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**BeiGene**

**BeiGene, Ltd.**

*(incorporated in the Cayman Islands with limited liability  
and trading as “百濟神州” or “百濟神州有限公司”)*

**(Stock Code: 06160)**

## **BUSINESS UPDATE**

### **BEIGENE ANNOUNCES PRELIMINARY RESULTS ON ANTI-PD-1 ANTIBODY TISLELIZUMAB IN PATIENTS WITH MICROSATELLITE INSTABILITY-HIGH OR MISMATCH REPAIR-DEFICIENT SOLID TUMORS AT ANNUAL MEETING OF THE CHINESE SOCIETY OF CLINICAL ONCOLOGY.**

On September 20, 2018, BeiGene, Ltd. (“**BeiGene**” or the “**Company**”) presented preliminary clinical data from Chinese patients with microsatellite instability-high (MSI-H) or mismatch repair-deficient (dMMR) solid tumors enrolled in an ongoing Phase 1/2 clinical trial of tislelizumab, an investigational anti-PD-1 antibody, at the 21st Annual Meeting of the Chinese Society of Clinical Oncology (CSCO) in Xiamen, China.

“Tislelizumab is being developed in a broad clinical program as both a monotherapy and in combination with other treatments for a number of potential clinical indications. We are encouraged by the preliminary results presented today with tislelizumab for patients with MSI-H or dMMR solid tumors and are excited about starting a Phase 2 trial in China in patients with advanced forms of these tumors to test our belief that they are sensitive to immune checkpoint inhibition. We hope this further enables the availability of new treatments options, which are urgently needed, especially in China,” commented Amy Peterson, M.D., Chief Medical Officer, Immuno-Oncology, at BeiGene.

“This is the first presentation of tislelizumab data in the population of patients with MSI-H or dMMR solid tumors, and we are encouraged by the objective response rate of 29 percent in a difficult-to-treat patient population. Tislelizumab was also

generally well-tolerated in these patients,” said Lin Shen, M.D., Vice President of Clinical Oncology at Beijing Cancer Hospital and Peking University, and study presenter. “We hope that further study of tislelizumab may lead to a new treatment for patients with these tumors.”

### **Summary of Results from the MSI-H and dMMR Cohorts in the Phase 1/2 Trial**

The multi-center, open-label Phase 1/2 trial of tislelizumab as monotherapy in advanced solid tumors in China (CTR20160872) consists of a Phase 1 dose verification component and a Phase 2 component of indication expansion in disease-specific cohorts, which includes MSI-H and dMMR solid tumors.

Data presented at CSCO on September 20, 2018 were from 22 patients enrolled in the cohort, of which 14 patients with centrally confirmed MSI-H/dMMR tumors were evaluable for antitumor activity per RECIST v1.1 criteria. Patients were treated with tislelizumab at a dose of 200 mg every three weeks. Colorectal cancer was the most common primary tumor type and 82 percent of the study population received one or more prior lines of systemic therapy. At the time of the data cutoff on May 11, 2018, median treatment duration was 2.2 months (0.69-11.1 months), median follow-up time was 4.4 months (0.10-10.7 months), and ten patients remained on treatment.

Adverse events (AEs) assessed by the investigator to be related to treatment occurred in 18 patients (82%). Of those, the most common treatment-related AEs (TRAEs) (occurring in  $\geq 15\%$  of patients) were increased bilirubin (36%), increased transaminase (27%), increased blood creatine phosphokinase (23%), anemia (23%) and decreased white blood cell and/or neutrophil count (18%). All of the TRAEs were grades 1 or 2. Immune-related AEs (irAEs) occurred in 13 patients (59%) and many were overlapping with the TRAE cases. All irAEs were grade 1 or 2 as well.

At the time of the data cutoff, the efficacy evaluation was early and 14 patients, including 12 patients with colorectal cancer, with centrally confirmed MSI-H/dMMR tumors were evaluable for response. The objective response rate was 29 percent (four patients, all with colorectal cancer), with the median duration of response still maturing. Additionally, three patients centrally confirmed as negative for MSI-H/dMMR were evaluable for response, and progressive disease was the best response in all three of these patients.

