target's board of directors.

The Cayman Companies Act has no comparable statute. As a result, we cannot avail ourselves of the types of protections afforded by the Delaware business combination statute. However, although the Cayman Companies Act does not regulate transactions between a company and its significant shareholders, it does provide that such transactions must be entered into bona fide in the best interests of the company and for a proper corporate purpose and not with the effect of constituting a fraud on the minority shareholders.

Dissolution; Winding Up

Under the Delaware General Corporation Law, unless the board of directors approves the proposal to dissolve, dissolution must be approved by shareholders holding 100% of the total voting power of the corporation. Only if the dissolution is initiated by the board of directors may it be approved by a simple majority of the corporation's outstanding shares. Delaware law allows a Delaware corporation to include in its certificate of incorporation a supermajority voting requirement in connection with dissolutions initiated by the board of directors.

Under the Cayman Companies Act and our articles, our company may be wound up only upon resolution of shareholders holding 100% of the total voting rights entitled to vote or if the winding up is initiated by our board of directors, by either a special resolution of our members or, if our company is unable to pay its debts as they fall due, by an ordinary resolution of our members. In addition, a company may be wound up by an order of the courts of the Cayman Islands. The court has authority to order winding up in a number of specified circumstances including where it is, in the opinion of the court, just and equitable to do so.

Variation of Rights of Shares

Under the Delaware General Corporation Law, a corporation may vary the rights of a class of shares with the approval of a majority of the outstanding shares of such class, unless the certificate of incorporation provides otherwise. Under the Cayman Companies Act and our articles, if our share capital is divided into more than one class of shares, we may materially and adversely vary the rights attached to any class only with the consent in writing of the holders of two-thirds of the shares of that class or with the sanction of a special resolution passed at a general meeting of the holders of the shares of that class.

Amendment of Governing Documents

Under the Delaware General Corporation Law, a corporation's certificate of incorporation may be amended only if adopted and declared advisable by the board of directors and approved by a majority of the outstanding shares entitled to vote, and the bylaws may be amended with the approval of a majority of the outstanding shares entitled to vote and may, if so provided in the certificate of incorporation, also be amended by the board of directors. Under the Cayman Companies Act and our articles, our articles may only be amended by special resolution of our shareholders.

Rights of Non-Resident or Foreign Shareholders

There are no limitations imposed by our articles on the rights of non-resident or foreign shareholders to hold or exercise voting rights on our shares. In addition, there are no provisions in our articles governing the ownership threshold above which shareholder ownership must be disclosed.

Directors' Power to Issue Shares

Under our articles, our board of directors is empowered to issue or allot shares or grant options, restricted shares, restricted share units, share appreciation rights, dividend equivalent rights, warrants and analogous equity-based rights with or without preferred, deferred, qualified or other special rights or restrictions. In particular, pursuant to our articles, our board of directors has the authority, without further action by the shareholders, to issue all or any part of our capital and to fix the designations, powers, preferences, privileges, and relative participating, optional or special rights and the qualifications, limitations or restrictions therefrom, including dividend rights, conversion rights, voting rights, terms of redemption and liquidation preferences, any or all of which may be greater than the rights of our ordinary shares. Our board of directors, without shareholder approval, may issue preferred shares with voting, conversion or other rights that could adversely affect the voting power and other rights of holders of our ordinary shares. Subject to the directors' duty of acting in the best interest of our company, preferred shares can be issued quickly with terms calculated to delay or prevent a change in control of us or make removal of management more difficult. Additionally, the issuance of preferred shares may have the effect of decreasing the market price of the ordinary shares, and may adversely affect the voting and other rights of the holders of ordinary shares.

Inspection of Books and Records

Holders of our ordinary shares will have no general right under the Cayman Companies Act to inspect or obtain copies of our list of shareholders or our corporate records. However, we will provide our shareholders with annual audited financial statements.

Registration Rights

On November 16, 2016, we entered into a registration rights agreement with 667, L.P., Baker Brothers Life Sciences, L.P. and 14159, L.P. ("the Baker Entities"), Hillhouse BGN Holdings Limited, HHLR Fund, L.P. (formerly known as Gaoling Fund, L.P.) and YHG Investment, L.P. ("the Hillhouse Entities"), (each an "Investor" and collectively, the "Investors"), all of which were existing shareholders. The registration rights agreement provides that, subject to certain limitations, if at any time and from time to time, the Investors demand that we register our ordinary shares and any other securities held by the Investors at the time any such demand is made on a Registration Statement on Form S-3 for resale under the Securities Act, we would be obligated to effect such registration. Our registration obligations under the registration rights agreement will continue in effect for up to four years, and include our obligation to facilitate certain underwritten public offerings of our ordinary shares or ADSs by the Investors in the future. The registration rights agreement also requires us to pay expenses relating to such registrations and indemnify the Investors against certain liabilities. On December 1, 2020, we and the Investors entered into an Amendment No.1 to the Registration Rights Agreement, effective December 31, 2020, pursuant to which our registration obligations under the Registration Rights Agreement will continue in effect for up to another three years, until December 31, 2023.

Pursuant to the Share Purchase Agreement (the "Share Purchase Agreement") dated October 31, 2019, as amended, by and between us and Amgen Inc. ("Amgen"), Amgen will have specified registration rights upon expiration of a lock-up period. Following demand by Amgen at any time after the expiration of the lock-up period or such earlier time as we in our sole discretion may agree in writing, we shall, subject to certain limits as specified under the Share Purchase Agreement, file with the SEC a Registration Statement on Form S-3 (except if we are not then eligible to register for resale the registrable shares on Form S-3, in which case such registration shall be on another appropriate form in accordance with the Securities Act) covering the resale of the registrable shares of Amgen. In addition, where we propose to register any of our ordinary shares or ADSs under the Securities Act for sale to the public (other than a registration effected solely to implement an employee benefit plan or a transaction to which Rule 145 of the Securities Act is applicable, or a registration statement in a form not available for registering registrable shares for sale to the public), we will give notice to Amgen of our intention to do so and, upon the

request of Amgen, use our reasonable best efforts to cause all the registrable shares of Amgen to be registered under the Securities Act in connection therewith, under specified circumstances and as set forth in the Share Purchase Agreement.

Description of American Depositary Shares

Citibank, N.A. (“Citibank”) acts as the depositary bank for the ADSs. Citibank's depositary offices are located at 388 Greenwich Street, New York, New York 10013. American Depositary Shares are frequently referred to as "ADSs" and represent ownership interests in securities that are on deposit with the depositary bank. ADSs may be represented by certificates that are commonly known as "American Depositary Receipts" or "ADRs." *The depositary bank typically appoints a custodian to safekeep the securities on deposit. In this case, the custodian is Citibank, N.A. - Hong Kong, presently located at 9/F, Citi Tower, One Bay East, 83 Hoi Bun Road, Kwun Tong, Kowloon, Hong Kong.*

We have appointed Citibank as depositary bank pursuant to a deposit agreement. A copy of the deposit agreement, as amended, is on file with the SEC under cover of a Registration Statement on Form F-6. You may obtain a copy of the deposit agreement from the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549 and from the SEC's website (www.sec.gov). Please refer to Registration Number 333-209044 when retrieving such copy.

