BeiGene, Ltd. Form S-1/A November 17, 2016

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As filed with the United States Securities and Exchange Commission on November 17, 2016

Registration No. 333-214540

# SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

Amendment No. 1 to

# FORM S-1

REGISTRATION STATEMENT UNDER THE SECURITIES ACT OF 1933

# **BEIGENE, LTD.**

(Exact Name of Registrant as Specified in Its Charter)

**Cayman Islands** 

(State or Other Jurisdiction of Incorporation or Organization)

2834 (Primary Standard Industrial Classification Code Number) c/o Mourant Ozannes Corporate Services (Cayman) Limited 94 Solaris Avenue, Camana Bay Grand Cayman KY1-1108 Cayman Islands +1 (345) 949 4123 **98-1209416** (I.R.S. Employer Identification Number)

(Address, Including Zip Code, and Telephone Number, Including Area Code, of Registrant's Principal Executive Offices)

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### Approximate date of commencement of proposed sale to the public: As soon as practicable after the effective date of this registration statement.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, as amended, check the following box. o

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o

If this form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o

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

Large Accelerated Filer o

Accelerated Filer o

Non-Accelerated Filer ý

Smaller Reporting Company o

(Do not check if a smaller reporting company)

CALCULATION OF REGISTRATION FEE

| Title of Each Class of Securities<br>to be Registered <sup>(1)</sup> | Proposed Maximum<br>Aggregate Offering<br>Price <sup>(2)(3)</sup> | Amount of<br>Registration Fee <sup>(4)</sup> |
|--|---|--|
| Ordinary Shares, par value \$0.0001 per share                        | \$201,250,000   | \$23,325                                     |

(1)

American depositary shares, or ADSs, evidenced by American depositary receipts issuable upon deposit of the ordinary shares registered hereby have been registered under a separate registration statement on Form F-6 (File No. 333-209044). Each ADS represents 13 ordinary shares.

(2)

Includes (i) ordinary shares represented by ADSs that may be purchased by the underwriters pursuant to their option to purchase additional ADSs and (ii) all ordinary shares represented by ADSs initially offered or sold outside the United States that are thereafter resold from time to time in the United States.

(3)

Estimated solely for the purpose of computing the amount of the registration fee pursuant to Rule 457(o) under the Securities Act of 1933, as amended.

(4)

A registration fee of \$17,385 was previously paid in connection with the Registration Statement. An additional \$5,940 is paid herewith.

The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until this registration statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

The information in this preliminary prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell nor does it seek an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

# Subject to Completion. Dated November 17, 2016.

# \$175,000,000 of American Depositary Shares

Representing

**Ordinary Shares** 

# BeiGene, Ltd.

We are offering \$160 million (approximately 4,336,043) American Depositary Shares, or ADSs, in this offering, assuming a public offering price of \$36.90 per ADS. The selling shareholders identified in this prospectus are offering \$15 million (approximately 406,503) ADSs. Each ADS represents 13 ordinary shares, par value \$0.0001 per share. We will not receive any proceeds from the sale of ADSs by the selling shareholders.

The ADSs are listed on the NASDAQ under the symbol "BGNE." The last reported sale price of the ADSs on the NASDAQ on November 16, 2016 was \$36.90 per ADS.

We are an "emerging growth company" as that term is used in the U.S. Jumpstart Our Business Startups Act of 2012 and, as such, have elected to comply with certain reduced public company reporting requirements for this prospectus and future filings.

Investing in the ADSs involves a high degree of risk. See "Risk Factors" on page 22 to read about factors you should consider before buying the ADSs.

Neither the Securities and Exchange Commission nor any other state securities commission has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus. Any representation to the contrary is a criminal offense.

|  | Per ADS | Total |
|--|---------|-------|
| Public offering price                                  | \$      | \$    |
| Underwriting discounts <sup>(1)</sup>                  | \$      | \$    |
| Proceeds, before expenses, to us                       | \$      | \$    |
| Proceeds, before expenses, to the selling shareholders | \$      | \$    |

<sup>(1)</sup> 

We refer you to "Underwriting" beginning on page 151 for additional information regarding total underwriting compensation.

To the extent the underwriters sell more than \$175,000,000 of ADSs (approximately 4,742,546 ADSs), the underwriters have the option to purchase up to an additional \$26,250,000 of ADSs (approximately 711,381 ADSs) from us at the public offering price less the underwriting discounts.

Our existing affiliates, including investors affiliated with Baker Bros. Advisors and Hillhouse Capital Management, Ltd., have indicated an interest in purchasing up to an aggregate of \$59.1 million in ADSs in this offering. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, less or no shares in this offering to any of these investors,

or any of these investors may determine to purchase more, less or no shares in this offering, including as a result of the pricing terms. See "Prospectus Summary The Offering."

The underwriters expect to deliver the ADSs against payment in New York, New York on

, 2016.

| Morgan  | Goldman,    | Cowen and |
|---------|-------------|-----------|
| Stanley | Sachs & Co. | Company   |

, 2016

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We have not, and the underwriters have not, authorized any person to provide you with information different from that contained in this prospectus or any related free-writing prospectus that we authorize to be distributed to you. This prospectus is not an offer to sell, nor is it seeking an offer to buy, these securities in any jurisdiction where the offer or sale is not permitted. The information in this prospectus speaks only as of the date of this prospectus unless the information specifically indicates that another date applies, regardless of the time of delivery of this prospectus or of any sale of the securities offered hereby.

