
BeiGene Announces Clinical Results on Tislelizumab Presented at the 22nd Annual Meeting of the Chinese Society of Clinical Oncology (CSCO)

BEIJING, China and CAMBRIDGE, Mass., September 22, 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 results on its investigational anti-PD-1 antibody tislelizumab from three ongoing clinical trials in China. These new or updated data were presented in five of the seven oral presentations on tislelizumab at the 22nd Annual Meeting of the Chinese Society of Clinical Oncology (CSCO), taking place September 18-22, 2019 in Xiamen, China. Additional BeiGene clinical data being presented at CSCO include four poster presentations on tislelizumab, zanubrutinib, and pamiparib.

“Taken together these data show the potential for tislelizumab to benefit patients across a number of indications where we see unmet need in China and around the world,” said Yong (Ben) Ben, M.D., Chief Medical Officer, Immuno-Oncology at BeiGene. “In anticipation of our first regulatory approvals in China for tislelizumab in classical Hodgkin’s lymphoma and urothelial carcinoma, we are nearing the first stage of completion on our state-of-the art biologics manufacturing facility, which we expect will be a model for quality biologics manufacturing operations at a global scale.”

Clinical Results from a Phase 2 Trial of Tislelizumab Plus Chemotherapy as First-Line Treatment for Patients with Lung Cancer

This open-label, multi-cohort, Phase 2 trial of tislelizumab in combination with chemotherapy as first-line treatment for patients with advanced lung cancer (clinicaltrials.gov identifier: NCT03432598) is being conducted in China.

Patients with non-squamous non-small cell lung cancer (NSCLC) were treated with tislelizumab at a dose of 200mg and doublet chemotherapy on day one of each three-week cycle; chemotherapy was given for up to four cycles, with pemetrexed and tislelizumab continued as scheduled if clinically appropriate. Patients with squamous NSCLC (two cohorts) and small cell lung cancer (SCLC) were treated with tislelizumab at a dose of 200mg and doublet chemotherapy every three weeks, for four-six cycles, with tislelizumab continued as scheduled if clinically appropriate.

As of February 25, 2019, 54 patients had received tislelizumab, with a median duration of treatment of 38.4 weeks (3-79). Fourteen patients remained on treatment as of the data cutoff. Results included:



- The confirmed overall response rate (ORR) across all cohorts was 66.7% (n=36), with ORRs of 43.8% (7/16) in patients with non-squamous NSCLC; 80.0% (12/15) in patients with squamous NSCLC (cohort A); 66.7% (4/6) in patients with squamous NSCLC (cohort B); and 76.5% (13/17) in patients with SCLC;
- Median progression-free survival (PFS) was measured at a later data cutoff on June 30, 2019, and was 9.0 months in patients with non-squamous NSCLC, 7.0 months in squamous NSCLC (cohort A), 6.9 months in SCLC, and in squamous NSCLC (cohort B) the median PFS had not yet been reached;
- At the median follow-up of 15.3 months, overall survival (OS) in patients with SCLC was 15.6 months; OS in other cohorts had not yet been reached;
- Treatment-emergent adverse events (TEAEs) occurred in all 54 patients; adverse events (AEs) reported as related to tislelizumab occurred in 46 patients (85.2%), and seven patients (13%) discontinued tislelizumab treatment due to AEs;
- Grade ≥ 3 TEAEs occurred in 43 patients, with the most common being decreased neutrophil count (48.1%), anemia (18.5%), decreased white blood cell count (13%), decreased platelet count (13%), thrombocytopenia (11.1%), neutropenia (7.4%), and increased alanine aminotransferase (ALT; 5.6%).
- A total of 14 patients (25.9%) experienced at least one immune-related adverse event (irAE), with the most common being thyroid disorders (16.7%), immune-mediated pneumonitis (7.4%), and immune-mediated hepatitis (3.7%);
- The most common TEAEs of any grade reported to be related to tislelizumab included asthenia (18.5%); hypothyroidism (13%); decreased appetite (11.1%); increased ALT (11.1%); and increased aspartate aminotransferase (AST; 11.1%); and
- Fourteen patients (25.9%) experienced at least one serious TEAE; one patient with squamous NSCLC (cohort A) had a fatal AE of immune-mediated myositis/rhabdomyolysis/cardiomyopathy after one dose of tislelizumab.

Updated Clinical Results from a Phase 2 Trial of Tislelizumab in Combination with Chemotherapy in Patients with ESCC

This open-label, multi-cohort, Phase 2 trial of tislelizumab in combination with chemotherapy as first-line treatment for patients with advanced esophageal, gastric or gastroesophageal junction carcinoma (clinicaltrials.gov identifier: NCT03469557) is

being conducted in China. Updated results from the ESCC cohort were reported in an oral presentation at CSCO.

