
BeiGene Announces Clinical Data on Tislelizumab and Pamiparib Presented at the European Society for Medical Oncology (ESMO) Congress 2019

CAMBRIDGE, Mass. and BEIJING, China, September 30, 2019 (GLOBE NEWSWIRE) -- BeiGene, Ltd. (NASDAQ: BGNE; HKEX: 06160), a commercial-stage biopharmaceutical company focused on developing and commercializing innovative molecularly-targeted and immuno-oncology drugs for the treatment of cancer, today announced clinical data on its investigational anti-PD-1 antibody tislelizumab and its investigational PARP inhibitor pamiparib that were presented at the European Society for Medical Oncology (ESMO) Congress 2019 in Barcelona, Spain.

“We are excited to present the pivotal data for tislelizumab in the second indication in China, urothelial carcinoma, and look forward to continued regulatory discussions on our supplemental new drug application (sNDA) which is under priority review by the National Medical Products Administration (NMPA),” said Yong (Ben) Ben, M.D., Chief Medical Officer, Immuno-Oncology at BeiGene. “We also presented additional clinical data on pamiparib monotherapy and its combination with low-dose temozolomide and we are looking forward to Phase 3 and pivotal Phase 2 data of pamiparib trials in China next year. We are hopeful that these treatments will provide meaningful benefit to patients battling these and other forms of cancer.”

First Report of Efficacy and Safety from a Phase 2 Trial of Tislelizumab for the Treatment of Locally Advanced or Metastatic Urothelial Carcinoma in Asian Patients

Presentation 920P

This multi-center, open-label Phase 2 trial (NCT04004221) of tislelizumab is being conducted in patients in China and South Korea with PD-L1+ locally advanced or metastatic urothelial carcinoma (UC) previously treated with ≥ 1 platinum-containing therapy. The trial was designed to assess safety, tolerability and efficacy of tislelizumab at the recommended Phase 2 dose (200 mg IV every three weeks), with a primary endpoint of objective response rate (ORR) as assessed by an independent review committee (IRC) per RECIST v1.1.

As of February 28, 2019, 113 patients were enrolled in the trial, including 38.9% of patients who had received two (32.7%) or at least three (6.2%) prior therapies, and 23.9% of patients with liver metastasis. The median duration of treatment for all patients

was 15.3 weeks (2–72). At the time of the data cutoff, 30 patients (26.5%) remained on treatment.

- Of the 104 patients evaluable for response, the confirmed ORR was 23.1%, with 8 complete responses (CRs) and 16 partial responses (PRs) per IRC assessment. Additional results included:
 - Median duration of response (DoR) was not reached. Of the 24 responders, 19 (79%) had maintained response as of the data cutoff; and
 - Median progression-free survival (PFS) and overall survival (OS) were 2.1 and 9.8 months, respectively;
- Tislelizumab was generally well-tolerated. There were 105 patients with ≥ 1 treatment-related adverse event (TRAE); the most common TRAEs of any grade were anemia (26.5%), decreased appetite (18.6%), pyrexia (16.8%), aspartate aminotransferase increased (15%), and pruritus (15%);
- Thirty-nine patients experienced grade ≥ 3 TRAEs related to the study drug. The most common grade ≥ 3 TRAEs were anemia (7.1%), urinary tract infection (4.4%), decreased appetite (3.5%), and hyponatremia (3.5%);
- Twelve (11%) patients experienced adverse events (AEs) related to the study drug that resulted in treatment discontinuation. Serious AEs related to study treatment were reported in 11 (9.7%) patients;
- Immune-related treatment-emergent adverse events (TEAEs) occurred in 64% of patients. Common immune-related TEAEs included immune-mediated skin adverse reaction (34%), immune-mediated hepatitis (24%), thyroid disorders (13%), and immune-mediated nephritis and renal dysfunction (12%); and
- Four (3.5%) patients experienced AEs with fatal outcome, including hepatic failure (n=2), respiratory arrest (n=1), and renal impairment (n=1). The events of hepatic failure and respiratory arrest were reported as possibly related to the study drug by the investigator. The event of renal impairment was reported as possibly unrelated to the study drug.

Updated Results of Pamiparib in Combination with Low-Dose Temozolomide in Patients with Locally Advanced or Metastatic Solid Tumors

Presentation 451PD

This open-label, multi-center Phase 1b dose-escalation/expansion trial (NCT03150810) of pamiparib plus low-dose temozolomide (TMZ) was designed to evaluate the safety, tolerability, maximum tolerated dose (MTD), and preliminary antitumor activity of the combination in patients with locally advanced and metastatic tumors. Patients received full-dose pamiparib in combination with escalating doses of TMZ, administered in both pulse and continuous dosing schedules.