For investors outside of the United States: Neither we, the selling shareholders, nor any of the underwriters have done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than the United States. Persons outside of the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the ADSs and the distribution of this prospectus outside of the United States.

This prospectus 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.

All references in this prospectus to "\$," "US\$," "U.S.\$," "U.S. dollars," "dollars" and "USD" mean U.S. dollars and all references to "¥" and "RMB," mean Renminbi, unless otherwise noted. All references to "PRC" or "China" in this prospectus refer to the People's Republic of China. Please see the Glossary of Scientific Terms on page 159 for definitions of scientific terms.

#### PROSPECTUS SUMMARY

This summary highlights information contained elsewhere in this prospectus and does not contain all of the information that you should consider in making your investment decision. Before investing in the ADSs, you should carefully read the entire prospectus, including the information in our filings with the U.S. Securities and Exchange Commission, or SEC, incorporated by reference in this prospectus. You should also consider, among other things, the matters described under "Risk Factors" beginning on page 22 of this prospectus and those identified in our most recent Quarterly Report on Form 10-Q for the quarter ended September 30, 2016, or our September 2016 Quarterly Report, and the matters discussed under "Management's Discussion and Analysis of Financial Condition and Results of Operations" in our Annual Report on Form 10-K for the year ended December 31, 2015, or our 2015 Annual Report, and our September 2016 Quarterly Report, each of which is incorporated by reference herein. Unless otherwise stated, all references to "us," "our," "BeiGene," "we," the "company" and similar designations refer to BeiGene, Ltd. and its consolidated subsidiaries, as a whole.

#### Overview

We are a globally focused biopharmaceutical company dedicated to becoming a leader in the discovery and development of innovative, molecularly targeted and immuno-oncology drugs for the treatment of cancer. We believe the next generation of cancer treatment will utilize therapeutics both as monotherapies and in combination to attack multiple underlying mechanisms of cancer cell growth and survival. We further believe that discovery of next-generation cancer therapies requires new research tools. To that end, we have developed a proprietary cancer biology platform that addresses the importance of tumor-immune system interactions and the value of primary biopsies in developing new models to support our drug discovery effort.

Our strategy is to advance a pipeline of drug candidates with the potential to be best-in-class monotherapies and also important components of multiple-agent combination regimens. Over the last six years, using our cancer biology platform, we have developed clinical-stage drug candidates that inhibit the important oncology targets Bruton's tyrosine kinase, or BTK, RAF dimer protein complex and PARP family of proteins, and an immuno-oncology agent that inhibits the immune checkpoint protein receptor PD-1. Our drug candidates targeting BTK, PD-1, PARP and RAF dimer have demonstrated early activity and favorable safety profiles in the dose-escalation phases of clinical trials conducted in Australia and New Zealand, and all four of our drug candidates are currently in the dose-expansion phases of their respective clinical trials. As of November 7, 2016, our four clinical-stage drug candidates, as monotherapies and in combination, have been dosed in a total of 803 patients and healthy subjects. We have Investigational New Drug Applications in effect for our BTK, PD-1 and PARP inhibitors with the U.S. Food and Drug Administration, or FDA. We have also received approval of our Clinical Trial Applications, or CTAs, for each of our clinical-stage drug candidates is the first in their respective classes being developed in China under the Category 1.1 domestic regulatory pathway to enter the clinic and to present clinical data.

Our research operations are in China, which we believe confers several advantages including access to a deep scientific talent pool and proximity to extensive preclinical study and clinical trial resources through collaborations with leading cancer hospitals in China. Beyond the substantial market opportunities we expect to have in the United States, Europe and Japan, we believe our location in China provides us the opportunity to bring best-in-class monotherapies and combination therapeutics to our home market where many global standard-of-care therapies are not currently approved or available. We have assembled a team of 318 employees and consultants in China, the United States, Australia, and Taiwan with deep scientific talent and extensive global pharmaceutical experience who are deeply committed to advancing our mission to become a leader in next-generation cancer therapies.

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We believe that oncology treatment has entered an era of revolutionary change in which cancer drugs will be used both as monotherapy and in combination to attack multiple underlying mechanisms of cancer cell growth and survival. Due to breakthroughs in gene sequencing and methods of tumor characterization, cancer is rapidly being redefined from a paradigm of classification based on tissue of origin to one of specific molecular characteristics. As a result, many more specific disease subpopulations can be targeted with more effective treatment than has been possible in the past. This ability to better classify cancers has allowed the development of molecularly targeted drugs that address specific cancer subpopulations and provide high response rates in tumors with particular mutations. In addition, the development of immuno-oncology agents such as antibodies targeting the CTLA-4 and PD-1 protein receptors and the PD-L1 protein has demonstrated the importance of the human immune system in cancer therapy and the potential for high rates of more durable responses from agents that activate the immune system to identify and eliminate tumors. We believe that the future of cancer therapy will involve combinations of molecularly targeted and immuno-oncology drugs tailored to particular tumor sub-groups and have directed our research efforts at both types of drugs.

