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

VOLUNTARY ANNOUNCEMENT — UPDATE REGARDING RECENT BUSINESS DEVELOPMENTS

BeiGene Announces European Medicines Agency Acceptance of Marketing Authorization Applications for Tislelizumab for the Treatment of Patients with ESCC and NSCLC

On April 6, 2022, BeiGene, Ltd. ("**BeiGene**" or the "**Company**") announced that marketing authorization applications (MAA) for tislelizumab, submitted by Novartis, the license holder in Europe, have been validated for regulatory review by the European Medicines Agency (EMA) for patients with advanced or metastatic esophageal squamous cell carcinoma (ESCC) after prior systemic chemotherapy and for patients with non-small cell lung cancers (NSCLC) including:

- As monotherapy for the treatment of locally advanced or metastatic NSCLC after prior chemotherapy in adults,

- In combination with carboplatin and either paclitaxel or nab-paclitaxel for the first-line treatment of locally advanced or metastatic squamous NSCLC in adults, and

- In combination with pemetrexed and platinum-containing chemotherapy for the first-line treatment of locally advanced or metastatic non-squamous NSCLC in adults whose tumors have no EGFR or ALK positive mutations.

"In our global Phase 3 trials in second line ESCC and NSCLC, tislelizumab monotherapy demonstrated significant improvements in overall survival and was generally well-tolerated in these patient groups. In the two Phase 3 studies in first line NSCLC, tislelizumab in combination with chemotherapy demonstrated significant improvements in progression free survival compared to chemotherapy alone in both non-squamous and squamous histology, and the addition of tislelizumab to chemotherapy was generally well-tolerated with no new safety signal observed. These first submissions for tislelizumab to the EMA highlight the momentum in our collaboration with Novartis, and we look forward to continued progress as they submit tislelizumab for approvals in their licensed territories," commented Mark Lanasa, M.D., Ph.D., Senior Vice President, Chief Medical Officer, Solid Tumors, at BeiGene. "We are motivated each day to advance tislelizumab's progress on behalf of the many patients in Europe and around the world with these cancers, for whom we hope to provide an important new treatment option."

The MAA for tislelizumab in NSCLC is supported by clinical results from three BeiGene-sponsored trials (NCT03358875, NCT03594747, NCT03663205) of 1,499 patients, including the global randomized, open-label, Phase 3 RATIONALE 303 trial comparing tislelizumab to docetaxel in the second-or third-line setting in patients with locally advanced or metastatic NSCLC who have progressed on prior platinum-based chemotherapy. In this trial, 805 patients in 10 countries across the Americas, Europe, Asia, and Oceania were enrolled in the trial, randomized 2:1 to either the tislelizumab arm or the docetaxel arm. As announced in November 2020, the trial met the primary endpoint of overall survival (OS) at the planned interim analysis, as recommended by the independent Data Monitoring Committee (IDMC). Tislelizumab was generally well-tolerated, consistent with known safety risks from previously reported results across different tumor types, with no new safety signals identified. The results of the interim analysis of the trial were presented at the American Association for Cancer Research (AACR) Annual Meeting in April 2021.

The MAA submission for ESCC is based on results from BeiGene's RATIONALE 302, a randomized, open-label, multicenter global Phase 3 trial (NCT03430843) designed to evaluate the efficacy and safety of tislelizumab when compared to investigator's choice chemotherapy as a second-line treatment for patients with advanced or metastatic ESCC. Results of this trial were presented at the 2021 American Society of Clinical Oncology Annual Meeting (ASCO 2021). The submission also included safety data on 1,972 patients who received tislelizumab as a monotherapy from seven clinical trials. A biologics license application (BLA) in this indication is currently under review by the U.S. FDA. In addition to the EU and the U.S., this indication is also under regulatory review in China.

About Esophageal Squamous Cell Carcinoma (ESCC)

Globally, esophageal cancer is one of the most frequently reported malignancies and a leading cause of cancer deaths.[i] Esophageal cancer ranks seventh in terms of incidence (604,000 new cases) and sixth in mortality overall (544,000 deaths), the latter signifying that esophageal cancer is responsible for one in every 18 cancer deaths in 2020.[ii]

There are two main types of esophageal cancer, based on the cells where cancer develop: squamous cell carcinoma (ESCC) and adenocarcinoma (EAC).[iii] Because many patients are diagnosed at later stages of disease, management of ESCC is challenging and the overall prognosis remains poor.[iv,v]

About Non-Small Cell Lung Cancer

Lung cancer remains the second most common type of cancer and the leading cause of cancer-related death worldwide.[vi] Lung cancer is the third most common cancer in Europe; NSCLC represents 85-90% of all lung cancers[vii]. In 2018, the number of new cases of lung cancer diagnosed in Europe was estimated at more than 470,000 (Ferlay et al., 2018).[viii] The five-year survival rate with treatment for stage IIIB and stage IV NSCLC is 5% and 2%, respectively.[ix]

