BRUKINSA® Approved in the U.S. for Chronic Lymphocytic Leukemia

Two global Phase 3 trials in adult CLL patients demonstrated superior efficacy for BRUKINSA (zanubrutinib) in first-line and relapsed/refractory treatment settings

BRUKINSA is the only BTKi to demonstrate superior PFS vs IMBRUVICA® (ibrutinib)

BASEL & BEIJING & CAMBRIDGE, Mass. – January 19, 2023 – BeiGene (NASDAQ: BGNE; HKEX: 06160; SSE: 688235), a global biotechnology company, today announced that the U.S. Food and Drug Administration (FDA) has approved its Bruton's tyrosine kinase inhibitor (BTKi) BRUKINSA (zanubrutinib) for the treatment of adult patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL).

"With four US approvals in just over three years and demonstrated superiority versus ibrutinib in the final progression-free survival (PFS) analysis of the ALPINE trial, we believe BRUKINSA is well-positioned to become the BTKi of choice across multiple indications," said Mehrdad Mobasher, M.D., M.P.H., Chief Medical Officer, Hematology at BeiGene. "We're grateful to the patients who participated in the ALPINE and SEQUOIA studies; and with this new approval, we're excited to expand our impact to even more patients."

The U.S. approval is based on two global Phase 3 clinical trials demonstrating superior efficacy and a favorable safety profile for BRUKINSA in CLL:

- With a median follow-up of 26.2 months in the SEQUOIA trial, BRUKINSA demonstrated a significant PFS benefit versus bendamustine plus rituximab, (HR 0.42, [95% CI: 0.28, 0.63], P<0.0001), as assessed by an Independent Review Committee (IRC) in the first-line treatment setting.[1]
- BRUKINSA achieved a superior overall response rate versus ibrutinib in the relapsed/refractory (R/R) treatment setting (ORR 80.4% vs 72.9%, P=0.0264), as assessed by an IRC in the ALPINE trial.[2]
- The overall safety profile of BRUKINSA in the ALPINE and SEQUOIA trials was consistent with prior studies.

In the pooled safety population of CLL patients who received BRUKINSA across the clinical development program (N=1,550), the most common adverse reactions (≥30%), were decreased neutrophil count (42%), upper respiratory tract infection (39%), decreased platelet count (34%), hemorrhage (30%), and musculoskeletal pain (30%).[3]

The pre-defined final PFS analysis of the ALPINE study demonstrating superior efficacy and a favorable cardiac safety profile for BRUKINSA versus IMBRUVICA in patients with R/R CLL, was presented in a late-breaking session at the 64th Annual American Society for Hematology (ASH) Meeting and published simultaneously in The New England Journal of Medicine. With a median follow-up of 29.6 months, BRUKINSA demonstrated superior PFS compared with ibrutinib in patients with R/R CLL (HR: 0.65 [95% CI, 0.49-0.86] P=.0024, for both investigator and IRC). Additionally, BRUKINSA demonstrated a favorable cardiac safety profile, with significantly lower rates of atrial fibrillation/flutter (5.2% vs 13.3%) and zero deaths due to cardiac disorders with BRUKINSA vs. six with ibrutinib (0% vs 1.9%).[4,5]

Jennifer R. Brown, M.D., Ph.D., Director of the CLL Center of the Division of Hematologic Malignancies at Dana-Farber Cancer Institute, commented "We have seen striking data from the

BRUKINSA development program demonstrating significant and consistent efficacy across CLL patient sub-types, including the high-risk del17p/*TP53* mutated population, and regardless of treatment setting. With extensive follow-up across the CLL development program and the combined results from the SEQUOIA and ALPINE trials, BRUKINSA is established as a new standard of care for CLL."

"Thanks to research that has delivered innovative and effective medicines, people with CLL can remain on therapy for years so tolerability is an important consideration. I'm pleased that the approval of zanubrutinib provides a new BTKi option for people with CLL/SLL, with demonstrated efficacy as well as being very well tolerated long-term," said Brian Koffman, M.D., Chief Medical Officer and Executive Vice-President at CLL Society.

About ALPINE

ALPINE is a randomized, global Phase 3 trial (NCT03734016) comparing BRUKINSA against ibrutinib in previously treated patients with relapsed or refractory chronic lymphocytic leukemia CLL or SLL. In the trial, a total of 652 patients across Europe (60%), the United States (17%), China (14%), and New Zealand and Australia (9%) were randomized into two arms, with the first arm receiving BRUKINSA (160 mg orally twice daily) and the second arm receiving ibrutinib (420 mg orally once daily) until disease progression or unacceptable toxicity.