Our belief that this fundamental shift was about to occur in cancer research led us early in our history to develop a cancer biology platform that addresses the importance of tumor-immune system interactions and the value of primary tumor biopsies in developing new models. Our proximity to leading cancer treatment centers in Beijing and our close relationships with clinicians who treat patients and perform biopsies and surgeries at those centers have allowed us to develop an extensive collection of *in vivo*, *ex vivo* and *in vitro* cancer models. Given our belief that the human immune system can play an important role in combating cancer and that future treatments will involve combination therapies, we have introduced elements of a functional immune system into these models. Our proprietary models allow our research team to better select targets and to screen and evaluate therapeutic agents that we believe have significant potential alone or in combination for treating a variety of cancers. Our models are a key component in the screening cascade we follow in our drug discovery effort and permit us to evaluate potential drug candidates in conditions that much better approximate a patient's cancer at the time of treatment. This is particularly significant when drug discovery requires evaluation not only of monotherapies but also multiple combinations and regimens targeting specific mutations while simultaneously immobilizing the defenses cancer cells mount against the human immune system.

#### **Our Clinical Stage Drug Candidates**

We have used our cancer biology platform to develop four clinical-stage drug candidates that we believe have the potential to be best-in-class or first-in-class. In addition, we believe that each has the potential to be an important component of a drug combination addressing major unmet medical needs.

The following table summarizes our monotherapy clinical pipeline:

Limited collaboration with Merck KGaA

1

2

Partnered with Merck KGaA outside China

The following table summarizes our combination therapy pipeline:

**BGB-3111** is a potent and highly selective small molecule BTK inhibitor. We are currently developing BGB-3111 as a monotherapy and in combination with other therapies for the treatment of a variety of lymphomas. BGB-3111 has demonstrated higher selectivity against BTK than ibrutinib, the only BTK inhibitor currently approved by the FDA and the European Medicines Agency, or EMA, based on biochemical assays and higher exposure than ibrutinib based on their respective Phase I experience.

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In addition, we believe BGB-3111 is the only BTK inhibitor that has demonstrated sustained target inhibition in disease originating tissues. Our preclinical data of ibrutinib show that target inhibition at disease originating tissues, such as bone marrow and spleen, in mice and rats was not sustained over a 24-hour period. Published clinical data on ibrutinib show that ibrutinib's target inhibition in the blood is borderline at the approved dose of 420 mg once a day, with BTK occupancy in a significant portion of patients below 80%.

We have completed the 25-patient dose-escalation phase of our clinical trial, and we are currently conducting the dose-expansion phase in patients with different subtypes of B-cell malignancies, including chronic lymphocytic leukemia, diffuse large B-cell lymphoma, follicular lymphoma, mantle cell lymphoma, marginal zone lymphoma, Waldenström's Macroglobulinemia and hairy cell leukemia in Australia, New Zealand, the United States and South Korea. We have dosed 291 patients and healthy subjects as of November 7, 2016 in monotherapy and in combination trials.

As of June 10, 2016, the cutoff date for the most recent data analysis of the Phase I trial, the preliminary data suggest that BGB-3111 is well-tolerated. Proof-of-concept has been established for BGB-3111 with clinical data indicating that BGB-3111 is a potent BTK inhibitor with objective anti-tumor activity observed in multiple types of lymphomas starting at the lowest dose tested, 40 mg once daily, or QD.

The chart below shows the pharmacokinetic profile of BGB-3111 from this Phase I trial, in comparison to historical data with ibrutinib and acalabrutinib.

BGB-3111: Drug Exposure in Humans, Half-life, and In Vitro Potency Comparison to Historical Data on Ibrutinib and Acalabrutinib^

Note: Cmax = maximum plasma concentration; AUC = area under the concentration-time curve as a standard measurement of drug exposure; Free drug exposure = unbound AUC as a measurement of unbound drug exposure.

^ Cross-trial comparisons

<sup>1</sup> Tam *el al.*, ASH, 2015; <sup>2</sup> Byrd *el al.*, NEJM, 2015; <sup>3</sup> Lannutti *el al.*, AACR, 2015; <sup>4</sup> BeiGene data on file

In addition, sustained BTK occupancy was achieved both in the blood (peripheral blood mononuclear cells, or PBMC) starting at the lowest dose of 40 mg QD, and in the lymph node, with 160 mg twice daily, or BID, in particular, as shown below.

BGB-3111: Complete and Sustained BTK Inhibition in PBMC and Lymph Node

On October 7, 2016, we presented data from our Phase I trial for a total of 24 Waldenström's Macroglobulinemia patients at the 9th International Workshop on Waldenström's Macroglobulinemia and Symposium on Advances in Multiple Myeloma. 41 patients with Waldenström's Macroglobulinemia were enrolled in the Phase I trial as of September 9, 2016, of which 24 patients were evaluable for response at the cutoff date of June 10, 2016. These 24 patients were from the dose-escalation phase receiving doses ranging from 40 mg to 320 mg QD or 160 mg BID, and the ongoing dose-expansion phase receiving 160 mg BID or 320 mg QD. Responses were determined according to the modified Sixth International Workshop on Waldenström's Macroglobulinemia, or IWWM, criteria.

Adverse events were generally mild in severity and self-limited, as shown in the table below.

BGB-3111 Phase I Trial in WM: Adverse Events Independent of Causality

In the most recent data analysis, which had a cutoff date of June 10, 2016, the most frequent adverse events ( $\geq$ 20%) of any attribution were upper respiratory infection (25%); diarrhea (25%); petechiae, contusion, and bruising (21%); and nausea (21%), all grade 1 or 2 in severity. One patient developed grade 2 atrial fibrillation. Grade 3 or higher adverse events included two cases of anemia and one each of foot fracture, renal artery thrombosis, bronchiectasis, thrombocytopenia, hypertension, cryptococcal meningitis, and neutropenia. There were two serious adverse events assessed as possibly related to BGB-3111 by investigators, grade 2 atrial fibrillation and grade 3 cryptococcal meningitis; in both cases, BGB-3111 was temporarily held but safely resumed. No serious hemorrhage ( $\geq$ grade 3 or CNS hemorrhage of any grade) was reported.

