BeiGene Announces Phase 1b Clinical Results of Zanubrutinib in Combination with GAZYVA® (Obinutuzumab) in Patients with Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma or Follicular Lymphoma at the 15th International Conference on Malignant Lymphoma (ICML)

CAMBRIDGE, Mass. and BEIJING, China, June 20, 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 results from an ongoing Phase 1b clinical study of its investigational BTK inhibitor zanubrutinib in combination with GAZYVA® (obinutuzumab) in patients with relapsed/refractory (R/R) or treatment naïve (TN) chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL), and patients with R/R follicular lymphoma (FL). These data were included in an oral presentation at the 15th International Conference on Malignant Lymphoma (ICML), taking place June 18-22, 2019 in Lugano, Switzerland.

“These updated data provide further evidence for the rational combination of zanubrutinib and obinutuzumab, and build upon the foundation supporting our global pivotal Phase 2 trial comparing obinutuzumab plus zanubrutinib to obinutuzumab alone as a treatment for patients with R/R follicular lymphoma. It is our hope that we will continue to see deep and durable responses for these patients,” said Jane Huang, M.D., Chief Medical Officer, Hematology, at BeiGene.

“These data demonstrated that zanubrutinib, in combination with the anti-CD20 monoclonal antibody obinutuzumab was generally well-tolerated, with the majority of adverse events being grade 1 or 2. In addition, the early finding of peripheral blood MRD negativity in three out of six patients with CLL/SLL merits further investigation,” commented Constantine S. Tam, M.D., Disease Group Lead for Low Grade Lymphoma and Chronic Lymphocytic Leukemia at the Peter MacCallum Cancer Center and Director of Hematology at St. Vincent’s Hospital, Australia, and presenting author of the trial.

Summary of Updated Clinical Results from the Phase 1b Combination Trial with Obinutuzumab in Patients with TN or R/R CLL/SLL and R/R FL

The open-label, Phase 1b trial (clinicaltrials.gov identifier: NCT02569476) of zanubrutinib in combination with obinutuzumab in patients with B-cell malignancies is being conducted in Australia, the United States, and South Korea, and consists of a dose-escalation phase and a dose-expansion phase in disease-specific cohorts, including patients with TN or R/R CLL/SLL and patients with R/R FL. The dose-

escalation component tested zanubrutinib at 320 mg once a day (QD) or 160 mg twice daily (BID) in 28-day cycles, in combination with obinutuzumab; obinutuzumab was administered in line with standard CLL dosing (three loading doses of 1000 mg weekly followed by 1000 mg on day one of cycles 2–6). Patients enrolled in the Phase 1b dose-expansion received zanubrutinib at 160 mg twice daily (BID) in 28-day cycles, in combination with obinutuzumab, which was administered with standard CLL dosing (three loading doses of 1000 mg weekly followed by 1000 mg on the first day of cycles 2–6). As of the February 28, 2019 data cutoff, a total of 81 patients with CLL/SLL or FL were enrolled in the trial, including 45 patients with CLL/SLL and 36 patients with FL. The primary endpoint of the expansion trial was investigator-assessed overall response rate (ORR) and duration of response (DOR) by standard 2007 International Working Group criteria.

As of the data cutoff, 51 patients (62.9%) remained on study treatment, including 33 patients (73.3%) with CLL/SLL and 18 patients (50%) with FL. The median follow-up time for patients with CLL/SLL was 28.9 months (7.9-36.9) and 20.1 months (2.3-37.2) for patients with FL. Results included:

- Of the 20 patients with TN CLL/SLL, the ORR was 100%; the complete response (CR) rate was 30.0% (6/20); and the partial response (PR) rate was 70.0% (14/20). Median follow-up for these patients was 28.8 months (13.9-34.8);
- Of the 25 patients with R/R CLL/SLL, the ORR was 92.0% (23/25); the CR was 28.0% (7/25); and the PR was 64.0% (16/25). Median follow-up for these patients was 28.9 months (7.9-36.9);
- Of the six patients with CLL/SLL who achieved CR and were tested, three were observed to be MRD negative in the peripheral blood;
- Of the 36 patients with R/R FL, the ORR was 72.2% (26/36); the CR was 38.9% (14/36); and the PR was 33.3% (12/36). Median response follow-up was 20.1 months (2.3-37.2);
- For patients with TN or R/R CLL/SLL the median progression free survival (PFS) had not been reached, with 73.3% of patients remaining on treatment. For patients with R/R FL, the median PFS was 24.9 months (0.7-36.4), with 50% of patients remaining on treatment;
- The majority of treatment-emergent adverse events (TEAEs) were grade 1 or 2 in severity;

- The most common TEAEs in patients with CLL/SLL were upper respiratory tract infection (URTI, 51.2%), neutropenia (44.4%), contusion (33.3%), fatigue (26.7%), and diarrhea (26.7%). The most common adverse events (AEs) in patients with FL were URTI (38.9%), contusion (27.8%), fatigue (25.0%), cough (22.2%), and thrombocytopenia (19.5%);
- The most common grade ≥3 AEs in patients with CLL/SLL were neutropenia (31.1%), pneumonia (8.9%), and thrombocytopenia (6.7%). The most common grade ≥3 AEs in patients with FL were neutropenia (13.9%), thrombocytopenia (5.6%), and back pain (2.8%); and
- One patient with CLL/SLL had a TEAE leading to death (metastatic squamous cell carcinoma).

About Zanubrutinib

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

Clinical trials of zanubrutinib include a fully-enrolled, global Phase 3 clinical trial in patients with Waldenström macroglobulinemia (WM) comparing zanubrutinib to ibrutinib, currently the only approved BTK inhibitor for WM; a global Phase 3 clinical trial in patients with previously untreated chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL); a pivotal Phase 2 trial in patients with relapsed/refractory (R/R) follicular lymphoma in combination with GAZYVA® (obinutuzumab); a Phase 3 trial comparing zanubrutinib to ibrutinib in patients with R/R CLL/SLL; and a global Phase 1 trial. In China, BeiGene has completed two pivotal Phase 2 clinical trials of zanubrutinib in patients with R/R MCL and R/R CLL/SLL and the enrollment in the pivotal Phase 2 clinical trials in patients with WM.

Zanubrutinib has been granted by the U.S. Food and Drug Administration (FDA) Fast Track designation for the treatment of patients with WM, and Breakthrough Therapy designation for the treatment of adult patients with MCL who have received at least one prior therapy. The New Drug Applications (NDAs) in China for R/R MCL and R/R CLL/SLL have been accepted by the China National Medical Products Administration (NMPA) and granted priority review. BeiGene plans to submit its first NDA in the U.S. for zanubrutinib in 2019 or early 2020.

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 2,500 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 the encouraging clinical data from clinical trials of zanubrutinib, and BeiGene's advancement of, and anticipated clinical development, regulatory milestones and commercialization of 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 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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