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# BeiGene cancer drug misses mark in Phase III study

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**BeiGene Announces Results of Phase 3 ASPEN Trial of Zanubrutinib Compared to Ibrutinib for the Treatment of Patients with WaldenstrÃ?Â¶m's Macroglobulinemia**




China based BeiGene, a commercial-stage biopharmaceutical company focused on developing and commercializing innovative molecularly-targeted and immuno-oncology drugs for the treatment of cancer, has announced results from the Phase 3 ASPEN trial comparing its BTK inhibitor BRUKINSA™ (zanubrutinib) to ibrutinib for the treatment of Waldenström's macroglobulinemia (WM). While the trial did not achieve statistical significance on its primary endpoint of superiority in complete response (CR) and very good partial response (VGPR) rates for zanubrutinib compared to ibrutinib, zanubrutinib demonstrated a higher VGPR rate as well as improvements in safety and tolerability in this first randomized comparative trial to read out within the BTK inhibitor class.

The ASPEN trial is a randomized Phase 3 trial in 229 patients with WM conducted in 61 centers in Europe, Australia, and the United States. The study includes two cohorts, a randomized cohort (cohort 1) consisting of 201 patients with a MYD88 mutation and a non-randomized cohort (cohort 2) in which 28 patients with MYD88 wild-type (MYD88WT) received zanubrutinib because they have historically responded poorly to ibrutinib therapy. The randomized cohort 1 enrolled 102 patients (including 83 relapsed or refractory (R/R) patients and 19 treatment-naïve (TN) patients) in the zanubrutinib arm and 99 patients (including 81 R/R patients and 18 TN patients) in the ibrutinib arm. Patients in the zanubrutinib arm were assigned to receive zanubrutinib 160 mg twice daily (BID) and patients in the ibrutinib arm received 420 mg of ibrutinib once daily (QD).

“Our researchers sought to design a BTK inhibitor that would improve efficacy and decrease side effects in patients by maximizing BTK inhibition and minimizing off-target binding. We took a bold approach to our clinical development plan by evaluating zanubrutinib directly against ibrutinib in patients with WM and are encouraged by the improvements in VGPR rates and safety,” said Jane Huang, M.D., Chief Medical BeiGene, Ltd. 4 Officer, Hematology at BeiGene.

“The ASPEN trial, which was the largest prospective trial for patients with WM ever run, showed consistent safety advantages for patients treated with zanubrutinib compared to ibrutinib. While falling short of a statistically significant improvement in CR and VGPR, we believe the trial demonstrated that zanubrutinib is a highly potent BTK inhibitor that has clinical benefit and trends toward increased response quality.” Dr. Huang continued, “Today's results are consistent with what we know about zanubrutinib from our broad clinical development program – that it is a more selective BTK inhibitor with beneficial pharmacokinetics designed to provide deep, meaningful responses for many patients. We plan to discuss our findings with regulatory authorities in the U.S. and Europe and plan to submit these data for presentation, with additional analysis, to an

upcoming medical meeting. In addition, we will continue to evaluate zanubrutinib compared to ibrutinib in our ongoing Phase 3 ALPINE trial in patients with relapsed/refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL)."

"WM is a devastating and incurable disease with significant morbidity. These meaningful results help us advance the understanding of the role of BTK specificity and off-target effects during treatment," said 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 a member of the steering committee and principal investigator for the ASPEN trial. "Despite not reaching the primary endpoint, 28.4% of zanubrutinib patients achieved VGPR as compared to 19.2% in the ibrutinib arm, and zanubrutinib had a more favorable safety profile, suggesting improved clinical benefit for zanubrutinib over standard BTKi therapy in the treatment of patients with WM."