After a median follow-up of eight months (range: 3.3 21 months), 24 patients were evaluable for response and the rate of overall response including complete response, or CR, very good partial response, or VGPR, partial response, or PR, and minor response, or MR, was 92% (22 out of 24 patients). The major response rate (CR plus VGPR plus PR) was 83% (20 out of 24 patients), with VGPRs ( $\geq$ 90% reduction in IgM and reduction in extramedullary disease) observed in 33% (eight out of 24 patients) and PRs ( $\geq$ 50 90% reduction in IgM and reduction in extramedullary disease) observed in 50% (12 out of 24 patients) of patients.

BGB-3111 Phase I Trial in WM: Efficacy Summary

IgM decreased from a median of 29.9g/l at baseline to 3.0g/l, and hemoglobin increased from a median of 10.1g/dl at baseline to 13.5g/dl. Only one patient discontinued BGB-3111, due to exacerbation of pre-existing bronchiectasis while in VGPR. There have been no cases of disease progression. The remainder of patients remain on study treatment.

Comparison of Response Rates of BGB-3111 to Historical Data on Ibrutinib with Comparable Follow-Up Time^

BGB-3111 Phase I Trial in WM: Post-Treatment IgM (vs. Baseline)

Though MYD88 and CXCR4 sequencing was not included in the original protocol, samples were requested with additional consents, and MYD88 mutational analysis results were available for 15 of the patients who were evaluable for response at the data cutoff of June 10, 2016. Preliminary sequencing data suggest a high VGPR rate seen in six out of 12 evaluable patients with the MYD88<sup>L265P</sup> genotype that included five additional patients with PR and one patient with stable disease, or SD, as well as response in MYD88<sup>WT</sup> patients with one PR, one MR, and one SD observed among three evaluable patients.

BGB-3111 Phase I Trial in WM: Response Rate by MYD88 Mutation Status Preliminary Results

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An updated analysis is currently being conducted for presentation at the American Society of Hematology meeting in December 2016 based on a data cutoff date of October 3, 2016 and includes an additional eight patients (all with less than six months follow-up, median 3.8 months). Based on a provisional analysis, which is subject to ongoing data validation, the major response rate is 78% (25 out of 32 patients), with 34% (11 out of 32 patients) of patients achieving VGPR. Compared to the data presented at the IWWM conference, no additional patients have discontinued study treatment for adverse event or progressive disease, and, based on serious adverse event reporting, no new safety signals have been identified.

Based on these findings, we plan to initiate a Phase III study in the United States, the European Union, and Australia in late 2016 or early 2017 comparing BGB-3111 and ibrutinib in patients with Waldenström's Macroglobulinemia.

In addition to data in Waldenström's Macroglobulinemia patients, updated data on BGB-3111 in patients with chronic lymphocytic leukemia from the dose-escalation and dose-expansion phases of the Phase I trial has been accepted for presentation at the American Society for Hematology annual conference. An abstract for this presentation was released on November 3, 2016. 29 patients were included in the most recent data analysis with cutoff date of June 10, 2016, from the dose-escalation and dose-expansion phases of the Phase I trial of BGB-3111 as monotherapy.

BGB-3111 was well-tolerated in 69% of patients with no drug-related adverse events >grade 1 in severity within the first 12 weeks of therapy. The most frequent adverse events of any attribution were petechiae and bruising (38%), upper respiratory tract infection (31%, all grade 1 and 2), diarrhea (28%, all grade 1 and 2), fatigue (24%, all grade 1 and 2), and cough (21%, all grade 1 and 2). Three serious adverse events were assessed as possibly related to BGB-3111 by investigators, including one each of grade 2 cardiac failure and pleural effusion, and one grade 3 purpura, the only major bleeding event reported. One patient developed grade 2 atrial fibrillation. Three patients had temporary dose interruptions and one patient discontinued from the study due to adverse events.

After a median follow-up of 7.5 months (range: 2.9 17.3 months), 29 patients were evaluable and the response rate was 90% (26 out of 29 patients) with PR in 79% of patients (23 out of 29 patients) and partial response with lymphocytosis in 10% of patients (three out of 29 patients). SD were observed in 7% of patients (two out of 29 patients), and one patient had a non-evaluable response due to discontinuation of treatment prior to week 12, the time of first evaluation of tumor response. No instances of disease progression or Richter's transformation have occurred.

An updated analysis is currently being conducted for presentation at the American Society of Hematology meeting in December 2016 based on data cutoff date of October 3, 2016 and includes an additional 17 patients (all with less than six months follow-up). Based on a provisional analysis, which is subject to ongoing data validation, the objective response rate is 93% (43 out of 46 patients). Compared to the analysis for ASH abstract publication, no additional patients have discontinued study treatment for adverse event or progressive disease, and, based on serious adverse event reporting, no new safety signals have been identified.

We initiated a monotherapy Phase I clinical trial of BGB-3111 in China in July 2016, and we believe BGB-3111 is the first BTK inhibitor being developed in China under the Category 1.1 domestic regulatory pathway to enter the clinic and to present clinical data. In addition, we have seen favorable preclinical data for and initiated combination studies of BGB-3111 with obinutuzumab, a CD20 antibody, in January 2016. We have also initiated combination studies of BGB-A317, our PD-1 antibody, on June 30, 2016, based on encouraging synergistic effects observed in our preclinical models. In our primary diffuse large B-cell lymphoma tumor models, we observed enhancement of anti-tumor activity of BGB-A317, our PD-1 antibody, by BGB-3111 in both PD-L1-positive and especially in PD-L1-negative diffuse large B-cell lymphoma tumor models, thus supporting our combination strategy.