The recommended Phase 2 dose and schedule of the combination was determined to be 60 mg of pamiparib taken orally twice daily for 28 days, with TMZ at 60 mg orally once daily during days one through seven.

As of July 29, 2019, a total of 113 patients with solid tumors have been enrolled in the study. Enrolled patients received a median of three prior treatments. As of the data cutoff, a total of 17 patients (15.0%) remained on pamiparib and low-dose TMZ treatment.

- The combination was shown to be generally well-tolerated; 112 patients had ≥ 1 TEAE; the most common TEAEs occurring in 20% or more patients of any grade were anemia (57.5%), nausea (54.0%), fatigue (48.7%), decreased appetite (34.5%), neutropenia (32.7%), thrombocytopenia (31.9%), vomiting (29.2%), and decreased platelet count (23.0%);
- Sixty-three patients experienced grade ≥ 3 TEAEs related to the study drug. The most common grade ≥ 3 TEAEs were cytopenias (anemia, neutropenia, and thrombocytopenia), all of which were manageable and reversible. Related grade 4 AEs included thrombocytopenia (11.5%), neutropenia (9.7%), decreased neutrophil counts (8.8%), decreased platelet counts (7.1%), and decreased white blood cells (2.7%);
- Three (2.7%) patients experienced AEs related to the study drug that resulted in treatment discontinuation. Serious AEs related to study treatment were reported in 11 (9.7%) patients;
- Four (3.5%) patients experienced AEs with fatal outcome, all of which were considered by investigators to be unrelated to the study drug;

- As of the data cutoff 57 of 66 patients enrolled in the dose-escalation phase were evaluable for response; 52 patients had measurable disease and were evaluated by either RECIST v1.1 or Prostate Cancer Working Group 2 criteria. Results included:
 - ORR was 19.3% (11 PRs); 8 of 11 responses were confirmed. In addition, an unconfirmed PSA response was observed in one patient with prostate cancer;
 - Disease control rate (DCR) was 64.9% (95% CI, 51.1–77.1);
 - Median DoR was 6.4 months (95% CI, 2.1–7.7);
 - Median treatment duration was 3.7 months (range 0.2–18.1); and
 - In a biomarker analysis, 62.5% (5/8) of patients assessed as homologous recombination deficiency (HRD+) showed a response;
- There were 19 evaluable patients, with \leq two prior lines of chemotherapy, enrolled in the extensive-stage small cell lung cancer (ES SCLC) expansion cohort. ORR was 31.6%; with one CR and five PRs. The DCR was 78.9%, with 3.6 months median treatment duration (1.0–5.7) and five patients remained on treatment; and
- There were 15 evaluable patients enrolled in the gastric/gastroesophageal junction (G/GEJ) cancer expansion cohort. ORR was 0%; The DCR was 33.3%, with 1.9 months median treatment duration (0.3–5.8) and two patients remained on treatment.

Safety, Antitumor Activity, and Pharmacokinetics of Pamiparib in Patients with Advanced Solid Tumors: Updated Phase 1 Dose-Escalation/Expansion Results

Presentation 452PD

The multi-center, open-label Phase 1A/1B trial (NCT02361723) of pamiparib is being conducted in Australia in patients with advanced solid tumors. The Phase 1A dose-escalation and dose-finding component identified the recommended Phase 2 dose to be 60 mg orally twice daily (BID). The ongoing Phase 1B trial consists of a component to investigate the safety, tolerability, and antitumor activity of pamiparib in disease-specific

dose-expansion cohorts, and a component investigating the effects of food on the pharmacokinetic profile of a single dose. Data presented at ESMO include updated safety data from the study and updated efficacy data from the ovarian and associated cancer cohort.

As of June 1, 2019, 101 patients were enrolled in the trial, with 64 patients in the dose-escalation component, and 37 patients in the dose-expansion component. Enrolled patients had received a median of three prior treatments. At the time of the data cutoff, 11 patients (10.9%) remained on treatment.