The primary endpoint of ORR, defined by pre-specified non-inferiority of BRUKINSA versus ibrutinib, was assessed by investigator and IRC using the modified 2008 iwCLL guidelines, with modification for treatment-related lymphocytosis for patients with CLL, and per Lugano Classification for non-Hodgkin's lymphoma for patients with SLL. There was pre-specified hierarchical testing of non-inferiority followed by superiority in ORR as assessed by investigator and IRC. Key secondary endpoints include PFS and event rate of atrial fibrillation or flutter; other secondary endpoints include duration of response, overall survival, and incidence of adverse events.

Interim study results from ALPINE were published online in the Journal of Clinical Oncology in November 2022 and the final pre-defined PFS analysis was presented in a late-breaking session at the 64th Annual American Society for Hematology (ASH) Meeting and published simultaneously in The New England Journal of Medicine.[4,5]

About SEQUOIA

SEQUOIA is a randomized, multicenter, global Phase 3 trial (NCT03336333) designed to evaluate the efficacy and safety of BRUKINSA compared to bendamustine + rituximab (B+R) in patients with treatment-naïve CLL or SLL. The trial consists of three cohorts:

- Cohort 1 (n=479): randomized 1:1 to receive BRUKINSA (n=241) or B+R (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 (enrollment ongoing): patients with del(17p) or pathogenic TP53 variant receiving BRUKINSA in combination with venetoclax.

Patients with del(17p) were not randomized to Cohort 1, as they experience poor clinical outcomes and poor response to chemoimmunotherapy. The primary endpoint of the trial is IRC-

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.[6] 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.[1]

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IMPORTANT SAFETY INFORMATION

Warnings and Precautions

Hemorrhage

Fatal and serious hemorrhage has occurred in patients with hematological malignancies treated with BRUKINSA monotherapy. Grade 3 or higher hemorrhage, including intracranial and gastrointestinal hemorrhage, hematuria and hemothorax have been reported in 3.6% of patients treated with BRUKINSA monotherapy in clinical trials, with fatalities occurring in 0.3% of patients. Bleeding of any grade, excluding purpura and petechiae, occurred in 30% 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 pre- and post-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 monotherapy. Grade 3 or higher infections occurred in 24% of patients, most commonly pneumonia (11%), with fatal infections occurring in 2.9% 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 (22%), thrombocytopenia (8%) and anemia (7%) based on laboratory measurements, developed in patients treated with BRUKINSA monotherapy.

Grade 4 neutropenia occurred in 11% of patients, and Grade 4 thrombocytopenia occurred in 2.8% 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 13% of patients treated with BRUKINSA monotherapy. The most frequent second primary malignancy was non-melanoma skin cancer reported in 7% of patients. Other second primary malignancies included malignant solid tumors (5%), melanoma (1.2%), and hematologic malignancies (0.5%). 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 3.7% of 1550 patients treated with BRUKINSA monotherapy, including Grade 3 or higher cases in 1.7% 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 0.2% 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.

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

In this pooled safety population, the most common adverse reactions, including laboratory abnormalities, in ≥30% of patients who received BRUKINSA (N=1550) included decreased neutrophil count (42%), upper respiratory tract infection (39%), decreased platelet count (34%), hemorrhage (30%), and musculoskeletal pain (30%).

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.

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

The MCL and MZL indications are approved under accelerated approval based on overall response rate. Continued approval for these indications may be contingent upon verification and description of clinical benefit in confirmatory trials.

Please see full Prescribing Information at www.beigene.com/PDF/BRUKINSAUSPI.pdf **and Patient Information at** www.beigene.com/PDF/BRUKINSAUSPPI.pdf

About BeiGene

BeiGene is a global biotechnology company that is developing and commercializing innovative and affordable oncology medicines to improve treatment outcomes and access for far more 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 9,000 colleagues spans five continents, with administrative offices in Beijing, China; Cambridge, U.S.; and Basel, Switzerland. To learn more about BeiGene, please visit www.beigene.com and follow us on Twitter at @BeiGeneGlobal.

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 potential for BRUKINSA to provide clinical benefit to patients with CLL/SLL, the future development, regulatory filing and approval, commercialization, and market access of BRUKINSA in the U.S. and other markets, 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, 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; and 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 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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[3] US Prescribing Information www.beigene.com/PDF/BRUKINSAUSPI.pdf

[4] Brown JR, Eichhorst, B, Hillmen, P., et al.. (2022). Zanubrutinib or Ibrutinib in Relapsed or Refractory Chronic Lymphocytic Leukemia. *New England Journal of Medicine*. doi:10.1056/NEJMoa2211582

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