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**BGB-A317** is an investigational humanized monoclonal antibody against the immune checkpoint receptor PD-1. We are developing BGB-A317 as a monotherapy and as a combination agent for various solid-organ and blood-borne cancers. PD-1 is a cell surface receptor that plays an important role in down-regulating the immune system by preventing the activation of certain types of white blood cells called T-cells. PD-1 inhibitors remove the blockade of immune activation by cancer cells. We believe BGB-A317 is differentiated from the currently approved PD-1 antibodies with the ability to bind Fc gamma receptor I specifically engineered out, and we believe this could potentially result in improved activities. In addition, BGB-A317 has a unique binding signature to PD-1 with high affinity and superior target specificity.

We have dosed a total of 299 patients with BGB-A317 in either monotherapy or combination trials as of November 7, 2016. In April 2016, we completed the enrollment of the ongoing dose-escalation phase and, in May 2016, we initiated the dose-expansion phase of our clinical trial in relapsed or refractory solid tumor patients in Australia and New Zealand. As of September 30, 2016, the cutoff date for the most recent data analysis, the preliminary clinical data show that BGB-A317 is well-tolerated with adverse events in keeping with the class effect. Among 103 patients evaluable for safety at the time of the data cutoff for the current safety analysis, the most common treatment-related adverse events ( $\geq$ 5%) were fatigue (19%), diarrhea (13%), rash (11%), pruritus (11%), nausea (8%), hypothyroidism (7%), and infusion related reaction (6%). Treatment-related serious adverse events included four cases of colitis, two cases of hypotension, and one case each of diarrhea, diabetes mellitus, diabetic ketoacidosis, dyspnea, hypoxia, infusion-related reaction, and pneumonitis. Among these,  $\geq$  grade 3 treatment-related serious adverse events included the two cases of hypotension and one case each of colitis, diabetes mellitus, diabetic ketoacidosis, dyspnea, hypoxia, and pneumonitis. Other treatment-related grade  $\geq$  3 adverse events included two cases each of fatigue and hyperglycemia, and one case each of back pain, elevated alanine aminotransferase and elevated gamma-glutamyl transferase. Among 99 patients evaluable for efficacy as of September 30, 2016, anti-tumor activities were observed in 15 patients with a PR and 23 patients with a SD. The PRs include three PRs in nine renal cell carcinoma patients; three in six urothelial cancer patients; two in four gastric cancer patients; two in two Merkel cell carcinoma patients; one in four nasopharyngeal patients; one in one penis squamous cell carcinoma patient; one in one duodenal carcinoma patient; one in one evaluable patient of two patients with microsatellite instability high, or MSI-h, colorectal cancer, among 13 colorectal cancer patients; one in one pancreatic cancer patient with MSI-h status, among two pancreatic cancer patients. A mixed patient population of 27 different tumor types was included in this data analyses, in which patients with melanoma, non-small cell lung cancer or head and neck cancer were not enrolled, and patients with renal cell cancer and urothelial carcinoma together represented close to 15% of the enrolled patients.

To date, we have two internal combination trials ongoing BGB-A317 with BGB-290 in patients with advanced solid tumors and BGB-A317 with BGB-3111 in patients with various hematologic malignancies, respectively.

**BGB-290** is a molecularly targeted, orally available, potent and highly selective inhibitor of PARP1 and PARP2. We are currently developing BGB-290 as a monotherapy and in combination with other therapies for the treatment of homologous recombination deficient cancers, which are cancers that contain abnormalities in their DNA molecule repair mechanisms, making these cancers particularly sensitive to PARP inhibitors. We believe BGB-290 has the potential to be differentiated from other PARP inhibitors, including olaparib, the only PARP inhibitor currently approved by the FDA and the EMA, in terms of selectivity, DNA-trapping activity, oral bioavailability, and brain penetration. We have a limited collaboration with Merck KGaA on BGB-290.

We have dosed a total of 88 patients with BGB-290 in either monotherapy or combination trials as of November 7, 2016. We have completed the dose-escalation phase, and we are evaluating BGB-290 in the ongoing dose-expansion phase of our clinical trial in Australia.

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At the 2015 AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics, we presented clinical data from our Phase I clinical trial. 29 relapsed or refractory solid tumor patients were enrolled in seven cohorts receiving monotherapy BGB-290 in doses ranging from 2.5 mg BID to 80 mg BID, as of June 30, 2015. Initial analysis of data from this trial suggests that BGB-290 is well-tolerated. Few adverse events of myelosuppression, no liver toxicity signal, and few drug-related grade 3/4 adverse events were observed in the dose-escalation phase. The most common drug-related adverse events were grade 1 and 2 nausea (38%) and fatigue (28%). Drug-related grade 3/4 adverse events include one each (3%) of neutropenia, anaemia, hypophosphatemia and hypokalemia, all grade 3. As of January 19, 2016, drug-related serious adverse events reported by investigators were three cases of grade 3 anemia and one case of shortness of breath.

