A Phase 1/2 Dose Escalation and Expansion Study to Investigate the Safety, Pharmacokinetics and Antitumor Activity of the anti-PD-1 Monoclonal Antibody BGB-A317 in Subjects with Advanced Solid Tumors

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Introduction: The immune check point inhibitory receptor, programmed cell death-1 (PD-1), plays a key role in immune modulation of tumor progression. Antibodies against PD-1 are effective in the treatment of many advanced solid tumors. BGB-A317 is a humanized IgG4 anti-PD-1 monoclonal antibody blocking PD-L1/PD-L2 binding to PD-1, restoring T-cell-mediated tumor inhibition. It is differentiated from other checkpoint inhibitors by its engineered Fc-hinge region that precludes FcγR1 mediated binding to macrophages/myeloid-derived suppressor cells, a potential mechanism of T cell clearance. BGB-A317 has antitumor activity in mouse models of human epidermoid carcinoma, renal cell carcinoma, and non-small cell lung cancer.

Trial Design: This ongoing, first-in-human, dose-escalation/dose-expansion study of BGB-A317 (NCT02407990) in patients with advanced solid tumors is being conducted in two phases. A total of 116 subjects with advanced solid tumors were enrolled to phase 1A. In the first part, 22 patients received one of 4 escalating doses of BGB-A317 (0.5, 2, 5, and 10 mg/kg) administered intravenously (IV) every 2 weeks (Q2W) in 3+3 design. Part 2 characterized the pharmacokinetic profile in 81 patients who received 2 or 5 mg/kg administered on a Q2W or Q3W schedule. Part 3 evaluated the safety and PK of 200 mg IV Q3W dose in 13 patients. The phase 2 component is ongoing and will enroll ~330 patients into one of several expansion cohorts (**Table**). Enrolled subjects will receive BGB-A317 dosed either at 5mg/kg or 200 mg IV Q3W until disease progression, intolerable toxicity, or discontinuation/withdrawal.

Treatment Arm	Tumor type	Estimated sample size
Arm 1†	Non-small cell lung cancer	50
Arm 2	Ovarian cancer	20
Arm 3†	Gastric cancer	50
Arm 4†	Hepatocellular cancer	50
Arm5	Head and neck squamous cell carcinoma	20
Arm 6†	Esophageal carcinoma	50
Arm 7	Triple negative breast cancer	20
Arm 8	Cholangiocarcinoma	20
Arm 9	Renal cell carcinoma, bladder cancer, melanoma, Merkel-cell carcinoma, sarcoma, gastrointestinal stromal tumor, or cutaneous squamous cell carcinoma. Or any other solid tumors with microsatellite instability-high or mismatch repair deficient, such as colorectal or pancreatic cancer	50
†At least 20 subjects will be enrolled from Taiwan or Korea		