We are providing you with a summary description of the material terms of the ADSs and of your material rights as an owner of ADSs. Please remember that summaries by their nature lack the precision of the information summarized and that the rights and obligations of an owner of ADSs will be determined by reference to the terms of the deposit agreement and not by this summary. *We urge you to review the deposit agreement in its entirety. The portions of this summary description that are italicized describe matters that may be relevant to the ownership of ADSs but that may not be contained in the deposit agreement.*

Each ADS represents the right to receive, and to exercise the beneficial ownership interests in, 13 ordinary shares that are on deposit with the depositary bank and/or custodian. An ADS also represents the right to receive, and to exercise the beneficial interests in, any other property received by the depositary bank or the custodian on behalf of the owner of the ADS but that has not been distributed to the owners of ADSs because of legal restrictions or practical considerations. We and the depositary bank may agree to change the ADS-to-ordinary share ratio by amending the deposit agreement. This amendment may give rise to, or change, the depositary fees payable by ADS owners. The custodian, the depositary bank and their respective nominees will hold all deposited property for the benefit of the holders and beneficial owners of ADSs. The deposited property does not constitute the proprietary assets of the depositary bank, the custodian or their nominees. Beneficial ownership in the deposited property will under the terms of the deposit agreement be vested in the beneficial owners of the ADSs. *The depositary bank, the custodian and their respective nominees will be the record holders of the deposited property represented by the ADSs for the benefit of the holders and beneficial owners of the corresponding ADSs. A beneficial owner of ADSs may or may not be the holder of ADSs. Beneficial owners of ADSs will be able to receive, and to exercise beneficial ownership interests in, the deposited property only through the registered holders of the ADSs, the registered holders of the ADSs (on behalf of the applicable ADS owners) only through the depositary bank, and the depositary bank (on behalf of the owners of the corresponding ADSs) directly, or indirectly, through the custodian or their respective nominees, in each case upon the terms of the deposit agreement.*

If you become an owner of ADSs, you will become a party to the deposit agreement and therefore will be bound to its terms and to the terms of any ADR that represents your ADSs. The deposit agreement and the ADR specify our rights and obligations as well as your rights and obligations as an owner of ADSs and those of the depositary bank. As an ADS holder you appoint the depositary bank to act on your behalf in certain circumstances. The deposit agreement and the ADRs are governed by New York law. However, our obligations to the holders of the ordinary shares will continue to be governed by the laws of the Cayman Islands, which may be different from the laws in the United States.

In addition, applicable laws and regulations may require you to satisfy reporting requirements and obtain regulatory approvals in certain circumstances. You are solely responsible for complying with such reporting requirements and obtaining such approvals. Neither the depositary bank, the custodian, us or any of their or our respective agents or affiliates shall be required to take any actions whatsoever on your behalf to satisfy such reporting requirements or obtain such regulatory approvals under applicable laws and regulations.

The manner in which you own the ADSs (e.g., in a brokerage account vs. as registered holder, or as holder of certificated vs. uncertificated ADSs) may affect your rights and obligations, and the manner in which, and extent to which, the depositary bank's services are made available to you. As an owner of ADSs, we will not treat you as one of our shareholders and you will not have direct shareholder rights. The depositary bank will hold on your behalf the shareholder rights attached to the ordinary shares underlying your ADSs. As an owner of ADSs you will be able to exercise the shareholders rights for the ordinary shares represented by your ADSs through the depositary bank only to the extent contemplated in the deposit agreement. To exercise any shareholder rights not contemplated in the deposit agreement you will, as an ADS owner, need to arrange for the cancellation of your ADSs and become a direct shareholder.

As an owner of ADSs, you may hold your ADSs either by means of an ADR registered in your name, through a brokerage or safekeeping account, or through an account established by the depositary bank in your name reflecting the registration of uncertificated ADSs directly on the books of the depositary bank (commonly referred to as the "direct registration system" or "DRS"). The direct registration system reflects the uncertificated (book-entry) registration of ownership of ADSs by the depositary bank. Under the direct registration system, ownership of ADSs is evidenced by periodic statements issued by the depositary bank to the holders of the ADSs. The direct registration system includes automated transfers between the depositary bank and The Depository Trust Company ("DTC"), the central book-entry clearing and settlement system for equity securities in the United States. If you decide to hold your ADSs through your brokerage or safekeeping account, you must rely on the procedures of your broker or bank to assert your rights as ADS owner. Banks and brokers typically hold securities such as the ADSs through clearing and settlement systems such as DTC. The procedures of such clearing and settlement systems may limit your ability to exercise your rights as an owner of ADSs. Please consult with your broker or bank if you have any questions concerning these limitations and procedures. All ADSs held through DTC will be registered in the name of a nominee of DTC. This summary description assumes you have opted to own the ADSs directly by means of an ADS registered in your name and, as such, we will refer to you as the "holder." When we refer to "you," we assume the reader owns ADSs and will own ADSs at the relevant time.

The registration of the ordinary shares in the name of the depositary bank or the custodian shall, to the maximum extent permitted by applicable law, vest in the depositary bank or the custodian the record ownership in the applicable ordinary shares with the beneficial ownership rights and interests in such ordinary shares being at all times vested with the beneficial owners of the ADSs representing the ordinary shares. The depositary bank or the custodian shall at all times be entitled to exercise the beneficial ownership rights in all deposited property, in each case only on behalf of the holders and beneficial owners of the ADSs representing the deposited property.

Dividends and Distributions

As a holder of ADSs, you generally have the right to receive the distributions we make on the securities deposited with the custodian. Your receipt of these distributions may be limited, however, by practical considerations and legal limitations. Holders of ADSs will receive such distributions under the terms of the deposit agreement in proportion to the number of ADSs held as of the specified record date, after deduction of the applicable fees, taxes and expenses.

Distributions of Cash

Whenever we make a cash distribution for the securities on deposit with the custodian, we will deposit the funds with the custodian. Upon receipt of confirmation of the deposit of the requisite funds, the depositary bank will arrange for the funds received in a currency other than U.S. dollars to be converted into U.S. dollars and for the distribution of the U.S. dollars to the holders, subject to the applicable laws and regulations.

The conversion into U.S. dollars will take place only if practicable and if the U.S. dollars are transferable to the United States. The depositary bank will apply the same method for distributing the proceeds of the sale of any property (such as undistributed rights) held by the custodian in respect of securities on deposit.

The distribution of cash will be made net of the fees, expenses, taxes and governmental charges payable by holders under the terms of the deposit agreement. The depositary bank will hold any cash amounts it is unable to distribute in a non-interest bearing account for the benefit of the applicable holders and beneficial owners of ADSs until the distribution can be effected or

the funds that the depositary bank holds must be escheated as unclaimed property in accordance with the laws of the relevant states of the United States.

Distributions of Shares

Whenever we make a free distribution of the ordinary shares for the securities on deposit with the custodian, we will deposit the applicable number of the ordinary shares with the custodian. Upon receipt of confirmation of such deposit, the depositary bank will either distribute to holders new ADSs representing the ordinary shares deposited or modify the ADS-to-ordinary share ratio, in which case each ADS you hold will represent rights and interests in the additional ordinary shares so deposited. Only whole new ADSs will be distributed. Fractional entitlements will be sold and the proceeds of such sale will be distributed as in the case of a cash distribution.