Proof-of-concept was established, with significant anti-tumor activity seen in ovarian cancer patients starting at the lowest tested dose and data suggestive of a wide therapeutic window. Among 14 evaluable patients with ovarian cancer as of June 30, 2015, seven had an objective response (six PRs and one CR). Of the ten ovarian cancer patients with germ-line breast cancer susceptibility gene, or BRCA, mutation, five had an objective response (four PRs and one CR), and of the three ovarian cancer patients with germ-line BRCA wild-type, two had an objective response (two PRs). The remaining one patient had unknown BRCA status and progressive disease, or PD. When assessed by underlying mutations, of six evaluable patients with the BRAF V600E, there was one CR, one PR and four SDs.

On February 2, 2016, we initiated a trial with BGB-290 in combination with BGB-A317 for the treatment of cancers with BRCA mutations or deficiencies in homologous recombination or mismatch repair, including ovarian, breast, prostate, colorectal and pancreatic cancers, as well as platinum-sensitive ovarian cancer.

**BGB-283** is a small molecule inhibitor of both the monomer and dimer forms of the RAF kinase. We are currently developing BGB-283 for the treatment of cancers with aberrations in the mitogen-activated protein kinase, or MAPK, pathway, including BRAF gene mutations and KRAS/NRAS gene mutations where first generation BRAF inhibitors are not effective. The MAPK pathway is a chain of proteins in the cell that communicates a signal from a receptor on the surface of the cell to the DNA in the nucleus of the cell. This pathway plays an essential role in regulating cell proliferation and survival and is described in more detail in the section of our 2015 Annual Report, incorporated by reference herein, titled "Item 1 Business Product Pipeline BGB-283, RAF Dimer Inhibitor Mechanism of Action." We intend to develop BGB-283 to treat various malignancies, including colorectal cancer, non-small cell lung carcinoma, endometrial cancer, ovarian cancer, pancreatic cancer and papillary thyroid carcinoma. Currently approved first-generation BRAF inhibitors, vemurafenib and dabrafenib, are only active against the BRAF monomer. BGB-283 inhibits not only the monomer but also the dimer forms of BRAF. We believe BGB-283 has the potential to be a first-in-class RAF dimer inhibitor globally.

We have completed the 37-patient dose-escalation phase of our Phase I clinical trial, and we have completed the enrollment in April 2016 of the dose-expansion phase of our clinical trial in Australia and New Zealand in a broad range of patient populations, including BRAF mutated melanoma, thyroid cancer, colorectal cancer, non-small cell lung cancer and other non-BRAF mutated tumors as well as KRAS/NRAS mutated endometrial cancer, colorectal cancer, non-small cell lung cancer and other KRAS/NRAS mutation bearing cancers, where first-generation BRAF inhibitors have not been effective. We have also initiated a dose-escalation trial in China. We have dosed 168 patients in Australia, New Zealand and China as of November 7, 2016.

Initial analysis of data from these trials suggests that BGB-283 is well-tolerated with a favorable safety profile. We presented initial clinical data from our Phase I clinical trial of BGB-283 in patients with BRAF or KRAS/NRAS-mutated cancers at the 2016 American Association for Cancer Research annual conference. As of January 31, 2016, the data cutoff date, among 31 advanced solid tumor patients, the most frequent treatment-related adverse events were fatigue (52%), thrombocytopenia (39%), decreased

appetite (39%), hand-foot syndrome (35%), dermatitis acneiform (32%) and hypertension (32%). The most frequent treatment-related grade 3-4 adverse events included thrombocytopenia (13%), fatigue (10%) and liver enzyme elevation (10%).

We have achieved proof-of-concept in a range of cancers including those with KRAS and BRAF mutations. At the time of the data cutoff, among 29 patients enrolled in the dose-escalation phase of the trial evaluable for efficacy, one melanoma patient with BRAF V600E mutation had a CR, one endometrial cancer patient with KRAS mutation and one thyroid cancer patient with BRAF V600E mutation had a PR, and 15 patients had an SD, including one non-small cell lung cancer patient with KRAS mutation with a transient PR or durable SD. 15 patients had remained on treatment for over six months, and the patient with CR had ongoing treatment for 342 days, and the two patients with PR had received treatment for 455 days and 574+ days (ongoing), respectively, as of January 31, 2016. When assessed by underlying mutations, of six evaluable patients with the BRAF V600E mutation, there was one CR, one PR and four SDs. Of three evaluable patients with BRAF non-V600E mutation, there were two SDs. Of 20 evaluable patients with KRAS/NRAS mutations, there was one confirmed PR and nine SDs.

We have granted exclusive licenses for the rights to develop and commercialize BGB-283 to Merck KGaA worldwide (outside China). We are currently conducting all clinical development and will continue to do so until Merck KGaA exercises its Continuation Option as further described in the section of our 2015 Annual Report, incorporated by reference herein, titled "Item 1 Business Collaboration with Merck KGaA."

**Our Preclinical Programs.** Our proprietary cancer biology platform has also allowed us to develop several preclinical-stage drug candidates in potentially important targeted areas. These currently consist of targeted therapies and immuno-oncology agents including a PD-L1 monoclonal antibody, an additional RAF dimer inhibitor, a TIM-3 cell surface protein monoclonal antibody, and a BTK inhibitor for non-oncology indications. We anticipate advancing one or more of our preclinical assets into the clinic in the next 12 months. We believe we have the opportunity to combine our PD-1 monoclonal antibody with other clinical-stage and preclinical candidates in our pipeline portfolio to target multiple points in the cancer immunity cycle.

