BGB-A317-LBL-007-202: A phase 2, randomized, active-controlled, open-label study to evaluate the efficacy and safety of LBL-007 (anti-LAG-3) in combination with tislelizumab (TIS; anti-PD-1) plus chemotherapy (chemo) as first-line (1L) treatment in patients with unresectable locally advanced/metastatic esophageal squamous cell carcinoma (ESCC)

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Background: ESCC is the predominant histological subtype of esophageal cancer, accounting for 85% of cases. Patients (pts) with locally advanced/metastatic ESCC have poor clinical outcomes, with a 5-year survival rate of 6.1% for pts with distant metastases. 1L treatment with programmed cell death protein-1 (PD-1) inhibitors + platinum-based chemo has become the new standard of care for metastatic ESCC, however, there is an unmet need for enhanced treatment efficacy and a prolonged life span. LBL-007 is a monoclonal antibody (mAb) against lymphocyte activation gene-3 (LAG-3), an immune checkpoint receptor that negatively regulates T-cell activity. TIS is an anti-PD-1 mAb that blocks the PD-1/programmed death-ligand 1 (PD-L1) immune checkpoint, resulting in T-cell activation. This study (NCT06010303) aims to evaluate the efficacy and safety of LBL-007 + TIS + chemo as a 1L treatment in pts with unresectable, locally advanced/metastatic ESCC.

Methods: This phase 2 study will enroll approximately 116 pts with a pathologically confirmed diagnosis of unresectable, locally advanced/metastatic ESCC and no prior systemic therapy. Pts will be randomized 2:1 to either Arm A (LBL-007 600 mg intravenously [IV] every 3 weeks [Q3W] + TIS 200 mg IV Q3W + chemo doublet) or Arm B (TIS 200 mg IV Q3W + chemo doublet), stratified by PD-L1 expression (tumor area positivity score ≥10% or <10%). The chemo doublet will consist of either cisplatin (60-80 mg/m^2 IV Q3W) + 5-fluorouracil (750-800 mg/m^2 IV daily on Days 1-5 Q3W), or cisplatin + paclitaxel (175 mg/m^2 IV Q3W), determined by the investigator before randomization. Treatments will be administered until disease progression, intolerable toxicity, or withdrawal for other reasons. The primary endpoint is the overall response rate, as assessed by the investigator per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1. Secondary endpoints include progression-free survival, duration of response, and disease control rate (all by investigator per RECIST v1.1), and the incidence and severity of adverse events per National

Cancer Institute-Common Terminology Criteria for Adverse Events v5.0. A safety monitoring committee is monitoring the safety of LBL-007 + TIS + chemo vs TIS + chemo. Exploratory endpoints include comparison of overall survival, assessment of predictive, prognostic, and pharmacodynamic biomarkers, pharmacokinetic evaluation of LBL-007 and TIS, and immunogenicity. The study is currently recruiting at approximately 46 sites across Asia, including Taiwan, mainland China, South Korea, and Thailand.