About Tislelizumab

Tislelizumab is a humanized IgG4 anti-PD-1 monoclonal antibody specifically designed to minimize binding to FcγR on macrophages. In pre-clinical studies, binding to FcγR on macrophages has been shown to compromise the anti-tumor activity of PD-1 antibodies through activation of antibody-dependent macrophage-mediated killing of T effector cells. Tislelizumab is the first drug from BeiGene's immuno-oncology biologics program and is being developed internationally as a monotherapy and in combination with other therapies for the treatment of a broad array of both solid tumor and hematologic cancers.

The China National Medical Products Administration (NMPA) has approved tislelizumab in seven indications, including full approval for 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, and for second – or third-line treatment of patients with locally advanced or metastatic NSCLC who progressed on prior platinum-based chemotherapy. The NMPA has 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, and for the treatment of patients with 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 or other confirmatory trials approved by the health authority.

In addition, two supplemental Biologics License Applications for tislelizumab are under review by the Center for Drug Evaluation (CDE) of the NMPA, including 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).

In the U.S., a Biologics License Application for tislelizumab as a treatment for patients with unresectable recurrent locally advanced or metastatic ESCC after prior systemic therapy is currently under review by the U.S. Food and Drug Administration.

BeiGene has initiated or completed more than 20 potentially registration-enabling clinical trials in China and globally, including 17 Phase 3 trials and four pivotal Phase 2 trials. In addition, tislelizumab is being investigated in combination with several other therapies including ociperlimab, sitravatinib, and zanidatamab.

In January 2021, BeiGene and Novartis entered into a collaboration and license agreement granting Novartis rights to develop, manufacture, and commercialize tislelizumab in North America, Europe, and Japan.

Tislelizumab is not approved for use outside of China.

About the Tislelizumab Clinical Program

Clinical trials of tislelizumab include:

- Phase 3 trial comparing tislelizumab with docetaxel in the second-or third-line setting in patients with NSCLC (NCT03358875);
- Phase 3 trial comparing tislelizumab to salvage chemotherapy in patients with relapsed or refractory classical Hodgkin Lymphoma (cHL; NCT04486391);
- Phase 3 trial in patients with locally advanced or metastatic urothelial carcinoma (NCT03967977);
- Phase 3 trial of tislelizumab in combination with chemotherapy versus chemotherapy as first-line treatment for patients with advanced squamous NSCLC (NCT03594747);
- Phase 3 trial of tislelizumab in combination with chemotherapy versus chemotherapy as first-line treatment for patients with advanced non-squamous NSCLC (NCT03663205);
- Phase 3 trial of tislelizumab in combination with platinum-based doublet chemotherapy as neoadjuvant treatment for patients with NSCLC (NCT04379635);
- Phase 3 trial of tislelizumab combined with platinum and etoposide versus placebo combined with platinum and etoposide in patients with extensive-stage small cell lung cancer (NCT04005716);
- Phase 3 trial comparing tislelizumab with sorafenib as first-line treatment for patients with hepatocellular carcinoma (HCC; NCT03412773);
- Phase 2 trial in patients with previously treated unresectable HCC (NCT03419897);
- Phase 2 trial in patients with locally advanced or metastatic urothelial bladder cancer (NCT04004221);
- Phase 3 trial comparing tislelizumab with chemotherapy as second-line treatment for patients with advanced esophageal squamous cell carcinoma (ESCC; NCT03430843);
- Phase 3 trial of tislelizumab in combination with chemotherapy as first-line treatment for patients with ESCC (NCT03783442);
- Phase 3 trial of tislelizumab versus placebo in combination with chemoradiotherapy in patients with localized ESCC (NCT03957590);

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

- Phase 3 trial comparing tislelizumab in combination with sitravatinib versus docetaxel in patients with advanced NSCLC that progressed on chemotherapy and anti-PD-(L)1 antibody (NCT04921358);

- Phase 3 trial of zanidatamab in combination with chemotherapy plus or minus tislelizumab as first-line treatment for patients with HER2-positive advanced gastric and esophageal cancers (NCT05152147);

- Phase 2 trial of tislelizumab in patients with relapsed or refractory cHL (NCT03209973);

- Phase 2 trial in patients with MSI-H/dMMR solid tumors (NCT03736889); and

- Phase 3 trial of tislelizumab combined with chemotherapy versus placebo combined with chemotherapy as first-line treatment in patients with nasopharyngeal cancer (NCT03924986).