Our research operations are in China, which we believe confers clinical, commercial and regulatory advantages. Our location provides us with access to a deep scientific talent pool and proximity to extensive clinical trial resources through collaborations with leading cancer hospitals in China. In addition, China accounts for approximately 20 25% of the world's cancer population and is experiencing rapid growth in the market for cancer therapeutics. According to CFDA Southern Medicine Economic Research Institute, targeted oncology therapies achieved significant revenues last year in China, maintaining rapid growth. Despite currently requiring out-of-pocket payment by patients, three EGFR targeted therapies (Iressa, Conmana and Tarceva) combined had a revenue of \$462 million in 2015, exemplifying a large cancer therapeutics market.

Currently, many global standard-of-care therapies are not approved or available in China, resulting in a significant need for innovative drugs with strong efficacy and safety profiles for patients who are naive to such treatments. While we plan to seek worldwide regulatory approval for our drug candidates, we also plan to seek expedited approval from the CFDA for our drug candidates as locally developed (Category 1) drugs. In August 2015, the Chinese State Council issued a statement, *Opinions on reforming the review and approval process for pharmaceutical products and medical devices*. In November 2015, the CFDA issued the *Circular Concerning Several Policies on Drug Registration Review and Approval*. In February 2016, the CFDA released the *Opinions on Priority Review and Approval for Resolving Drug Registration Applications Backlog*. The foregoing developments aimed to accelerate and improve the drug clinical development process in China. The CFDA is soliciting public opinions on detailed policies regarding the circular, however, how and when the clinical trial approval and drug registration pathway will be changed is still subject to further policies to be issued by the CFDA. We believe these announcements on regulatory developments could

significantly accelerate development of innovative oncology agents. Expedited approval of our drug candidates in China will address the current unmet need in China and further our understanding and characterization of these drugs for approval in other markets.

As of September 30, 2016, we had a global team of 318 employees and consultants, including a global research and development team of 214 scientists, clinicians, and staff. Our team shares the vision of improving the lives of cancer patients globally and has built a scientifically-driven and collaborative culture fostering both nimble and rational decision-making. Our management team and world-renowned scientific advisory board have deep experience and capabilities in biology, chemistry, drug discovery, clinical development, manufacturing and commercialization. Our scientific advisory board is chaired by our co-founder Xiaodong Wang, Ph.D., a highly respected cancer scientist, member of the U.S. National Academy of Sciences and the Chinese Academy of Sciences and head of China's National Institute of Biological Sciences. Our scientific advisory board also includes Ronald Levy, M.D., Ph.D.; Neal Rosen, M.D., Ph.D.; Charles Sawyers, M.D.; David Schenkein, M.D.; Jedd Wolchok, M.D., Ph.D.; and Steve Young, Ph.D.

#### **Our Mission and Strategy**

Our mission is to become a global leader in the discovery and development of innovative, molecularly targeted and immuno-oncology drugs for the treatment of cancer. To achieve our mission, we intend to pursue the following strategies:

**Rapidly advance our pipeline programs through global development.** In the next 12 months, we plan to make significant advances within our clinical-stage pipeline. We have moved all four of our drug candidates into the dose-expansion phases of their respective clinical trials as monotherapies, and we will continue to enroll multiple expansion cohorts and significantly increase the number of sites globally participating in these trials. We plan to present data from these trials at medical conferences in late 2016 and 2017. We plan to advance BGB-3111 into late-stage development in late 2016 or early 2017 with the initiation of the global Phase III trial for BGB-3111 in Waldenström's Macroglobulinemia. We also have a robust pipeline of preclinical programs and are planning to advance one or more of these programs into the clinic in the next 12 months.

**Pursue global development of combination therapies.** We believe our ownership of both molecularly targeted and immuno-oncology drugs puts us in an advantageous position to develop potentially best-in-combination or first-in-combination therapies that could produce high rates of more durable responses in patients. We have four clinical-stage, independently discovered drug candidates in important and combinable molecularly targeted and immuno-oncology drug classes including BTK inhibitor, PD-1 inhibitor, PARP inhibitor and RAF dimer inhibitor. We believe that we are one of only two companies today to wholly own both a clinical-stage BTK inhibitor for cancer treatment and PD-1 inhibitor or a BRAF inhibitor and PD-1 inhibitor for use as combination therapies. In addition to monotherapy trials, we have initiated and are planning combination trials using wholly-owned drug candidates as well as third-party agents. For BGB-3111, in January 2016 we initiated a combination trial with the anti-CD20 antibody, obinutzumab, and the trial is currently in the dose-expansion phase. On June 30, 2016, we initiated a combination trial with BGB-A317 on February 2, 2016. We plan to present data from these combination trials at medical conferences in 2017.

**Continue to use our cancer biology platform to discover additional candidates with best-in-class characteristics and potential for use in rational combinations.** We plan to use our cancer biology platform to discover additional drug candidates with the potential to be best-in-class monotherapies and also important components of multiple-agent combination regimens. In the last six years, we



have been successful in discovering four clinical stage and numerous promising preclinical drug candidates. By further investing in and improving our cancer biology platform, we expect that the platform will continue to help us select relevant drug targets, identify potential best-in-class drug candidates and develop regimens for rational drug combinations.