The distribution of new ADSs or the modification of the ADS-to-ordinary share ratio upon a distribution of the ordinary shares will be made net of the fees, expenses, taxes and governmental charges payable by holders under the terms of the deposit agreement. In order to pay such taxes or governmental charges, the depositary bank may sell all or a portion of the new ordinary shares so distributed.

No such distribution of new ADSs will be made if it would violate a law (e.g., the U.S. securities laws) or if it is not operationally practicable. If the depositary bank does not distribute new ADSs as described above, it may sell the ordinary shares received upon the terms described in the deposit agreement and will distribute the proceeds of the sale as in the case of a distribution of cash.

Distributions of Rights

Whenever we intend to distribute rights to subscribe for additional ordinary shares, we will give prior notice to the depositary bank and we will assist the depositary bank in determining whether it is lawful and reasonably practicable to distribute rights to subscribe for additional ADSs to holders.

The depositary bank will establish procedures to distribute rights to subscribe for additional ADSs to holders and to enable such holders to exercise such rights if it is lawful and reasonably practicable to make the rights available to holders of ADSs, and if we provide all of the documentation contemplated in the deposit agreement (such as opinions to address the lawfulness of the transaction). You may have to pay fees, expenses, taxes and other governmental charges to subscribe for the new ADSs upon the exercise of your rights. The depositary bank is not obligated to establish procedures to facilitate the distribution and exercise by holders of rights to subscribe for new ordinary shares other than in the form of ADSs.

The depositary bank will *not* distribute the rights to you if:

- We do not timely request that the rights be distributed to you or we request that the rights not be distributed to you;
- We fail to deliver satisfactory documents to the depositary bank; or
- It is not reasonably practicable to distribute the rights.

The depositary bank will sell the rights that are not exercised or not distributed if such sale is lawful and reasonably practicable. The proceeds of such sale will be distributed to holders as in the case of a cash distribution. If the depositary bank is unable to sell the rights, it will allow the rights to lapse.

Elective Distributions

Whenever we intend to distribute a dividend payable at the election of shareholders either in cash or in additional shares, we will give prior notice thereof to the depositary bank and will indicate whether we wish the elective distribution to be made available to you. In such case, we will assist the depositary bank in determining whether such distribution is lawful and reasonably practicable.

The depositary bank will make the election available to you only if it is reasonably practicable and if we have provided all of the documentation contemplated in the deposit agreement. In such case, the depositary bank will establish procedures to enable you to elect to receive either cash or additional ADSs, in each case as described in the deposit agreement.

If the election is not made available to you, you will receive either cash or additional ADSs, depending on what a shareholder in the Cayman Islands would receive upon failing to make an election, as more fully described in the deposit agreement.

Other Distributions

Whenever we intend to distribute property other than cash, ordinary shares or rights to subscribe for additional ordinary shares, we will notify the depositary bank in advance and will indicate whether we wish such distribution to be made to you. If so, we will assist the depositary bank in determining whether such distribution to holders is lawful and reasonably practicable.

If it is reasonably practicable to distribute such property to you and if we provide all of the documentation contemplated in the deposit agreement to the depositary bank, the depositary bank will distribute the property to the holders in a manner it deems practicable.

The distribution will be made net of fees, expenses, taxes and governmental charges payable by holders under the terms of the deposit agreement. In order to pay such taxes and governmental charges, the depositary bank may sell all or a portion of the property received.

The depositary bank will not distribute the property to you and will sell the property if:

- We do not request that the property be distributed to you or if we request that the property not be distributed to you; or
- We do not deliver satisfactory documents to the depositary bank; or
- The depositary bank determines that all or a portion of the distribution to you is not reasonably practicable.

The proceeds of such a sale will be distributed to holders as in the case of a cash distribution.

Redemption

Whenever we decide to redeem any of the securities on deposit with the custodian, we will notify the depositary bank in advance. If it is practicable and if we provide all of the documentation contemplated in the deposit agreement, the depositary bank will provide notice of the redemption to the holders.

The custodian will be instructed to surrender the shares being redeemed against payment of the applicable redemption price. The depositary bank will convert into U.S. dollars the redemption funds received in a currency other than U.S. dollars upon the terms of the deposit agreement and will establish procedures to enable holders to receive the net proceeds from the redemption upon surrender of their ADSs to the depositary bank. You may have to pay fees, expenses, taxes and other governmental charges upon the redemption of your ADSs. If less than all ADSs are being redeemed, the ADSs to be retired will be selected by lot or on a pro rata basis, as the depositary bank may determine.

Changes Affecting Ordinary Shares

The ordinary shares held on deposit for your ADSs may change from time to time. For example, there may be a change in nominal or par value, split-up, cancellation, consolidation or any other reclassification of such ordinary shares or a recapitalization, reorganization, merger, consolidation or sale of assets of the company.

If any such change were to occur, your ADSs would, to the extent permitted by law and the deposit agreement, represent the right to receive the property received or exchanged in respect of the ordinary shares held on deposit. The depositary bank may in such circumstances deliver new ADSs to you, amend the deposit agreement, the ADRs and the applicable Registration Statement(s) on Form F-6, call for the exchange of your existing ADSs for new ADSs and take any other actions that are appropriate to reflect as to the ADSs the change affecting the ordinary shares. If the depositary bank may not lawfully distribute

such property to you, the depositary bank may sell such property and distribute the net proceeds to you as in the case of a cash distribution.

Issuance of ADSs Upon Deposit of Ordinary Shares

The depositary bank may create ADSs on behalf of investors who deposit ordinary shares with the custodian. The depositary bank will deliver these ADSs to the person you indicate only after you pay any applicable issuance fees and any charges and taxes payable for the transfer of the ordinary shares to the custodian. Your ability to deposit ordinary shares and receive ADSs may be limited by U.S. and Cayman Islands legal considerations applicable at the time of deposit.

The issuance of ADSs may be delayed until the depositary bank or the custodian receives confirmation that all required approvals have been given and that the ordinary shares have been duly transferred to the custodian. The depositary bank will only issue ADSs in whole numbers.

When you make a deposit of the ordinary shares, you will be responsible for transferring good and valid title to the depositary bank. As such, you will be deemed to represent and warrant that:

- The ordinary shares are duly authorized, validly issued, fully paid, non-assessable and legally obtained.
- All preemptive (and similar) rights, if any, with respect to such ordinary shares have been validly waived or exercised.
- You are duly authorized to deposit the ordinary shares.
- The ordinary shares presented for deposit are free and clear of any lien, encumbrance, security interest, charge, mortgage or adverse claim, and are not, and the ADSs issuable upon such deposit will not be, "restricted securities" (as defined in the deposit agreement).
- The ordinary shares presented for deposit have not been stripped of any rights or entitlements.

If any of the representations or warranties are incorrect in any way, we and the depositary bank may, at your cost and expense, take any and all actions necessary to correct the consequences of the misrepresentations.

Transfer, Combination and Split Up of ADRs

As an ADR holder, you will be entitled to transfer, combine or split up your ADRs and the ADSs evidenced thereby. For transfers of ADRs, you will have to surrender the ADRs to be transferred to the depositary bank and also must:

- ensure that the surrendered ADR is properly endorsed or otherwise in proper form for transfer;
- provide such proof of identity and genuineness of signatures as the depositary bank deems appropriate;
- provide any transfer stamps required by the State of New York or the United States; and
- pay all applicable fees, charges, expenses, taxes and other government charges payable by ADR holders pursuant to the terms of the deposit agreement, upon the transfer of ADRs.