In addition to this Phase 1/2 trial, tislelizumab is being investigated in two pivotal Phase 2 clinical trials in China in relapsed/refractory (R/R) classical Hodgkin's lymphoma and in urothelial cancer, Phase 3 trials in China and globally in a number of malignancies including non-small cell lung cancer, hepatocellular carcinoma, and esophageal squamous cell carcinoma; as well as two global Phase 2 trials in patients with previously treated hepatocellular carcinoma or with R/R mature T- and NK-cell lymphomas.

### **About Microsatellite Instability-High or Mismatch Repair Deficient Solid Tumors**

Microsatellite instability-high (MSI-H) cancer cells have a greater than normal number of genetic markers called microsatellites, which are short, repeated sequences of DNA. Cancer cells that have large numbers of microsatellites may have defects in the ability to correct mistakes (also known as mismatch repair deficiency, or dMMR) that occur when DNA is copied in the cell. MSI-H and dMMR tumors are found most often in colorectal cancer, other types of gastrointestinal cancer and endometrial cancer, although they may also be found in cancers of the breast, prostate, bladder and thyroid.

### **About Tislelizumab**

Tislelizumab (BGB-A317) is an investigational humanized monoclonal antibody that belongs to a class of immuno-oncology agents known as immune checkpoint inhibitors. Discovered by BeiGene scientists in Beijing, tislelizumab is designed to bind to PD-1, a cell surface receptor that plays an important role in downregulating the immune system by preventing the activation of T-cells. Tislelizumab has demonstrated high affinity and specificity for PD-1. It is potentially differentiated from the currently approved PD-1 antibodies in an engineered Fc region, which is believed to minimize potentially negative interactions with other immune cells, based on preclinical data. Tislelizumab is being developed as a monotherapy and in combination with other therapies for the treatment of a broad array of both solid tumor and hematologic cancers. BeiGene and Celgene Corporation have a global strategic collaboration for the development of tislelizumab in solid tumor cancers outside of Asia (except Japan).

### **BEIGENE ANNOUNCES RESULTS ON ANTI-PD-1 ANTIBODY TISLELIZUMAB IN CHINESE PATIENTS WITH LUNG CANCERS AT THE ANNUAL MEETING OF THE CHINESE SOCIETY OF CLINICAL ONCOLOGY**

On September 20, 2018, BeiGene presented clinical data on tislelizumab, an investigational anti-PD-1 antibody, in Chinese patients with lung cancers, in two oral presentations at the 21st Annual Meeting of the Chinese Society of Clinical Oncology (CSCO) in Xiamen, China.

“Advanced lung cancer is one of our focus areas for development of tislelizumab, where we hope to have an impact on the way patients are treated both in China and worldwide. This complex and difficult-to-treat disease has proven to be susceptible to treatment with immunotherapies,” commented Amy Peterson, M.D., Chief Medical Officer, Immuno-Oncology, at BeiGene. “The preliminary data presented today demonstrate that tislelizumab is generally well tolerated and has antitumor activity both as monotherapy and in combination with several chemotherapy regimens used in small cell and non-small cell lung cancer patients. We are hopeful that further study of tislelizumab may lead to a new treatment option for a broad array of patients with lung cancers.”

### **Summary of Preliminary Results of Phase 2 Trial in China of Tislelizumab Combined with Chemotherapy as First-Line Treatment in Advanced Lung Cancer Setting**

The multi-center, open-label Phase 2 trial in China (CTR20170361) of tislelizumab in combination with chemotherapy enrolled 54 patients with previously untreated locally advanced or metastatic lung cancer. All patients received tislelizumab at 200 mg every three weeks, plus platinum doublet until disease progression. Patients with non-squamous non-small cell lung cancer (NSCLC) (n=16) received pemetrexed plus platinum; patients with squamous NSCLC received either paclitaxel plus platinum (cohort A, n=15) or gemcitabine plus platinum (cohort B, n=6); and patients with small cell lung cancer (SCLC) received etoposide plus platinum (n=17).

