NEWS RELEASE

BeiGene to Present New Data from SEQUOIA Study Evaluating BRUKINSA® plus Venetoclax in High-Risk First-Line CLL/SLL at EHA2024

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Arm D of SEQUOIA study evaluated treatment-naïve patients with high-risk chronic lymphocytic leukemia or small lymphocytic lymphoma with del(17p) and/or TP53 mutation

Preliminary data suggest promising efficacy and tolerability

Safety profile was consistent with results of prior BRUKINSA studies

SAN MATEO, Calif.--(BUSINESS WIRE)-- BeiGene, Ltd. (NASDAQ: BGNE; HKEX: 06160; SSE: 688235), a global oncology company, announced the presentation of new data from the SEQUOIA study of BRUKINSA® (zanubrutinib) today at the European Hematology Association 2024 Hybrid Congress (EHA2024) in Madrid, Spain in an oral session (**Abstract S160**). The presentation will feature data from arm D of SEQUOIA evaluating BRUKINSA in combination with venetoclax in treatment-naïve (TN) patients with high-risk chronic lymphocytic leukemia (CLL) and/or small lymphocytic lymphoma (SLL) with del(17p) and/or TP53 mutation. The preliminary data demonstrate that in the 65 response-evaluable patients treated with the combination, the overall response rate (ORR) was 100%, and the rate of complete response (CR) plus CR with incomplete hematopoietic recovery (CRi) was 48%. The safety profile of the combination is consistent with that of the treatment components, and no new safety signals were seen.

“Patients with untreated CLL with del(17p) or TP53 mutations often face a poor prognosis, even in the front-line setting, so there is a critical need to better understand how this patient population responds to combination approaches,” said Alessandra Tedeschi, M.D., Ph.D., consultant in hematology and Medical Director of the Department of Hematology at the Niguarda Cancer Center in Milan, Italy. “This arm of the SEQUOIA study showed

that zanubrutinib in combination with a BCL2 inhibitor demonstrates promising efficacy and tolerability for high-risk CLL patients, providing important information about the clinical profile of this regimen."

Overall, 66 patients with centrally assessed del(17p) and/or TP53 mutation were enrolled in this arm of the SEQUOIA study. Patients received BRUKINSA at 160 mg twice daily for three months, followed by combination treatment of BRUKINSA at the same dose and venetoclax with a ramp-up dosing to 400 mg once daily for 12 to 24 cycles until progressive disease, unacceptable toxicity or confirmed undetectable minimal residual disease (MRD). In the 65 response-evaluable patients, ORR was 100%; the rate of CR+CRi was 48% (CR=46%; CRi=2%). Undetectable MRD was achieved in 59% of patients in ≥1 peripheral blood sample and with a median study follow up of 31.6 months. Median progression-free survival (PFS) was not reached; 12- and 24-month PFS estimates were 95% and 94%, respectively.

"SEQUOIA has shown that BRUKINSA is a highly effective monotherapy treatment for TN CLL patients, including those with high-risk markers like del(17p) and/or TP53 mutation. With one of the largest pools of high-risk patients of any published study to date, SEQUOIA arm D demonstrates how BCL2 inhibitor therapies can complement BRUKINSA as a backbone therapy to achieve deep clinical response even in this patient population," said Mehrdad Mobasher, M.D., M.P.H., Chief Medical Officer, Hematology at BeiGene. "We look forward to evaluating the potential for time-limited therapy with longer follow-up and incorporating these findings into our development program for our investigational next-generation BCL2 inhibitor sonrotoclax."

The safety profile of BRUKINSA plus venetoclax was consistent with results of prior studies of both medicines, and no new safety signals were identified. In total, 97% of patients experienced ≥1 treatment emergent adverse effect (TEAE). The most common all-grade non-hematologic TEAEs were infections (71%), COVID-19 (55%), diarrhea (39%), nausea (30%) and contusion (29%). Grade ≥3 non-hematologic TEAEs occurred in 44% of patients; the most common were infections (15%), diarrhea (9%), hypertension (8%) and second primary malignancies (8%). The most common all grade and grade ≥3 hematologic toxicity was neutropenia (22% and 17%, respectively). The proportion of patients at high risk for tumor lysis syndrome (TLS) decreased 91% from 35% at screening to 3% after three cycles of lead-in BRUKINSA, and no TLS was reported.

About SEQUOIA

SEQUOIA (**NCT03336333**) is a randomized, multicenter, global Phase 3 trial designed to evaluate the efficacy and safety of BRUKINSA in patients with TN CLL or SLL. The trial consists of three cohorts:

- Cohort 1 (n=479): randomized 1:1 to receive BRUKINSA (n=241) or bendamustine plus rituximab (n=238) until disease progression or unacceptable toxicity, in patients not harboring del(17p); data from this group comprise the primary endpoint;

- Cohort 2 (n=110): patients with del(17p) receiving BRUKINSA as a monotherapy; and
- Cohort 3/arm D (n=114): 66 patients with del(17p) and/or pathogenic TP53 mutation received BRUKINSA in combination with venetoclax. While patients without del(17p) (n=48) were later included in this cohort, the data presented at EHA2024 do not include these patients.