To have your ADRs either combined or split up, you must surrender the ADRs in question to the depositary bank with your request to have them combined or split up, and you must pay all applicable fees, charges and expenses payable by ADR holders, pursuant to the terms of the deposit agreement, upon a combination or split up of ADRs.

Withdrawal of Ordinary Shares Upon Cancellation of ADSs

As a holder, you will be entitled to present your ADSs to the depositary bank for cancellation and then receive the corresponding number of underlying ordinary shares at the custodian's offices. Your ability to withdraw the ordinary shares held in respect of the ADSs may be limited by U.S. and Cayman Islands legal considerations applicable at the time of withdrawal. In order to withdraw the ordinary shares represented by your ADSs, you will be required to pay to the depositary bank the fees for cancellation of ADSs and any charges and taxes payable upon the transfer of the ordinary shares. You assume

the risk for delivery of all funds and securities upon withdrawal. Once canceled, the ADSs will not have any rights under the deposit agreement.

If you hold ADSs registered in your name, the depositary bank may ask you to provide proof of identity and genuineness of any signature and such other documents as the depositary bank may deem appropriate before it will cancel your ADSs. The withdrawal of the ordinary shares represented by your ADSs may be delayed until the depositary bank receives satisfactory evidence of compliance with all applicable laws and regulations. Please keep in mind that the depositary bank will only accept ADSs for cancellation that represent a whole number of securities on deposit.

You will have the right to withdraw the securities represented by your ADSs at any time except for:

- temporary delays that may arise because (i) the transfer books for the ordinary shares or ADSs are closed, or (ii) the ordinary shares are immobilized on account of a shareholders' meeting or a payment of dividends;
- obligations to pay fees, taxes and similar charges; or
- restrictions imposed because of laws or regulations applicable to ADSs or the withdrawal of securities on deposit.

The deposit agreement may not be modified to impair your right to withdraw the securities represented by your ADSs except to comply with mandatory provisions of law.

Voting Rights

As a holder, you generally have the right under the deposit agreement to instruct the depositary bank to exercise the voting rights for the ordinary shares represented by your ADSs. The voting rights of holders of ordinary shares are described in "— Ordinary Shares".

At our request, the depositary bank will distribute to you any notice of shareholders' meeting received from us together with information explaining how to instruct the depositary bank to exercise the voting rights of the securities represented by ADSs. In lieu of distributing such materials, the depositary bank may distribute to holders of ADSs instructions on how to retrieve such materials upon request.

If the depositary bank timely receives voting instructions from a holder of ADSs, it will endeavor to vote the securities (in person or by proxy) represented by the holder's ADSs in accordance with the voting instructions received from the holders of ADSs.

Our memorandum and articles of association provide that voting of shareholders at any meeting is by poll. Holders of ADSs in respect of which no timely voting instructions have been received, or timely voting instructions have been received however such instructions fail to specify the manner in which the depositary is to vote, shall be deemed to have instructed the depositary to give a discretionary proxy to a person designated by us to vote the ordinary shares represented by such holders' ADSs; provided, that no such instruction shall be deemed given and no such discretionary proxy shall be given with respect to any matter as to which we inform the depositary that we do not wish such proxy to be given; provided, further, that no such discretionary proxy shall be given with respect to any matter as to which we inform the depositary that (i) there exists substantial opposition, or (ii) the rights of shareholders of our company will be materially adversely affected.

Please note that the ability of the depositary bank to carry out voting instructions may be limited by practical and legal limitations and the terms of the securities on deposit. We cannot assure you that you will receive voting materials in time to enable you to return voting instructions to the depositary bank in a timely manner.

Fees and Charges

As an ADS holder, you will be required to pay the following fees under the terms of the deposit agreement:

Service	Fees
• Issuance of ADSs upon deposit of ordinary shares (excluding issuances as a result of distributions of ADSs pursuant to (i) stock dividends or other free stock distributions, or (ii) exercise of rights to purchase additional ADSs)	Up to U.S. $5.00 per 100 ADSs (or fraction thereof) issued
• Delivery of deposited property against surrender of ADSs	Up to U.S. $5.00 per 100 ADSs (or fraction thereof) canceled
• Distribution of cash dividends or other cash distributions (i.e., sale of rights and other entitlements)	Up to U.S. $5.00 per 100 ADSs (or fraction thereof) held
• Distribution of ADSs pursuant to (i) stock dividends or other free stock distributions, or (ii) exercise of rights to purchase additional ADSs	Up to U.S. $5.00 per 100 ADSs (or fraction thereof) held
• Distribution of securities other than ADSs or rights to purchase additional ADSs (i.e., spin-off shares)	Up to U.S. $5.00 per 100 ADSs (or fraction thereof) held
• ADS Services	Up to U.S. $5.00 per 100 ADSs (or fraction thereof) held on the applicable record date(s) established by the depositary bank

As an ADS holder you will also be responsible to pay certain charges such as:

- taxes (including applicable interest and penalties) and other governmental charges;
- the registration fees as may from time to time be in effect for the registration of the ordinary shares on the share register and applicable to transfers of the ordinary shares to or from the name of the custodian, the depositary bank or any nominees upon the making of deposits and withdrawals, respectively;
- such cable, telex and facsimile transmission and delivery expenses as are expressly provided in the deposit agreement to be at the expense of the person depositing ordinary shares or withdrawing deposited securities or of the holders and beneficial owners of ADSs;
- the expenses and charges incurred by the depositary bank in the conversion of foreign currency;
- the fees and expenses incurred by the depositary bank in connection with compliance with exchange control regulations and other regulatory requirements applicable to the ordinary shares, deposited securities, ADSs and ADRs; and
- the fees and expenses incurred by the depositary bank, the custodian or any nominee in connection with the servicing or delivery of deposited property.

ADS fees and charges payable upon (i) deposit of the ordinary shares against issuance of ADSs and (ii) surrender of ADSs for cancellation and withdrawal of the ordinary shares are charged to the person to whom the ADSs are delivered (in the case of ADS issuances) and to the person who delivers the ADSs for cancellation (in the case of ADS cancellations). In the case of ADSs issued by the depositary bank into DTC or presented to the depositary bank via DTC, the ADS issuance and cancellation fees and charges will be payable by the DTC participant(s) receiving the ADSs from the depositary bank or the DTC participant(s) surrendering the ADSs to the depositary bank for cancellation, as the case may be, on behalf of the beneficial

owner(s) and will be charged by the DTC participant(s) to the account(s) of the applicable beneficial owner(s) in accordance with the procedures and practices of the DTC participant(s) as in effect at the time. ADS fees and charges in respect of distributions and the ADS service fee are payable by holders as of the applicable ADS record date established by the depositary bank. In the case of distributions of cash, the amount of the applicable ADS fees and charges is deducted from the funds being distributed. In the case of (i) distributions other than cash and (ii) the ADS service fee, holders as of the ADS record date will be invoiced for the amount of the ADS fees and charges and such ADS fees and charges may be deducted from distributions made to holders of ADSs. For ADSs held through DTC, the ADS fees and charges for distributions other than cash and the ADS service fee may be deducted from distributions made through DTC, and may be charged to the DTC participants in accordance with the procedures and practices prescribed by DTC and the DTC participants in turn charge the amount of such ADS fees and charges to the beneficial owners for whom they hold ADSs.