As of the June 5, 2018 data cutoff, 35 patients remain on treatment. Treatment discontinuation due to adverse events (AEs) occurred in three patients. Fifty-one patients had at least one post-baseline tumor assessment and were evaluable for efficacy. Objective responses (including confirmed and unconfirmed partial responses) were observed in 56 percent (31 percent confirmed; all patients with an unconfirmed partial response remained on treatment) of 16 evaluable patients with non-squamous NSCLC; 80 percent (all confirmed) in 15 evaluable patients with squamous NSCLC, cohort A; 67 percent (all confirmed) in six patients with squamous NSCLC, cohort B; and 82 percent (47 percent confirmed; all patients with an unconfirmed partial response remained on treatment) in 17 evaluable patients with SCLC. Data continue to mature with follow-up.

AEs were considered manageable and reversible, with chemotherapy dose modifications or tislelizumab dose holds, except for one fatal event of myocarditis/myositis. Five patients (9.3%) experienced at least one grade  $\geq 3$  AE (polymyositis, dyspnea, rhabdomyolysis, myocarditis/myositis, and myasthenia

gravis) that were considered to be possibly related to tislelizumab. Immune-related AEs (irAEs) occurred in 13 patients (24%) and included hypothyroidism (n=3), decreased tri-iodothyronine (n=2), hyperthyroidism (n=2), pneumonitis (n=2), pyrexia (n=2), and rash (n=2).

“We are excited by the preliminary data of tislelizumab combined with chemotherapy in patients with advanced lung cancer. The safety and tolerability appear consistent with previous data, and high response rates of up to 80 percent in a squamous NSCLC cohort along with low discontinuation rates support continued investigation of tislelizumab in patients with advanced lung cancer. We are hopeful that this combination therapy will offer improved outcomes in this advanced disease setting,” said Professor Jie Wang, M.D., from the National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College in Beijing, China, and lead author of the presentation.”

### **Summary of Preliminary Results of Tislelizumab in Chinese Patients with NSCLC from Phase 1/2 Trial**

The multi-center, open-label Phase 1/2 trial in China (CTR20160872) of tislelizumab enrolled 46 patients with NSCLC in the Phase 2 indication expansion portion of the trial, with 21 patients having expression of PD-L1 in 10 percent or more of their tumor cells (PD-L1+); the remaining 25 patients were considered PD-L1 negative (PD-L1-).

As of the May 11, 2018 data cutoff, 15 patients (33%) remained on treatment with the median treatment duration of 4.1 months (0.2—11.3 months) and a median follow-up of 8.4 months (0.2—11.8 months). Treatment discontinuation due to adverse events (AEs) occurred only in one patient. The median duration of treatment was 3.5 months (0.2-11.2 months) and 4.4 months (0.7—11.3 months) in PD-L1+ and PD-L1- cohorts, respectively. A total of 42 patients had at least 1 post-baseline tumor assessment and were evaluable for antitumor activity. Confirmed partial responses were observed in 17 percent of the evaluable patients, including 12 percent and 20 percent in PD-L1+ and PD-L1- patients, respectively.

Across the two arms, the most common treatment-related AEs (TRAEs) (occurring in  $\geq 10\%$  of patients) were increased transaminases (26%), rash (11%) and hypothyroidism (11%). A total of 14 patients had serious AEs and three of these patients experienced serious TRAEs, including nausea and vomiting (n=1), increased aspartate aminotransferase (AST) (n=1) and hyperglycemia (n=1). Three patients experienced a serious AE with a fatal outcome (multiple organ dysfunction syndrome [n=1], central nervous system metastases [n=1], hypotension [n=1]); none were determined to be related to treatment. Immune-related AEs occurred in 26 patients (57%) and many were overlapping with the TRAE cases.