The results of Cohort 1 of the SEQUOIA study led to the regulatory approval of zanubrutinib monotherapy in the treatment of TN CLL in many countries across the world, including approvals by the U.S. Food and Drug Administration and the European Medicines Agency. Patients with del(17p) were not randomized in the Cohort 1 study, as these patients are known to experience poor clinical outcomes and poor response to chemoimmunotherapy, the control arm of the study. The primary endpoint of the trial is independent review committee-assessed PFS. Secondary endpoints include investigator-assessed PFS, IRC- and investigator-assessed ORR, overall survival, PFS and ORR in patients with del(17p), and safety. Results for Cohort 2 (arm C), representing high-risk patients treated with BRUKINSA monotherapy, were presented at the 62nd ASH Annual Meeting in December 2020.1 This cohort of patients with del(17p) achieved significant efficacy, with an 18-month PFS of 90.6%, as assessed by investigator. Full study results were published in **Lancet Oncology** .2

About BRUKINSA® (zanubrutinib)

BRUKINSA is a small molecule inhibitor of Bruton's tyrosine kinase (BTK) designed to deliver complete and sustained inhibition of the BTK protein by optimizing bioavailability, half-life, and selectivity. With differentiated pharmacokinetics compared with other approved BTK inhibitors, BRUKINSA has been demonstrated to inhibit the proliferation of malignant B cells within a number of disease-relevant tissues.

U.S. Indications and Important Safety Information for BRUKINSA (zanubrutinib)

INDICATIONS

BRUKINSA is a kinase inhibitor indicated for the treatment of adult patients with:

- Chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL).
- Waldenström's macroglobulinemia (WM).
- Mantle cell lymphoma (MCL) who have received at least one prior therapy.
- Relapsed or refractory marginal zone lymphoma (MZL) who have received at least one anti-CD20-based regimen.
- Relapsed or refractory follicular lymphoma (FL), in combination with obinutuzumab, after two or more lines of systemic therapy.

The MCL, MZL and FL indications are approved under accelerated approval based on overall response rate and

durability of response. Continued approval for these indications may be contingent upon verification and description of clinical benefit in confirmatory trials.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions

Hemorrhage

Fatal and serious hemorrhage has occurred in patients with hematological malignancies treated with BRUKINSA. Grade 3 or higher hemorrhage including intracranial and gastrointestinal hemorrhage, hematuria, and hemothorax was reported in 3.8% of patients treated with BRUKINSA in clinical trials, with fatalities occurring in 0.2% of patients. Bleeding of any grade, excluding purpura and petechiae, occurred in 32% of patients.

Bleeding has occurred in patients with and without concomitant antiplatelet or anticoagulation therapy. Coadministration of BRUKINSA with antiplatelet or anticoagulant medications may further increase the risk of hemorrhage.

Monitor for signs and symptoms of bleeding. Discontinue BRUKINSA if intracranial hemorrhage of any grade occurs. Consider the benefit-risk of withholding BRUKINSA for 3-7 days before and after surgery depending upon the type of surgery and the risk of bleeding.

Infections

Fatal and serious infections (including bacterial, viral, or fungal infections) and opportunistic infections have occurred in patients with hematological malignancies treated with BRUKINSA. Grade 3 or higher infections occurred in 26% of patients, most commonly pneumonia (7.9%), with fatal infections occurring in 3.2% of patients. Infections due to hepatitis B virus (HBV) reactivation have occurred.

Consider prophylaxis for herpes simplex virus, pneumocystis jirovecii pneumonia, and other infections according to standard of care in patients who are at increased risk for infections. Monitor and evaluate patients for fever or other signs and symptoms of infection and treat appropriately.

Cytopenias

Grade 3 or 4 cytopenias, including neutropenia (21%), thrombocytopenia (8%) and anemia (8%) based on laboratory measurements, developed in patients treated with BRUKINSA. Grade 4 neutropenia occurred in 10% of patients, and Grade 4 thrombocytopenia occurred in 2.5% of patients.

Monitor complete blood counts regularly during treatment and interrupt treatment, reduce the dose, or discontinue treatment as warranted. Treat using growth factor or transfusions, as needed.

Second Primary Malignancies

Second primary malignancies, including non-skin carcinoma, have occurred in 14% of patients treated with BRUKINSA. The most frequent second primary malignancy was non-melanoma skin cancers (8%), followed by other solid tumors in 7% of the patients (including melanoma in 1% of patients) and hematologic malignancies (0.7%). Advise patients to use sun protection and monitor patients for the development of second primary malignancies.