In the event of refusal to pay the depositary bank fees, the depositary bank may, under the terms of the deposit agreement, refuse the requested service until payment is received or may set off the amount of the depositary bank fees from any distribution to be made to the ADS holder. Certain of the depositary fees and charges (such as the ADS services fee) may become payable shortly after the closing of the ADS offering. Note that the fees and charges you may be required to pay may vary over time and may be changed by us and by the depositary bank. You will receive prior notice of such changes. The depositary bank may reimburse us for certain expenses incurred by us in respect of the ADR program, by making available a portion of the ADS fees charged in respect of the ADR program or otherwise, upon such terms and conditions as we and the depositary bank agree from time to time.

Amendments and Termination

We may agree with the depositary bank to modify the deposit agreement at any time without your consent. We undertake to give holders 30 days' prior notice of any modifications that would materially prejudice any of their substantial rights under the deposit agreement. We will not consider to be materially prejudicial to your substantial rights any modifications or supplements that are reasonably necessary for the ADSs to be registered under the Securities Act or to be eligible for book-entry settlement, in each case without imposing or increasing the fees and charges you are required to pay. In addition, we may not be able to provide you with prior notice of any modifications or supplements that are required to accommodate compliance with applicable provisions of law.

You will be bound by the modifications to the deposit agreement if you continue to hold your ADSs after the modifications to the deposit agreement become effective. The deposit agreement cannot be amended to prevent you from withdrawing the ordinary shares represented by your ADSs (except as permitted by law).

We have the right to direct the depositary bank to terminate the deposit agreement. Similarly, the depositary bank may in certain circumstances on its own initiative terminate the deposit agreement. In either case, the depositary bank must give notice to the holders at least 30 days before termination. Until termination, your rights under the deposit agreement will be unaffected.

After termination, the depositary bank will continue to collect distributions received (but will not distribute any such property until you request the cancellation of your ADSs) and sell the securities held on deposit. After the sale, the depositary bank will hold the proceeds from such sale and any other funds then held for the holders of ADSs in a non-interest bearing account. At that point, the depositary bank will have no further obligations to holders other than to account for the funds then held for the holders of ADSs still outstanding (after deduction of applicable fees, taxes and expenses).

Books of Depositary

The depositary bank will maintain ADS holder records at its depositary office. You may inspect such records at such office during regular business hours but solely for the purpose of communicating with other holders in the interest of business matters relating to the ADSs and the deposit agreement.

The depositary bank will maintain in New York facilities to record and process the issuance, cancellation, combination, split-up and transfer of ADSs. These facilities may be closed from time to time, to the extent not prohibited by law.

Limitations on Obligations and Liabilities

The deposit agreement limits our obligations and the depositary bank's obligations to you. Please note the following:

- We and the depositary bank are obligated only to take the actions specifically stated in the deposit agreement without negligence or bad faith.
- The depositary bank disclaims any liability for any failure to carry out voting instructions, for any manner in which a vote is cast or for the effect of any vote, provided it acts in good faith and in accordance with the terms of the deposit agreement.
- The depositary bank disclaims any liability for any failure to determine the lawfulness or practicality of any action, for the content of any document forwarded to you on our behalf or for the accuracy of any translation of such a document, for the investment risks associated with investing in the ordinary shares, for the validity or worth of the ordinary shares, for any tax consequences that result from the ownership of ADSs, for the credit-worthiness of any third party, for allowing any rights to lapse under the terms of the deposit agreement, for the timeliness of any of our notices or for our failure to give notice.
- We and the depositary bank will not be obligated to perform any act that is inconsistent with the terms of the deposit agreement.
- We and the depositary bank disclaim any liability if we or the depositary bank are prevented or forbidden from or subject to any civil or criminal penalty or restraint on account of, or delayed in, doing or performing any act or thing required by the terms of the deposit agreement, by reason of any provision, present or future of any law or regulation, or by reason of present or future provision of any provision of our memorandum and articles of association, or any provision of or governing the securities on deposit, or by reason of any act of God or war or other circumstances beyond our control.
- We and the depositary bank disclaim any liability by reason of any exercise of, or failure to exercise, any discretion provided for in the deposit agreement or in our memorandum and articles of association or in any provisions of or governing the securities on deposit.
- We and the depositary bank further disclaim any liability for any action or inaction in reliance on the advice or information received from legal counsel, accountants, any person presenting ordinary shares for deposit, any holder of ADSs or authorized representatives thereof, or any other person believed by either of us in good faith to be competent to give such advice or information.
- We and the depositary bank also disclaim liability for the inability by a holder to benefit from any distribution, offering, right or other benefit that is made available to holders of ordinary shares but is not, under the terms of the deposit agreement, made available to you.
- We and the depositary bank may rely without any liability upon any written notice, request or other document believed to be genuine and to have been signed or presented by the proper parties.
- We and the depositary bank also disclaim liability for any consequential or punitive damages for any breach of the terms of the deposit agreement.
- No disclaimer of any Securities Act liability is intended by any provision of the deposit agreement.
- Nothing in the deposit agreement gives rise to a partnership or joint venture, or establishes a fiduciary relationship among us, the depositary bank and you as ADS holder.
- Nothing in the deposit agreement precludes Citibank (or its affiliates) from engaging in transactions in which parties adverse to us or the ADS owners have interests, and nothing in the deposit agreement obligates Citibank to disclose

those transactions, or any information obtained in the course of those transactions, to us or to the ADS owners, or to account for any payment received as part of those transactions.

As the above limitations relate to our obligations and the depositary bank's obligations to you under the deposit agreement, we believe that, as a matter of construction of the clause, such limitations would likely to continue to apply to ADS holders who withdraw the ordinary shares from the ADS facility with respect to obligations or liabilities incurred under the deposit agreement before the cancellation of the ADSs and the withdrawal of the ordinary shares, and such limitations would most likely not apply to ADS holders who withdraw the ordinary shares from the ADS facility with respect to obligations or liabilities incurred after the cancellation of the ADSs and the withdrawal of the ordinary shares and not under the deposit agreement.

In any event, you will not be deemed, by agreeing to the terms of the deposit agreement, to have waived our or the depositary bank's compliance with U.S. federal securities laws and the rules and regulations promulgated thereunder. In fact, you cannot waive our or the depositary bank's compliance with U.S. federal securities laws and the rules and regulations promulgated thereunder.

Pre-Release Transactions

The depositary bank has informed us that it no longer engages in pre-release transactions and has no intention to do so in the future.

Taxes

You will be responsible for the taxes and other governmental charges payable on the ADSs and the securities represented by the ADSs. We, the depositary bank and the custodian may deduct from any distribution the taxes and governmental charges payable by holders and may sell any and all property on deposit to pay the taxes and governmental charges payable by holders. You will be liable for any deficiency if the sale proceeds do not cover the taxes that are due.