Tislelizumab is also currently being investigated in combination with ociperlimab, BeiGene's investigational potent TIGIT inhibitor with intact Fc function, in multiple ongoing trials, including:

- AdvanTIG-301: Phase 3 trial (NCT04866017) in locally advanced, unresectable non-small cell lung cancer;

- AdvanTIG-302: Phase 3 trial in untreated non-small cell lung cancer (NCT04746924);

- AdvanTIG-202: Phase 2 trial in metastatic cervical cancer (NCT04693234);

- AdvanTIG-203: Phase 2 trial in advanced esophageal squamous cell carcinoma (NCT04732494);

- AdvanTIG-204: Phase 2 trial in untreated limited-stage small cell lung cancer (NCT04952597);

- AdvanTIG-205: Phase 2 trial in untreated metastatic non-small cell lung cancer (NCT05014815);

- AdvanTIG-206: Phase 2 trial in first-line advanced hepatocellular carcinoma (NCT04948697); and

- Phase 1b trial in advanced solid tumors (NCT04047862).

About BeiGene Oncology

BeiGene 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. We have a growing R&D and medical affairs team of approximately 2,900 colleagues dedicated to advancing more than 100 clinical trials that have involved more than 14,500 subjects. Our expansive portfolio is directed predominantly by our internal colleagues supporting clinical trials in more than 45 countries and regions. Hematology-oncology and solid tumor targeted therapies and immuno-oncology are key focus areas for the Company, with both mono-and combination therapies prioritized in our research and development. BeiGene currently has three approved medicines discovered and developed in our own labs: BTK inhibitor BRUKINSA in the United States, China, the EU and U.K., Canada, Australia and additional international markets; and the non-FC-gamma receptor binding anti-PD-1 antibody tislelizumab as well as the PARP inhibitor pamiparib in China.

BeiGene also partners with innovative companies who share our goal of developing therapies to address global health needs. We commercialize a range of oncology medicines in China licensed from Amgen, Bristol Myers Squibb, EUSA Pharma and Bio-Thera. We also plan to address greater areas of unmet need globally through our other collaborations including with Mirati Therapeutics, Seagen, and Zymeworks.

In January 2021 BeiGene and Novartis announced a collaboration granting Novartis rights to co-develop, manufacture, and commercialize BeiGene's anti-PD1 antibody tislelizumab in North America, Europe, and Japan. Building upon this productive collaboration, including a biologics license application (BLA) under FDA review, BeiGene and Novartis announced an option, collaboration and license agreement in December 2021 for BeiGene's TIGIT inhibitor ociperlimab that is in Phase 3 development. Novartis and BeiGene also entered into a strategic commercial agreement through which BeiGene will promote five approved Novartis Oncology products across designated regions of China.

References

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About BeiGene

BeiGene is a global, science-driven biotechnology company focused on developing innovative and affordable medicines to improve treatment outcomes and access for patients worldwide. With a broad portfolio of more than 40 clinical candidates, we are expediting development of our diverse pipeline of novel therapeutics through our own capabilities and collaborations. We are committed to radically improving access to medicines for two billion more people by 2030. BeiGene has a growing global team of over 8,000 colleagues across five continents. To learn more about BeiGene, please visit www.beigene.com and follow us on Twitter at @BeiGeneGlobal.

Forward-Looking Statements

This announcement contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 and other federal securities laws, including statements regarding data from the Phase 3 trials of tislelizumab in patients with ESCC and NSCLC, the potential clinical benefits of tislelizumab in patients with ESCC and NSCLC, the filing and potential approval of the MAAs for tislelizumab in ESCC and NSCLC in the European Union, expectations for continued progress in regulatory submissions and approvals under the collaboration with Novartis, BeiGene's advancement, anticipated clinical development, regulatory milestones and commercialization of tislelizumab, and BeiGene's plans, commitments, aspirations and goals under the headings "About BeiGene Oncology" and "About BeiGene". 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 medicines and drug candidates, if approved; BeiGene's ability to obtain and maintain protection of intellectual property for its medicines and technology; BeiGene's reliance on third parties to conduct drug development, manufacturing and other services; BeiGene's limited experience in obtaining regulatory approvals and commercializing pharmaceutical products and its ability to obtain additional funding for operations and to complete the development and commercialization of its drug candidates and achieve and maintain profitability; the impact of the COVID-19 pandemic on BeiGene's clinical development, regulatory, commercial, manufacturing and other operations, as well as those risks more fully discussed in the section entitled "Risk Factors" in BeiGene's most recent annual report on Form 10-K as well as discussions of potential risks, uncertainties, and other important factors in BeiGene's subsequent filings with the U.S. Securities and Exchange Commission and The Stock Exchange of Hong Kong Limited. 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, April 6, 2022

As of 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 and Mr. Anthony C. Hooper as Non-executive Directors, and Mr. Timothy Chen, 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.