Cardiac Arrhythmias

Serious cardiac arrhythmias have occurred in patients treated with BRUKINSA. Atrial fibrillation and atrial flutter were reported in 4.4% patients treated with BRUKINSA, including Grade 3 or higher cases in 1.9% of patients. Patients with cardiac risk factors, hypertension, and acute infections may be at increased risk. Grade 3 or higher ventricular arrhythmias were reported in 0.3% of patients.

Monitor for signs and symptoms of cardiac arrhythmias (e.g., palpitations, dizziness, syncope, dyspnea, chest discomfort), manage appropriately, and consider the risks and benefits of continued BRUKINSA treatment.

Hepatotoxicity, Including Drug-Induced Liver Injury

Hepatotoxicity, including severe, life-threatening, and potentially fatal cases of drug-induced liver injury (DILI), has occurred in patients treated with Bruton tyrosine kinase inhibitors, including BRUKINSA.

Evaluate bilirubin and transaminases at baseline and throughout treatment with BRUKINSA. For patients who develop abnormal liver tests after BRUKINSA, monitor more frequently for liver test abnormalities and clinical signs and symptoms of hepatic toxicity. If DILI is suspected, withhold BRUKINSA. Upon confirmation of DILI, discontinue BRUKINSA.

Embryo-Fetal Toxicity

Based on findings in animals, BRUKINSA can cause fetal harm when administered to a pregnant woman. Administration of zanubrutinib to pregnant rats during the period of organogenesis caused embryo-fetal toxicity, including malformations at exposures that were 5 times higher than those reported in patients at the recommended dose of 160 mg twice daily. Advise women to avoid becoming pregnant while taking BRUKINSA and

for 1 week after the last dose. Advise men to avoid fathering a child during treatment and for 1 week after the last dose. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to a fetus.

Adverse Reactions

The most common adverse reactions (≥30%), including laboratory abnormalities, in patients who received BRUKINSA (N=1729) are decreased neutrophil count (51%), decreased platelet count (41%), upper respiratory tract infection (38%), hemorrhage (32%), and musculoskeletal pain (31%).

Drug Interactions

CYP3A Inhibitors: When BRUKINSA is co-administered with a strong CYP3A inhibitor, reduce BRUKINSA dose to 80 mg once daily. For coadministration with a moderate CYP3A inhibitor, reduce BRUKINSA dose to 80 mg twice daily.

CYP3A Inducers: Avoid coadministration with strong or moderate CYP3A inducers. Dose adjustment may be recommended with moderate CYP3A inducers.

Specific Populations

Hepatic Impairment: The recommended dose of BRUKINSA for patients with severe hepatic impairment is 80 mg orally twice daily.

Please see full **U.S. Prescribing Information** including **U.S. Patient Information** .

This information is intended for a global audience. Product indications vary by region.

About BeiGene

BeiGene is a global oncology company that is discovering and developing innovative treatments that are more affordable and accessible to cancer patients worldwide. With a broad portfolio, we are expediting development of our diverse pipeline of novel therapeutics through our internal capabilities and collaborations. We are committed to radically improving access to medicines for far more patients who need them. Our growing global team of more than 10,000 colleagues spans five continents. To learn more about BeiGene, please visit **www.beigene.com** and follow us on **LinkedIn**, **X** (formerly known as Twitter), and **Facebook**.

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 efficacy and tolerability of zanubrutinib in combination with a BCL2 inhibitor for high-risk CLL patients; BRUKINSA's ability to complement BCL2 therapies to achieve clinical response in high-risk CLL patients; the future progression of the SEQUOIA trial; and BeiGene's plans, commitments, aspirations, and goals under the heading "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, commercialization, and other services; BeiGene's limited experience in obtaining regulatory approvals and commercializing pharmaceutical products; BeiGene's ability to obtain additional funding for operations and to complete the development of its drug candidates and achieve and maintain profitability; and 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.

To access BeiGene media resources, please visit our **News & Media** site.

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1 Tam CS, Giannopoulos K, Jurczak W, et al. SEQUOIA: Results of a Phase 3 Randomized Study of Zanubrutinib versus Bendamustine + Rituximab (BR) in Patients with Treatment-Naïve (TN) Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL), Blood. 2021;138(Supplement 1, p396) doi:10.1182/blood-2021-148457

2 Tam CS, Brown JR, Kahl BS, et al. Zanubrutinib versus bendamustine and rituximab in untreated chronic lymphocytic leukaemia and small lymphocytic lymphoma (SEQUOIA): a randomised, controlled, phase 3 trial. Lancet Oncology. 2022;23(8):1031-1043. doi:10.1016/S1470-2045(22)00293-5.

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