Patients were treated with tislelizumab at a dose of 200mg and cisplatin on day one, and fluorouracil (5-FU) on days one through five during each 21-day cycle. At the time of data cutoff on March 31, 2019, 15 patients with ESCC had received treatment with tislelizumab, and four remained on treatment. Results included:

- As of the data cutoff, seven patients achieved a confirmed partial response (PR) and the ORR was 46.7%;
- Median duration of response (DoR) was 12.8 months; median PFS was 10.4 months (5.6-15.1);
- Despite a median follow-up of 13.0 months, median OS had not been reached;
- AEs reported in this cohort were consistent with the safety profile of tislelizumab observed in previous studies with other tumor types and were generally of low severity; AEs reported in this cohort were consistent with the known tolerability profile of PD-1 inhibitors in combination with chemotherapy;
- The most common TEAEs were anemia (n=12) and decreased appetite (n=11)
- Five patients discontinued tislelizumab treatment due to TEAEs, including pneumonitis, tracheal fistula, increased AST, lung infection, and autoimmune dermatitis (n=1, each);
- Twelve patients (80%) experienced 23 irAEs, with the most common being rash (20%), pruritis (20%), increased AST (13.3%), increased ALT (13.3%), lung infection (13.3%), and autoimmune dermatitis (13.3%). The majority of irAEs were mild to moderate in severity; five grade ≥ 3 irAEs were reported in four patients (26.7%) and lung infection was the only irAE of grade ≥ 3 occurring in two patients (13.3%);
- The most common AEs of any grade reported to be related to tislelizumab included decreased appetite (66.7%), anemia (60%), nausea (40%), leukopenia (40%), decreased neutrophil count (40%), vomiting (33.3%), decreased weight (33.3%), decreased white blood cell count (33.3%), asthenia (33.3%), hypoalbuminemia (33.3%), and hyponatremia (33.3%);
- The most common grade > 3 AEs considered related to treatment with tislelizumab included vomiting (20%), hyponatremia (20%); anemia (13.3%); and leukopenia (13.3%);



- The only serious TEAE of any attribution occurring in more than one patient were dysphagia (n=3) and fatigue (n=2); one case of each was considered possibly related to tislelizumab; and
- One patient experienced a fatal AE of hepatic dysfunction, which was considered mainly related to progressive disease and also possibly related to study treatment or underlying type B hepatitis.

Clinical Results of Tislelizumab from a Phase 1/2 Trial in Patients with Advanced Solid Tumors

This multi-center, open-label Phase 1/2 trial of tislelizumab as monotherapy in patients with advanced solid tumors (chinadrugtrials.org registration number: CTR20160872) is being conducted in China and consists of a Phase 1 dose verification and pharmacokinetics component, and a Phase 2 indication expansion in disease-specific cohorts, including patients with non-small cell lung cancer (NSCLC), melanoma, urothelial carcinoma (UC), renal cell carcinoma (RCC), esophageal squamous cell carcinoma (ESCC), gastric cancer (GC), hepatocellular carcinoma (HCC), and microsatellite instability-high/mismatch repair deficient (MSI-H/dMMR) solid tumors.

As of December 1, 2018, 300 patients across all indications had been treated in this study with tislelizumab at a dose of 200mg every three weeks.

Safety Profile in All Indications (N=300):

- Tislelizumab was generally well tolerated among patients with advanced solid tumors;
- Most treatment-related adverse events (TRAEs) were grade ≤ 2 in severity, with the most common being anemia (23%), increased AST (22%), increased ALT (20%), proteinuria (14%), increased blood bilirubin (13%), hypothyroidism (11%), decreased white blood cell count (11%), increased conjugated bilirubin (11%) and pyrexia (10%);
- The most common grade ≥ 3 TRAEs were increased gammaglutamyl transferase (GGT) (4%), anemia (3%), and increased AST (3%);
- One patient with GC experienced a fatal brain edema, which was considered possibly related to tislelizumab treatment by the investigator;
- Most irAEs were grade ≤ 2 in severity, with the most common being increased AST/ALT (24%) and hyperbilirubinemia (15%); and



- The most common grade ≥ 3 irAEs were increased GGT (4%) and increased AST/ALT (3%).

Efficacy Profile:

Cohort	Patient Number (all evaluable for response)	Median Number of Prior Lines of Systemic Anti-Cancer Therapy	Median Follow-up (months)	Responses	Median OS (months)
NSCLC	56	2	9 (0-19)	ORR 18% <ul style="list-style-type: none"> 10 confirmed PRs 21 SDs 	Not reached; Median PFS was 4.0 (2.1-8.1)
Melanoma	34	2	8 (1-18)	ORR 15% <ul style="list-style-type: none"> 5 confirmed PRs 8 SDs 	11.3
UC	22	1	4.2 (1-22)	ORR 14% <ul style="list-style-type: none"> 3 confirmed PRs 6 SDs 	4.3
RCC	21	2	16 (3-18)	ORR 10% <ul style="list-style-type: none"> 2 confirmed PRs 9 SDs 	Not reached
ESCC	26	2	5 (2-19)	ORR 8% <ul style="list-style-type: none"> 2 confirmed PRs 7 SDs 	4.8
GC	24	2	6 (1-18)	ORR 17%	4.7



				<ul style="list-style-type: none"> • 4 confirmed PRs • 3 SDs 	
HCC	18 All patients had Child-Pugh A liver status. Sixteen patients had hepatitis B virus infection, one had hepatitis C virus infection, and one patient was uninfected	1.5	8 (3-17)	ORR 17% <ul style="list-style-type: none"> • 3 confirmed PRs • 7 SDs 	Not reached
MSI-H/dMMR Solid Tumor	16 (all evaluable for response) Among the 16 patients, 14 patients had colorectal carcinoma, one had GC and one had unknown primary tumor site	2	11 (2-17)	ORR 19% <ul style="list-style-type: none"> • 3 confirmed PRs • 5 SDs 	Not reached

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 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, the mechanism of action of tislelizumab, BeiGene's advancement of, and anticipated clinical development, regulatory milestones and commercialization of tislelizumab. 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.

Investor Contact

Craig West

+1 857-302-5189

ir@beigene.com

Media Contact

Liza Heapes

+1 857-302-5663

media@beigene.com

¹ ABRAXANE®, REVLIMID® and VIDAZA® are registered trademarks of Celgene Corporation.