- Of the 101 patients, the most common (occurring in 20% or more patients) TEAEs of any grade were nausea (69.3%), fatigue (48.5%), anemia (35.6%), diarrhea (33.7%), vomiting (31.7%), decreased appetite (22.8%), and constipation (21.8%);
- The most common grade 3 or higher TEAE occurring in 5% or more patients were anemia (24.8%) and alanine aminotransferase (ALT) increase (5%);
- TEAEs led to treatment discontinuation in 6.9% of patients. Five (5%) patients experienced TEAEs with a fatal outcome, all of which were considered by investigators to be unrelated to the study drug;
- As of the data cutoff, 58 patients with ovarian and associated cancer were evaluable for efficacy per RECIST v1.1 criteria. Of these patients, 23 (39.7%) achieved a confirmed objective response, with four CRs (6.9%) and 19 PRs (32.8%). Additional results included:
 - The clinical benefit rate was 53.4%;
 - The median duration of response was 14.9 months (11–17.9);
 - The ORR was higher (61.3%) in 31 patients with germline or somatic BRCA mutation (g/s BRCA^{mut+}) as compared to 14.8% in 27 patients who were BRCA wild-type or unknown (BRCA^{wt} or BRCA^{unk}) status;
 - There were 22 patients with platinum sensitivity, 23 patients were platinum-resistant, and 12 patients were platinum-refractory. The ORR was 77.3% for platinum-sensitive patients, 17.4% for platinum-resistant and 8.3% for platinum-refractory patients;

- In patients who were platinum-sensitive with BRCA^{mut+} the ORR was 83.3% (15/18); in patients who were BRCA^{wt} or BRCA^{unk} the ORR was 50% (2/4); and
- In patients who were platinum-resistant with BRCA^{mut+} the ORR was 20% (2/10); and in patients who were BRCA^{wt} or BRCA^{unk} the ORR was 15.4% (2/13);
- Pharmacokinetic data showed that the plasma exposure of pamiparib increased nearly proportionally with increase in dose with a terminal half-life of approximately 13 hours, and supported administration of pamiparib, with or without food.

About Tislelizumab

Tislelizumab (BGB-A317) is an investigational 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 candidate produced from BeiGene's immuno-oncology biologics program and 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.

Ongoing clinical trials of tislelizumab include a Phase 3 clinical trial in patients with second-line or third-line non-small cell lung cancer (NSCLC); a Phase 3 clinical trial in first-line patients with hepatocellular carcinoma (HCC); a Phase 3 clinical trial in second-line patients with esophageal squamous carcinoma (ESCC); a Phase 3 clinical trial in first-line patients with gastric cancer (GC); a Phase 3 clinical trial in first-line patients with ESCC; and a Phase 2 clinical trial in second- or third-line patients with HCC. The aforementioned trials are enrolling patients in multiple countries, including the United States, Europe, and China.

In addition to a pivotal Phase 2 clinical trial in patients with relapsed or refractory (R/R) classical Hodgkin's lymphoma (cHL) and a pivotal Phase 2 clinical trial in patients with locally advanced or metastatic urothelial cancer, BeiGene is conducting a Phase 3 clinical trial in first-line patients with non-squamous NSCLC; a Phase 3 clinical trial in first-line patients with squamous NSCLC; a Phase 3 clinical trial in patients with first-line nasopharyngeal cancer (NPC); a Phase 3 clinical trial in first-line patients with urothelial

carcinoma (UC); a Phase 3 clinical trial in patients with localized ESCC; and a Phase 2 trial in patients with MSI-H or dMMR solid tumors. These studies have been enrolling patients primarily in China.

New drug applications (NDA) for tislelizumab in patients with R/R cHL and in patients with previously treated locally advanced or metastatic UC have been accepted and granted priority review by the China National Medical Products Administration (NMPA, formerly known as CFDA). BeiGene has full development and commercial rights to tislelizumab worldwide.

About Pamiparib

Pamiparib (BGB-290) is an investigational inhibitor of PARP1 and PARP2 which has demonstrated pharmacological properties such as brain penetration and PARP-DNA complex trapping in preclinical models. Discovered by BeiGene scientists in Beijing, pamiparib is currently in global clinical development as a monotherapy and in combination with other agents for a variety of solid tumor malignancies.

About BeiGene

BeiGene is a global, commercial-stage, research-based biotechnology company focused on molecularly-targeted and immuno-oncology cancer therapeutics. With a team of over 2,700 employees in China, the United States, Australia and Europe, BeiGene is advancing a pipeline consisting of novel oral small molecules and monoclonal antibodies for cancer. BeiGene is also working to create combination solutions aimed to have both a meaningful and lasting impact on cancer patients. BeiGene markets ABRAXANE[®] (nanoparticle albumin-bound paclitaxel), REVLIMID[®] (lenalidomide), and VIDAZA[®] (azacitidine) in China under a license from Celgene Corporation.¹

Forward-Looking Statements

This press release 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 ongoing clinical trials of tislelizumab and pamiparib, the mechanism of action of tislelizumab, BeiGene's advancement of, and anticipated clinical development, regulatory milestones and commercialization of tislelizumab and pamiparib. 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 filings with the U.S. Securities and Exchange Commission. All information in this press release is as of the date of this press release, and BeiGene undertakes no duty to update such information unless required by law.

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