“The prognosis for patients with late stage non-small cell lung cancer remains particularly poor. We are pleased that this trial demonstrated that treatment with tislelizumab was generally well tolerated. We are excited to see that Phase 3 trials evaluating tislelizumab, either as monotherapy or in combination with chemotherapy, in patients with advanced NSCLC are underway and look forward to the results,” said Yi-Long Wu, M.D., President of Chinese Thoracic Oncology Group (CTONG) and lead author of the presentation.

Trial data with the same cut off time will be presented at the International Association for the Study of Lung Cancer (IASLC) 19th World Conference on Lung Cancer (WCLC), which takes place September 23-26 in Toronto.

### **About Tislelizumab**

Tislelizumab (BGB-A317) is an investigational humanized monoclonal antibody that belongs to a class of immuno-oncology agents known as immune checkpoint inhibitors. Discovered by BeiGene scientists in Beijing, tislelizumab is designed to bind to PD-1, a cell surface receptor that plays an important role in downregulating the immune system by preventing the activation of T-cells. Tislelizumab has demonstrated high affinity and specificity for PD-1. It is potentially differentiated from the currently approved PD-1 antibodies in an engineered Fc region, which is believed to minimize potentially negative interactions with other immune cells, based on preclinical data. Tislelizumab is being developed as a monotherapy and in combination with other therapies for the treatment of a broad array of both solid tumor and hematologic cancers. BeiGene and Celgene Corporation have a global strategic collaboration for the development of tislelizumab in solid tumor cancers outside of Asia (except Japan).

### **BEIGENE ANNOUNCES PRELIMINARY RESULTS FROM THE PHASE 1 CLINICAL TRIAL OF ZANUBRUTINIB IN CHINESE PATIENTS WITH B-CELL LYMPHOMA AT ANNUAL MEETING OF THE CHINESE SOCIETY OF CLINICAL ONCOLOGY**

On September 21, 2018, BeiGene presented preliminary results from the Phase 1 trial of its investigational BTK inhibitor zanubrutinib in Chinese patients with B-cell lymphoma in an oral presentation at the 21st Annual Meeting of the Chinese Society of Clinical Oncology (CSCO) in Xiamen, China.

“We continue to be encouraged by clinical data on zanubrutinib, including these results, which we believe support its broad global clinical development. Our recent new drug application filing for zanubrutinib in China for patients with relapsed/refractory mantle cell lymphoma (MCL), a type of B-cell lymphoma, is currently under review by the National Medical Products Administration of China,

and we are hopeful that it will give patients in China, and across the world, a new treatment option where it is so greatly needed,” said Jane Huang, M.D., Chief Medical Officer, Hematology, at BeiGene.

### **Summary of Preliminary Results from the Phase 1 Trial of Zanubrutinib in Chinese Patients with B-Cell Lymphoma**

An ongoing Phase 1 trial of zanubrutinib as a monotherapy in patients with different subtypes of B-cell malignancies, including Waldenström macroglobulinemia (WM), chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) and other non-Hodgkin’s lymphomas (NHL), is being conducted in China. The trial is fully enrolled and comprised of two parts — a dose escalation phase involving 21 patients and a doseexpansion phase of 23 patients treated with zanubrutinib at the recommended Phase 2 dose of 160 mg taken orally twice daily.

Preliminary findings suggested that there was no significant difference in the pharmacokinetic profile of zanubrutinib between Chinese and nonChinese patients. Preliminary findings also showed complete or greater than 80 percent sustained BTK occupancy was achieved among these patients with both single- and multiple-dose administrations.

As of June 15, 2018, after a median follow-up of 9.5 months (2.3 months— 23.4 months), 21 patients (47%) remained on treatment. With 44 patients enrolled in the trial, 34 were evaluable for response. Of the nine patients with CLL/SLL, the overall response rate (ORR) was 100 percent, with two complete responses (CRs), six partial responses (PRs), and a PR with lymphocytosis (PR-L). Of the two patients with mantle cell lymphoma (MCL), there was one CR and one stable disease (SD). Of the two patients with WM, there was one PR and one SD. Of the 26 patients with follicular lymphoma (FL), the ORR was 42 percent with two CRs and nine PRs. There were three patients with FL who were not evaluable at the time of the data cutoff. Of the five patients with marginal zone lymphoma (MZL), there were three SDs and two patients who were not evaluable.