The depositary bank may refuse to issue ADSs, to deliver, transfer, split and combine ADRs or to release securities on deposit until all taxes and charges are paid by the applicable holder. The depositary bank and the custodian may take reasonable administrative actions to obtain tax refunds and reduced tax withholding for any distributions on your behalf. However, you may be required to provide to the depositary bank and to the custodian proof of taxpayer status and residence and such other information as the depositary bank and the custodian may require to fulfill legal obligations. You are required to indemnify us, the depositary bank and the custodian for any claims with respect to taxes based on any tax benefit obtained for you.

Foreign Currency Conversion

The depositary bank will arrange for the conversion of all foreign currency received into U.S. dollars if such conversion is practical, and it will distribute the U.S. dollars in accordance with the terms of the deposit agreement. You may have to pay fees and expenses incurred in converting foreign currency, such as fees and expenses incurred in complying with currency exchange controls and other governmental requirements.

If the conversion of foreign currency is not practical or lawful, or if any required approvals are denied or not obtainable at a reasonable cost or within a reasonable period, the depositary bank may take the following actions in its reasonable discretion:

- convert the foreign currency to the extent practical and lawful and distribute the U.S. dollars to the holders for whom the conversion and distribution is lawful and practical;
- distribute the foreign currency to holders for whom the distribution is lawful and practical; and
- hold the foreign currency (without liability for interest) for the applicable holders.

Governing Law/Waiver of Jury Trial

The deposit agreement and the ADRs will be interpreted in accordance with the laws of the State of New York. The rights of holders of ordinary shares (including the ordinary shares represented by ADSs) is governed by the laws of the Cayman Islands.

AS A PARTY TO THE DEPOSIT AGREEMENT, YOU **IRREVOCABLY WAIVE, TO THE FULLEST EXTENT PERMITTED BY APPLICABLE LAW**, YOUR RIGHT TO TRIAL BY JURY IN ANY LEGAL PROCEEDING ARISING OUT OF THE DEPOSIT AGREEMENT OR THE ADRs AGAINST US AND/OR THE DEPOSITARY BANK.

The deposit agreement provides that, to the extent permitted by law, ADS holders waive the right to a jury trial of any claim they may have against us or the depositary bank arising out of or relating to our ordinary shares, the ADSs or the deposit agreement, including any claim under U.S. federal securities laws. If we or the depositary bank opposed a jury trial demand based on the waiver, the court would determine whether the waiver was enforceable in the facts and circumstances of that case in accordance with applicable case law. However, you will not be deemed, by agreeing to the terms of the deposit agreement, to have waived our or the depositary bank's compliance with U.S. federal securities laws and the rules and regulations promulgated thereunder.

BEIGENE, LTD.

AMENDMENT NO. 3 TO SHARE PURCHASE AGREEMENT

THIS AMENDMENT NO. 3 (this "**Amendment**") to the SHARE PURCHASE AGREEMENT, dated as of October 31, 2019, as amended on December 6, 2019 and September 24, 2020 (the "**Agreement**"), is made and entered into as of January 30, 2023 (the "**Amendment Effective Date**"), by and among BeiGene, Ltd., an exempted company incorporated in the Cayman Islands (the "**Company**"), and Amgen Inc., a Delaware corporation (the "**Investor**"). Capitalized terms used but not defined herein shall have the meanings ascribed to them in the Agreement.

RECITALS

WHEREAS, pursuant to Section 5.12 of the Agreement, Amgen has certain rights to designate a director for appointment to the Company's board of directors;

WHEREAS, Amgen has elected to waive its right to designate a director for appointment to the Company's board of directors;

WHEREAS, pursuant to Section 8.9 of the Agreement, no provision in the Agreement may be supplemented, deleted or amended except in a writing executed by an authorized representative of each of the Investor and the Company; and

WHEREAS, the Parties desire to enter into this Amendment, upon the terms and conditions set forth herein.

NOW, THEREFORE, in consideration of the foregoing and other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the parties hereby agree as follows:

1. **Definition of "Standstill Period"**. The definition of "Standstill Period" in the Agreement is hereby amended and restated in its entirety as follows:

> ""**Standstill Period**" shall mean the period from and after the Signing Date until the date as of which the Investor holds less than five percent (5%) of the then outstanding share capital of the Company."

2. **Section 2.3**. Section 2.3 of the Agreement is hereby amended by deleting subsection (a)(viii) and subsection (b)(iii) each in their entirety and renumbering subsection (a)(ix) to (a)(viii).

3. **Section 5.1(iv)**. Section 5.1(iv) of the Agreement is hereby amended and restated in its entirety as follows:

> "(iv) Seek to have called any meeting of the shareholders of the Company, propose or nominate for election to the Company's board of directors any person whose nomination has not been approved by a majority of the Company's board of directors or cause to be voted in favor of such person for election to the Company's board of directors any Ordinary Shares or American Depositary Shares of the then outstanding share capital of the Company or Ordinary Share Equivalents (including any Derivatives) other than as contemplated by Section 5.3 hereof;"

4. **Section 5.2**. Section 5.2 of the Agreement is hereby amended and restated in its entirety by deleting the second sentence.

5. **Section 5.3**. The first paragraph of Section 5.3 of the Agreement is hereby amended and restated in its entirety as follows:

> "**5.3 Voting of Securities**. From and after the Closing Date until the later of (i) the fifth (5th) anniversary of the Closing Date and (ii) the expiration of the Standstill Period, in any vote or action by written consent of the shareholders of the Company, except as provided by Section 5.4, the Investor shall, and shall cause its Affiliates to, vote or execute a written consent with respect to all voting securities of the Company as to which it is entitled to vote or execute a written consent (A) in accordance with the recommendation of a majority of the Company's board of directors, solely with respect to (i) the election of directors, provided that such directors are unanimously recommended by the Company's board of directors; (ii) the approval of the Company's auditor; (iii) the approval of, on a non-binding, advisory basis, the compensation of the Company's named executive officers; (iv) the approval of an increase to the number of shares reserved for issuance or the issuance of shares under the Plans; (v) within the parameters of Rule 13.36 of the HK Listing Rules, the approval of the granting of a share issue mandate to the Company's board of directors to issue, allot or deal with unissued Ordinary Shares and/or American Depositary Shares up to the next annual general meeting of shareholders of the Company, subject to the conditions described in the Company's definitive proxy statement; and (vi) subject to the Company's compliance with Section 5.16, the authorization of the Company and its underwriters, in their sole discretion, to allocate to each of Baker Bros. Advisors LP and Hillhouse Capital Management, Ltd. and parties affiliated with each of them (the "**Existing Shareholders**"), up to a maximum amount of shares in order to maintain the same shareholding percentage of each of the Existing Shareholders (based on the then-outstanding share capital of the Company) before and after the allocation of the corresponding securities issued pursuant to an offering for a period of five years, which period will be subject to an extension on a rolling basis each year, conditional on the approval of the shareholders who are not Existing Shareholders, subject to the conditions described in the Company's definitive proxy statement, provided that, to the extent permissible by the HK Listing Rules and subject to the Company's ability to obtain any necessary waiver thereunder to seek shareholder approval therefor, any such authorization or a similar authorization provides for an allocation to the Investor in the same manner as the Existing Shareholders, and (B) in accordance with and proportional to the votes cast by shareholders entitled to vote other than the Investor, in any matter that arises as a result of a conflict due to the Collaboration Agreement.