**Bring transformative oncology therapeutics to our home market in China.** We are committed to addressing the needs of cancer patients in our home market. China is one of the largest and fastest growing markets for cancer drugs worldwide, representing approximately 20 25% of the world's cancer population and an even greater proportion in lung, liver, and gastric cancers. Because many global standard-of-care therapies are not currently approved and available in China, there is a significant unmet need for innovative cancer drugs for patients who are naive to such treatments. In addition, focusing on cancer types of high prevalence in China will aid our global development efforts in these indications. We have received approval of CTAs in China for each of our four clinical-stage drug candidates from the CFDA to develop our drug candidates through the locally developed, Category 1 registration pathway. We plan to pursue accelerated development, single-arm registration studies and brief dose-escalation studies in China. We also strive to have our drug candidates selected and listed as national priorities. The ability to launch our cancer drugs in our home market, which has a large patient population, will also help us establish broad safety and efficacy profiles for each drug, enabling us to build a full portfolio for future drug combinations.

**Maintain our culture as we grow our business globally.** We believe our science-driven, cooperative and non-hierarchical culture is a key strength of our organization and will continue to be instrumental to our success. As an innovative biotechnology company with research facilities in China, we have been able to attract an internationally trained research team. Many members of our team moved back to China from other countries to join us because they share our goals of advancing the discovery and development of drugs in China and of working with Chinese clinicians to treat their patients with innovative and effective drugs not currently available to them. We intend to maintain our patient-focused and research-driven culture as we discover and develop new drugs for China and the rest of the world.

**Retain the value of our pipeline in our core focus area of oncology.** We currently collaborate with Merck KGaA on our BGB-283 program, but retain exclusive development and commercial rights in China, subject to certain non-compete restrictions. Additionally, we currently retain all worldwide development and commercial rights for our other clinical and preclinical therapeutics. We also have a limited collaboration with Merck KGaA on our BGB-290 program. We intend to protect our ability to direct global preclinical studies and clinical trials for our drug candidates as monotherapies and combination therapies and to maintain exclusive rights in our home market. However, we may opportunistically evaluate additional collaboration opportunities that could increase the value of our programs by accessing the expertise or infrastructure of strategic collaborators or by developing drug candidates with potential applications outside of our strategic focus on cancer.

## **Risks Associated with Our Business**

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

We have incurred net losses in each period since our inception and anticipate that we will continue to incur net losses for the foreseeable future.

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

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We depend substantially on the success of our drug candidates, particularly BGB-3111, BGB-A317, BGB-290, and BGB-283, which are in clinical development as monotherapies and in combination. Clinical trials of our drug candidates may not be successful. If we are unable to commercialize our drug candidates, or experience significant delays in doing so, our business will be materially harmed.

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

Even if any of our drug candidates receives regulatory approval, they may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.

If we are unable to obtain and maintain patent protection for our technology and drugs, our competitors could develop and commercialize technology and drugs similar or identical to ours, and our ability to successfully commercialize our technology and drugs may be adversely affected.

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 drug candidates and our business could be substantially harmed.

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

Changes in the political and economic policies of the PRC government 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.

We will need to increase the size and capabilities of our organization, and we may experience difficulties in managing our growth.

#### **Company and Other Information**

We are an exempted company incorporated in the Cayman Islands with limited liability on October 28, 2010. Any company that is registered in the Cayman Islands but conducts business mainly outside of the Cayman Islands may apply to be registered as an exempted company. The principal executive office of our research and development operations is located at No. 30 Science Park Road, Zhong-Guan-Cun Life Science Park, Changping District, Beijing 102206, People's Republic of China. Our telephone number at this address is +86 10 58958000. Our current registered office in the Cayman Islands is located at the offices of Mourant Ozannes Corporate 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 prospectus, and you should not consider any information on, or that can be accessed through, our website as part of this prospectus.

We own various applications and unregistered trademarks and servicemarks, including BeiGene, and our corporate logo. All other trade names, trademarks and service marks of other companies appearing in this prospectus are the property of their respective holders. Solely for convenience, the trademarks and trade names in this prospectus 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.

## Implications of Being an Emerging Growth Company

We qualify as an "emerging growth company" as defined in the U.S. Jumpstart Our Business Startups Act of 2012, or the JOBS Act. As an emerging growth company, we may take advantage of specified reduced disclosure and other requirements that are otherwise applicable generally to public companies. These provisions include:

not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002;

the ability to include only two years of audited financial statements in addition to any required interim financial statements and correspondingly reduced disclosure in management's discussion and analysis of financial condition and results of operations in the registration statement for this offering of which this prospectus forms a part;

reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements; and

exemptions from the requirements of holding a non-binding advisory vote on executive compensation, including golden parachute compensation.

We may take advantage of these exemptions for up to five years from our initial public offering or such earlier time that we are no longer an emerging growth company. We would cease to be an emerging growth company upon the earliest to occur of (1) the last day of the fiscal year in which we have more than \$1.0 billion in annual revenue; (2) the date we qualify as a "large accelerated filer," with at least \$700 million of equity securities held by non-affiliates; (3) the issuance, in any three-year period, by our company of more than \$1.0 billion in non-convertible debt securities; and (4) the last day of the fiscal year ending after the fifth anniversary of our initial public offering. We may choose to take advantage of some but not all of these exemptions. For example, Section 107 of the JOBS Act provides that an emerging growth company can use the extended transition period provided in Section 7(a)(2)(B) of the Securities Act of 1933, as amended, or the Securities Act, for complying with new or revised accounting standards. We have irrevocably elected not to avail ourselves of this extended transition period. However, we have taken advantage of other reduced reporting requirements in this prospectus. Accordingly, the information contained herein may be different than the information you receive from other public companies in which you hold equity securities.

The Offering

ADSs offered by us 4,336,043 ADSs ADSs offered by the selling shareholders 406,503 ADSs Ordinary shares outstanding immediately after this offering