BeiGene Announces FDA Accelerated Approval of BRUKINSA for the Treatment of Relapsed or Refractory Follicular Lymphoma

BRUKINSA is the first and only BTK inhibitor approved across five oncology indications and the first and only approved in follicular lymphoma

Approval based on positive results from ROSEWOOD trial showing BRUKINSA plus obinutuzumab achieved higher overall response rate versus obinutuzumab alone

BASEL, Switzerland & BEIJING & CAMBRIDGE, Mass., --- March 7, 2024---BeiGene, Ltd. (Nasdaq: BGNE; HKEX: 06160; SSE: 688235), a global oncology company, today announced that the U.S. Food and Drug Administration (FDA) has granted accelerated approval to BRUKINSA® (zanubrutinib) for the treatment of adult patients with relapsed or refractory (R/R) follicular lymphoma (FL), in combination with the anti-CD20 monoclonal antibody obinutuzumab, after two or more lines of systemic therapy. The indication is approved under accelerated approval based on response rate and durability of response, marking BRUKINSA's fifth indication in B-cell malignancies in the U.S.

"This accelerated approval of BRUKINSA represents an important advancement, offering the first and only BTK inhibitor treatment for follicular lymphoma patients in the U.S. who have either not responded to initial therapies or have experienced relapse," said Mehrdad Mobasher, M.D., M.P.H., Chief Medical Officer, Hematology at BeiGene. "BRUKINSA is the only BTK inhibitor to date that shows efficacy with this type of malignancy and now has the broadest label, including five oncology indications, of any medication in its class globally. This is a testament to BRUKINSA's differentiated clinical profile and our continued commitment to bringing this much-needed treatment option to patients around the world."

BRUKINSA was approved for the treatment of R/R FL under the FDA's accelerated approval program based on the overall response rate (ORR) from the ROSEWOOD trial (NCT03332017), as assessed by an independent review committee (IRC). Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory MAHOGANY (NCT05100862) trial, which is underway. The application for R/R FL was also granted Fast Track Designation and Orphan Drug Designation by the FDA.

The ROSEWOOD trial is a global, randomized, open-label Phase 2 study of BRUKINSA plus obinutuzumab compared with obinutuzumab alone in 217 patients with R/R FL who received at least two prior lines of systemic therapy. In the study, the ORR by IRC was 69% in the BRUKINSA plus obinutuzumab arm versus 46% in the obinutuzumab arm (P=0.0012), with a median follow-up of approximately 20 months. Responses were durable, with an 18-month landmark duration of response (DOR) of 69% in the BRUKINSA combination arm.[i]

BRUKINSA plus obinutuzumab was generally well-tolerated, with safety results consistent with previous studies of both medicines.[i] Serious adverse reactions occurred in 35% of patients who received BRUKINSA in combination with obinutuzumab. Adverse reactions led to permanent discontinuation of BRUKINSA in 17% of patients.

Christopher Flowers, M.D., Division Head of Cancer Medicine and Chair of the Department of Lymphoma/Myeloma, The University of Texas MD Anderson Cancer Center commented, "Patients living with follicular lymphoma often experience relapse or do not respond to treatment and need options for treatment during the course of their illness. The findings from the ROSEWOOD trial highlight the significant clinical advantage of treating patients who experience relapse or have refractory follicular lymphoma with zanubrutinib plus obinutuzumab."

“Follicular lymphoma can significantly impact patients' lives and prove to be challenging, especially for those whose condition has advanced despite undergoing prior treatment or experienced relapse,” said the Follicular Lymphoma Foundation. “However, the emergence of new treatment options which have been shown to be effective and well-tolerated, including second generation BTK inhibitors such as zanubrutinib in combination with existing therapies, brings hope to those dealing with advanced follicular lymphoma.”

In addition to R/R FL, BRUKINSA is also approved in the U.S. as a treatment for adult patients with Waldenström’s macroglobulinemia; mantle cell lymphoma, who have received at least one prior therapy, R/R marginal zone lymphoma, who have received at least one anti-CD20-based regimen; and most recently chronic lymphocytic leukemia or small lymphocytic lymphoma. BRUKINSA is the first and only BTK inhibitor to demonstrate PFS superiority in a head-to-head clinical trial versus ibrutinib in patients with R/R CLL in the global Phase 3 ALPINE trial. In a recent presentation, BRUKINSA showed sustained PFS benefit versus ibrutinib in a longer term follow up. Durable PFS was observed across major subgroups, including in the high-risk 17p deletion/TP53 mutated patient population.

BRUKINSA is approved in 70 markets, including the U.S., EU, Great Britain, Canada, Australia, China, South Korea and Switzerland in selected indications, and it is under development for additional indications globally. The global BRUKINSA development program includes more than 5,000 subjects enrolled to date in 29 countries and regions.

About Follicular Lymphoma
Follicular lymphoma (FL) is the second most common type of non-Hodgkin lymphoma (NHL), accounting for 22% of all NHL cases.[ii] Approximately 15,000 cases are diagnosed in the U.S. each year.[iii] While FL remains incurable, people with the condition can live a long time. The five-year survival rate is about 90%, and approximately half of people diagnosed with FL can live with the disease for nearly 20 years.[iv]

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.

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**.**

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, with administrative offices in Basel, Beijing, and Cambridge, U.S. To learn more about BeiGene, please visit www.beigene.com and follow us on LinkedIn and X (formerly known as Twitter).

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 BeiGene's ability and commitment to bring BRUKINSA to patients around the world; the significance of the clinical advantages of treating R/R FL patients with BRUKINSA plus obinutuzumab; BeiGene's advancement, anticipated clinical development, regulatory submissions and commercialization of zanubrutinib, particularly as a treatment for R/R FL; 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 annual report on Form 10-K, 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.

References

[i] Zinsani PL, et al. ROSEWOOD: A Phase II Randomized Study of Zanubrutinib Plus Obinutuzumab Versus Obinutuzumab Monotherapy in Patients With Relapsed or Refractory Follicular Lymphoma. *J Clin Oncol*. 2023;41(33):5107-5117.

[ii] Leukemia & Lymphoma Society. Treatment for Indolent NHL Subtypes. Accessed February 16, 2024. Available at: https://www.lls.org/lymphoma/non-hodgkin-lymphoma/nhl-subtypes/treatment-indolent-nhl-subtypes.

[iii] Leukemia & Lymphoma Society. Follicular Lymphoma (FL). Accessed February 16, 2024. Available at: https://www.lls.org/research/follicular-lymphoma-fl#:~:text=FL%20has%20an%20annual%20incidence,having%20a%20higher%20survival%20rate.

[iv] Cleveland Clinic. Follicular Lymphoma. March 25, 2022. Accessed February 16, 2024. Available at: https://my.clevelandclinic.org/health/diseases/22606-follicular-lymphoma.

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