Efficacy, Safety, and Pharmacokinetics of the Anti-Programmed Cell Death Receptor-1 Monoclonal Antibody, Tislelizumab (BGB-A317), in a Phase 2, Open-label, Multicenter Study in Patients with Unresectable Hepatocellular Carcinoma: A Trial-in-Progress

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Background: Tislelizumab (BGB-A317) is a humanized IgG4 monoclonal antibody with high affinity and specificity for programmed cell death receptor-1 (PD-1). Tislelizumab was specifically engineered to minimize $F_c\gamma R$ binding on macrophages that, based on preclinical evidence, is believed to minimize potentially negative interactions with other immune cells. A first-in-human, phase 1A/1B study (NCT02407990) demonstrated that single-agent tislelizumab was generally well tolerated and showed preliminary evidence of antitumor activity in patients with advanced solid tumors, including hepatocellular carcinoma (HCC). A recommended dose of tislelizumab administered at 200 mg intravenously (IV) every 3 weeks (Q3W) has been established.

Trial Design: This phase 2, multicenter study (NCT03419897) is designed to evaluate the efficacy, safety, tolerability, and pharmacokinetics of tislelizumab in patients with previously treated, unresectable HCC. This study will enroll patients who are ≥18 years of age with histologically confirmed locally advanced or unresectable HCC. This includes patients who are not amenable to, or who have relapsed after, a curative treatment approach or locoregional therapy. To be enrolled, patients must also have a Child-Pugh score A, ECOG performance status ≤1 and must have experienced up to two lines of prior systemic therapy. Patients with prior PD-1 or PD-L1 treatment are excluded. In addition, those who received sorafenib or regorafenib within 14 days of the first study drug administration will be excluded. A total of 228 patients worldwide are planned to be treated with tislelizumab 200 mg IV Q3W. The primary endpoint of this study is objective response rate evaluated by Independent Review Committee per RECIST v1.1; radiological assessment of tumor-response status will be performed every 6 weeks in the first 18 weeks and then every 9 weeks thereafter. Secondary endpoints include duration of response, progression-free survival, disease control rate, clinical benefit rate, overall survival, quality-of-life outcomes, and assessment of the pharmacokinetic and safety/tolerability profiles of tislelizumab. Exploratory endpoints include assessment of potential biomarkers and assessment of host immunogenicity to tislelizumab. Safety/tolerability assessments will include monitoring of adverse events (AEs), including immune-related AEs, as well as physical examinations, vital signs, and electrocardiograms.