At the time of data cutoff, no dose-limiting toxicities occurred during dose escalation portion of the trial and there were no unexpected safety signals identified in the trial. No deaths related to adverse events were observed in the trial. The most common adverse events (occurring in  $\geq 20\%$  of patients) of any attribution among all 44 patients were neutrophil count decreased (50%), anemia (32%), upper respiratory tract infection (25%), white blood cell count decreased (25%), platelet count decreased (23%), rash (23%), hematuria (20%), and hyperuricemia (20%).

“These preliminary safety, tolerability and pharmacokinetics data of zanubrutinib support its ongoing clinical study. In this study, the preliminary results suggest zanubrutinib has a high rate of activity and is generally well-tolerated, which we believe is based on its potency and high-degree of selectivity,” said Jun Zhu, M.D., Medical Department Chief at the Beijing Cancer Hospital and study presenter.

### **About B-Cell Lymphomas**

Lymphoma is a diverse group of malignancies that originates from B, T or NK cells. The most common type of B-cell lymphomas is nonHodgkin’s lymphoma, of which diffuse large B-cell lymphoma (DLBCL) is the most common. Other types of B-cell non-Hodgkin’s lymphoma include FL, CLL/SLL, MCL, MZL, and WM.

### **About Zanubrutinib**

Zanubrutinib (BGB-3111) is an investigational small molecule inhibitor of Bruton’s tyrosine kinase (BTK) that is currently being evaluated in a broad pivotal clinical program globally and in China as a monotherapy and in combination with other therapies to treat various B-cell malignancies.

**Cautionary Statement required by Rule 18A.05 of the Rules Governing the Listing of Securities on The Stock Exchange of Hong Kong Limited:** BeiGene may not be able to ultimately develop and market Tislelizumab and Zanubrutinib successfully.

### **Forward-Looking Statements**

This announcement contains forward-looking statements, including statements regarding BeiGene’s advancement of, and anticipated clinical development, regulatory milestones and commercialization of tislelizumab and zanubrutinib. Actual results may differ materially from those indicated in the forward-looking statements as a result of various important factors, including BeiGene’s ability to demonstrate the efficacy and safety of its drug candidates; the clinical results for its drug candidates, which may not support further development or marketing approval; actions of regulatory agencies, which may affect the initiation, timing and progress of clinical trials and marketing approval; BeiGene’s ability to achieve commercial success for its marketed products and drug candidates, if approved; BeiGene’s ability to obtain and maintain protection of intellectual property for its technology and drugs; BeiGene’s reliance on third parties to conduct drug development, manufacturing and other services; BeiGene’s limited operating history and BeiGene’s ability to obtain additional funding for operations and to complete the development and commercialization of its drug candidates, as well as those risks more fully discussed in the section entitled “Risk Factors” in BeiGene’s most recent quarterly



report on Form 10-Q, as well as discussions of potential risks, uncertainties, and other important factors in BeiGene's subsequent announcements and filings with the U.S. Securities and Exchange Commission. All information in this announcement is as of the date of this announcement, and BeiGene undertakes no duty to update such information unless required by law.

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

Hong Kong, September 26, 2018

*As at the date of this announcement, the Board of Directors of the Company comprises Mr. John V. Oyler as Chairman and Executive Director, Dr. Xiaodong Wang as Non-executive Director, and Mr. Timothy Chen, Mr. Donald W. Glazer, Mr. Michael Goller, Mr. Ranjeev Krishana, Mr. Thomas Malley, Mr. Jing-Shyh (Sam) Su and Mr. Qingqing Yi as Independent Non-executive Directors.*