6. **Section 5.5**. Section 5.5 of the Agreement is hereby amended and restated in its entirety as follows:

> "**5.5 Sale Limitations**. Subject to the restrictions set forth in Section 5.2, from and after the Closing Date until the later of (i) the expiration of the Lock-Up Period and (ii) the expiration of the Standstill Period, the Investor agrees that it shall not, and shall cause its Affiliates not to, Dispose of any Ordinary Shares, American Depositary Shares or Ordinary Share Equivalents except (a) pursuant to a registered underwritten public offering in accordance with Section 5.11, (b) pursuant to Rule 144 under the Securities Act in accordance with the volume restrictions applicable thereto, (c) in a private sale exempt from the registration requirements of the Securities Act, or (d) in any transaction approved by the Company; provided, however, that in no event shall the Dispositions in clauses (a), (b) or (c), in any rolling twelve (12)-calendar month period, exceed five percent (5%) of the then outstanding share capital of the Company; and provided further, however, that in no event shall the Investor or any of its Affiliates Dispose of any

Ordinary Shares, American Depositary Shares or Ordinary Share Equivalents to any Person that the Investor or its Affiliate knows (after a reasonable inquiry in a non-public offering) is a Competitor or is an Activist Investor."

7. **Section 5.6**. The last sentence of Section 5.6 of the Agreement is hereby amended and restated in its entirety as follows:

"The foregoing provisions of this Section 5.6 shall not apply (a) if the Investor and its Affiliates collectively own less than five percent (5%) of Ordinary Shares or American Depositary Shares of the outstanding share capital of the Company or Ordinary Share Equivalents, (b) to the sale of any shares to an underwriter pursuant to an underwriting agreement, and shall be applicable to the Investor only if all officers and directors are subject to the same restrictions or (c) if any beneficial owner of at least five percent (5%) of Ordinary Shares or American Depositary Shares of the then outstanding share capital of the Company or Ordinary Share Equivalents (excluding Baker Bros. Advisors LP) is not subject to a Lock-Up Agreement upon the same terms and conditions as the Investor.

8. **Section 5.12**. Section 5.12 of the Agreement is hereby amended and restated in its entirety as follows:

"**5.12 [Reserved].**"

9. **Section 5.19**. Section 5.19 of the Agreement is hereby amended by deleting the last sentence.

10. General

A. Except as expressly modified by this Amendment, the terms and provisions of the Agreement shall remain unchanged and in full force and effect in accordance with its terms.

B. Each of the parties hereto shall bear its respective costs, including legal fees, and expenses incurred in connection with the preparation of this Amendment and the activities incurred in connection therewith.

C. This Amendment may be executed in one or more counterparts, each of which shall be deemed to be an original but all of which shall constitute one and the same agreement.

D. This Amendment shall be governed by and construed in accordance with the Laws of the State of New York, without regard to the conflict of laws principles thereof that would require the application of the Law of any other jurisdiction.

E. The Agreement and this Amendment constitute the full and entire understanding and agreement between the Company and the Investor with regard to the subject matter hereof and neither the Company nor the Investor shall be liable or bound to any other in any manner by any representations, warranties, covenants and agreements except as specifically set forth herein and therein.

F. This Amendment shall become effective immediately upon execution by the Company and the Investor.

[REMAINDER OF PAGE INTENTIONALLY LEFT BLANK]

IN WITNESS WHEREOF, the parties have executed this Amendment as of the date first written above.

THE COMPANY:

BEIGENE, LTD.

By: /s/ CHAN LEE
Name: Chan Lee
Title: Senior Vice President, General Counsel

IN WITNESS WHEREOF, the parties have executed this Amendment as of the date first written above.

INVESTOR:

AMGEN INC.

By: /s/ PETER GRIFFITH
Name: Peter H. Griffith
Title: Executive Vice President & Chief Financial Officer

Exhibit 21.1

Subsidiaries

Name of Subsidiary	Jurisdiction of Incorporation or Organization	Percentage of Ownership by the Registrant
B10 Health Technologies Private Limited	India	100 %
BeiGene 101	Cayman Islands	100 %
BeiGene AUS Pty Ltd	Australia	100 %
BeiGene Austria GmbH	Austria	100 %
BeiGene (Beijing) Co., Ltd.	People's Republic of China	100 %
BeiGene Biologics Co., Ltd.	People's Republic of China	100 %
BeiGene Brasil Ltda.	Brazil	100 %
BeiGene (Canada) ULC	Canada	100 %
BeiGene Colombia S.A.S.	Colombia	100 %
BeiGene ESP, S.L.	Spain	100 %
BeiGene France Sarl	France	100 %
BeiGene Germany GmbH	Germany	100 %
BeiGene Guangzhou Biologics Manufacturing Co., Ltd.	People's Republic of China	100 %
BeiGene (Guangzhou) Innovation Technology Co., Ltd.	People's Republic of China	100 %
BeiGene (Hong Kong) Co., Limited	Hong Kong	100 %
BeiGene Hopewell Urban Renewal, LLC	New Jersey, United States	100 %
BeiGene International GmbH	Switzerland	100 %
BeiGene Ireland Limited	Republic of Ireland	100 %
BeiGene (Italy) S.r.l.	Italy	100 %
BeiGene Japan GK	Japan	100 %
BeiGene Korea Y.H.	South Korea	100 %
BeiGene Netherlands B.V.	Netherlands	100 %
BeiGene NZ Unlimited	New Zealand	100 %
BeiGene Pharmaceuticals GmbH	Switzerland	100 %
BeiGene Pharmaceuticals (Guangzhou) Co., Ltd.	People's Republic of China	100 %
BeiGene Pharmaceuticals Israel Ltd.	Israel	100 %
BeiGene Pharmaceutical (Shanghai) Co., Ltd.	People's Republic of China	100 %
BeiGene Poland sp. z o.o.	Poland	100 %
BeiGene Shanghai	Cayman Islands	100 %
BeiGene Shanghai 101	Cayman Islands	100 %
BeiGene (Shanghai) Co., Ltd.	People's Republic of China	100 %
BeiGene (Shanghai) Management Consulting Co., Ltd.	People's Republic of China	100 %
BeiGene (Shanghai) Research & Development Co., Ltd.	People's Republic of China	100 %
BeiGene Singapore Pte. Ltd.	Singapore	100 %
BeiGene South Africa Pty Ltd.	South Africa	100 %
BeiGene (Suzhou) Co., Ltd.	People's Republic of China	100 %
BeiGene Sweden AB	Sweden	100 %
BeiGene Switzerland GmbH	Switzerland	100 %
BeiGene (Taiwan) Limited	Taiwan	100 %
BeiGene (Thailand) Ltd.	Thailand	100 %
BeiGene Turkey Medical Products Trade Limited Company	Turkey	100 %
BeiGene UK, Ltd.	United Kingdom	100 %
BeiGene United Kingdom, Ltd.	United Kingdom	100 %
BeiGene USA, Inc.	Delaware, United States	100 %

Exhibit 21.1

BeiGene US Holdings, LLC	Delaware, United States	100 %
BeiGene US Manufacturing Co., Inc.	Delaware, United States	100 %
Beijing Innerway Bio-tech Co., Ltd.	People's Republic of China	100 %
Newco 101	Cayman Islands	100 %
Pi Health Brasil Consultoria Ltda.	Brazil	100 %
Pi Health Hong Kong Limited	Hong Kong	100 %
Pi Health, Ltd.	Cayman Islands	100 %
Pi Health USA, LLC	Delaware, United States	100 %
SuGene Pharmaceuticals (Suzhou) Co., Ltd.	People's Republic of China	100 %

