Title: Phase 2 Obinutuzumab ± Zanubrutinib (BGB-3111) in Patients with Relapsed/Refractory Follicular Lymphoma (R/R FL)

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Background: Bruton's tyrosine kinase (BTK) plays a critical role in B-cell receptor signaling, which mediates B-cell proliferation, migration and adhesion. Inhibition of BTK has emerged as a strategy for targeting B-cell malignancies including CLL/SLL. Zanubrutinib has been shown to be a novel 2nd-generation, potent, and specific BTK inhibitor in clinical studies to date. Early clinical data suggest that zanubrutinib plus obinutuzumab (ob) in patients (pts) with R/R FL induced deep and sustained responses and was generally well tolerated, with an overall response rate (ORR) of 76.2% (Tam ASH 2017). We hypothesize that zanubrutinib + ob may have superior efficacy and potentially improved safety in pts with R/R FL.

Methods: This ongoing Phase 2, global, randomized, open label, active-controlled study (NCT03332017, BGB-3111-212) examines zanubrutinib + ob and ob monotherapy in pts with R/R FL with ≥2 prior lines of therapy (210 pts in 16 countries). Pts are randomized 2:1 to receive oral zanubrutinib 160 mg twice-daily + ob per the package insert (1000 mg IV on days 1, 8, and 15 of cycle 1 [28-d cycles], day 1 of cycles 2 to 6, then every 8 weeks) or ob alone (same dosing) until progressive disease (PD), toxicity, or max 30 mo for ob monotherapy. Randomization is stratified by prior therapies (2-3 vs > 3) and rituximab refractory status. Eligible pts must have histologically-confirmed Grade 1-3a B-cell FL, prior anti-CD20 antibody and alkylator-based combination therapy, and measurable disease. Disease response is assessed per the Lugano Classification for Non-Hodgkin Lymphoma. The primary endpoint is ORR determined by independent review committee (IRC). The analysis of ORR by IRC will be based on a Cochran-Mantel-Haenszel test adjusted for the randomization factors. Key secondary endpoints include ORR by investigator assessment, rate of complete response or complete metabolic response, time to and duration of response, progression-free and overall survival (all IRC and investigator assessment) and safety. At the discretion of the investigator, pts in the ob arm can crossover to the combination arm with PD or < partial response after 12 cycles. Study enrollment is ongoing.