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

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

1. Registration Statement (Form S-8 No. 333-209410) pertaining to the 2011 Option Plan, 2016 Share Option and Incentive Plan, and Non-Plan Share Options of BeiGene, Ltd.,
2. Registration Statement (Form S-8 No. 333-214064) pertaining to the 2011 Option Plan of BeiGene, Ltd.,
3. Registration Statement (Form S-8 No. 333-216885) pertaining to the 2016 Share Option and Incentive Plan of BeiGene, Ltd.,
4. Registration Statement (Form S-8 No. 333-223319) pertaining to the 2016 Share Option and Incentive Plan, as amended, of BeiGene, Ltd.,
5. Registration Statement (Form S-8 No. 333-225543) pertaining to the 2018 Employee Share Purchase Plan and the 2018 Inducement Equity Plan of BeiGene, Ltd.,
6. Registration Statement (Form S-8 No. 333-228786) pertaining to the Second Amended and Restated 2016 Share Option and Incentive Plan and the Second Amended and Restated 2018 Employee Share Purchase Plan of BeiGene, Ltd.,
7. Registration Statement (Form S-3 No. 333-238181) of BeiGene, Ltd. and the related prospectus,
8. Registration Statement (Form S-3 No. 333-238182) of BeiGene, Ltd. and the related prospectus,
9. Registration Statement (Form S-8 No. 333-241697) pertaining to the Second Amended and Restated 2016 Share Option and Incentive Plan, as amended, of BeiGene, Ltd., and
10. Registration Statement (Form S-8 No. 333-266639) pertaining to the Second Amended and Restated 2016 Share Option and Incentive Plan, as amended, of BeiGene, Ltd.;

of our reports dated February 27, 2023, with respect to the consolidated financial statements of BeiGene, Ltd. and the effectiveness of internal control over financial reporting of BeiGene, Ltd. included in this Annual Report (Form 10-K) of BeiGene, Ltd. for the year ended December 31, 2022.

/s/ Ernst & Young LLP
Boston, Massachusetts
February 27, 2023

Exhibit 23.2

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

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

1. Registration Statement (Form S-8 No. 333-209410) pertaining to the 2011 Option Plan, 2016 Share Option and Incentive Plan, and Non-Plan Share Options of BeiGene, Ltd.,
2. Registration Statement (Form S-8 No. 333-214064) pertaining to the 2011 Option Plan of BeiGene, Ltd.,
3. Registration Statement (Form S-8 No. 333-216885) pertaining to the 2016 Share Option and Incentive Plan of BeiGene, Ltd.,
4. Registration Statement (Form S-8 No. 333-223319) pertaining to the 2016 Share Option and Incentive Plan, as amended, of BeiGene, Ltd.,
5. Registration Statement (Form S-8 No. 333-225543) pertaining to the 2018 Employee Share Purchase Plan and the 2018 Inducement Equity Plan of BeiGene, Ltd.,
6. Registration Statement (Form S-8 No. 333-228786) pertaining to the Second Amended and Restated 2016 Share Option and Incentive Plan and the Second Amended and Restated 2018 Employee Share Purchase Plan of BeiGene, Ltd.,
7. Registration Statement (Form S-8 No. 333-241697) pertaining to the Second Amended and Restated 2016 Share Option and Incentive Plan, as amended, of BeiGene, Ltd.,
8. Registration Statement (Form S-8 No. 333-266639) pertaining to the Second Amended and Restated 2016 Share Option and Incentive Plan, as amended, of BeiGene, Ltd.;
9. Registration Statement (Form S-3 No. 333-238181) of BeiGene, Ltd. and the related prospectus, and
10. Registration Statement (Form S-3 No. 333-238182) of BeiGene, Ltd. and the related prospectus;

of our report dated February 28, 2022 (except for the effects on the consolidated financial statements of the correction of an error as described in Notes 2 and 3, as to which the date is February 27, 2023), with respect to the consolidated financial statements of BeiGene, Ltd. as of December 31, 2021 and for the years ended December 31, 2021 and 2020, included in this Annual Report (Form 10-K) for the year ended December 31, 2022.

/s/ Ernst & Young Hua Ming LLP
Beijing, People's Republic of China
February 27, 2023

Exhibit 31.1

CERTIFICATIONS UNDER SECTION 302

I, John V. Oyler, certify that:

1. I have reviewed this annual report on Form 10-K of BeiGene, Ltd.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
    (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
    (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
    (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
    (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
    (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
    (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 27, 2023

/s/ JOHN V. OYLER

John V. Oyler
Chief Executive Officer and Chairman
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATIONS UNDER SECTION 302

I, Julia Wang, certify that:

1. I have reviewed this annual report on Form 10-K of BeiGene, Ltd.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
    (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
    (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
    (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
    (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
    (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
    (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 27, 2023

/s/ JULIA WANG

Julia Wang

Chief Financial Officer

(Principal Financial and Accounting Officer)

Exhibit 32.1

CERTIFICATIONS UNDER SECTION 906

Pursuant to section 906 of the Sarbanes-Oxley Act of 2002 (subsections (a) and (b) of section 1350, chapter 63 of title 18, United States Code), each of the undersigned officers of BeiGene, Ltd., an exempted company incorporated in the Cayman Islands with limited liability (the "Company"), does hereby certify, to such officer's knowledge, that:

The Annual Report on Form 10-K for the year ended December 31, 2022 (the "Form 10-K") of the Company fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, and the information contained in the Form 10-K fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: February 27, 2023

/s/ JOHN V. OYLER

John V. Oyler
Chief Executive Officer and Chairman
(Principal Executive Officer)

Dated: February 27, 2023

/s/ JULIA WANG

Julia Wang
Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 99.1

DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS

In March 2022, the U.S. Securities and Exchange Commission ("SEC") added BeiGene, Ltd. (the "Company") to its conclusive list of issuers identified under the Holdings Foreign Companies Accountable Act ("HFCAA") following the filing of our annual report on Form 10-K with the SEC, which annual report was audited by Ernst & Young Hua Ming LLP, a registered public accounting firm in mainland China that the Public Company Accounting Oversight Board ("PCAOB") previously was unable to inspect or investigate completely, because of a position taken by an authority in the foreign jurisdiction. On March 23, 2022, Ernst & Young Hua Ming LLP resigned as our independent registered public accounting firm for the audit of our financial statements and internal control over financial reporting to be filed with the SEC and since that time, the Company has engaged Ernst & Young LLP, located in Boston, Massachusetts, United States, as the Company's independent registered public accounting firm for the audit of our financial statements and internal control over financial reporting for the fiscal year ending December 31, 2022.

The Company has determined that no governmental entity in mainland China or Hong Kong, directly or indirectly, possesses the power to direct or cause the direction of the management and policies of the Company or has a controlling financial interest. The Company has made this determination based on the fact that as of the date of this Annual Report on Form 10-K, no such governmental entity has filed a Schedule 13D or 13G, there are no material contracts with such a foreign governmental party, and there is no such foreign government representative on the Company's Board.