Preliminary results of a phase 1A/1B study of BGB-A317, an anti-PD-1 monoclonal antibody (mAb), in patients with advanced hepatocellular carcinoma (HCC)

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Background: BGB-A317 is a humanized IgG4 anti-PD-1 mAb blocking PD-L1/PD-L2 binding to PD-1, thereby restoring T-cell-mediated tumor inhibition. BGB-A317 is differentiated from other checkpoint inhibitors by its engineered Fc-hinge region that precludes FcγR1 mediated binding to macrophages/ myeloid-derived suppressor cells (MDSCs) - a potential mechanism by which PD1-bound T-cells may be cleared. Upregulation of PD-1 and PD-L1, and a predominance of macrophages and MDSCs have been reported in HCC supporting the rationale for evaluation of BGB-A317 in patients with HCC. At SITC 2016 we have reported the safety and efficacy data of a phase 1 study of BGB-A317 in patients with advanced solid tumors. Here we present the preliminary results in the HCC subset of patients enrolled in this ongoing phase 1 study.

Method: A phase 1A/1B, open-label, multi-center, dose-escalation and expansion study (NCT02407990) was conducted to evaluate the safety, tolerability and anti-tumor activity of BGB-A317 in patients with advanced solid tumors. Patients with histologically confirmed advanced HCC were eligible and treated every three weeks (Q3W) at a dose of 5 mg/kg. Adverse events (AEs) were assessed per NCI-CTCAE v4.03 and tumor assessments were performed Q9W using RECIST v1.1.

Results: As of 13 Jan 2017, 11 patients (pts) with sorafenib-refractory HCC were enrolled. The most common AEs included fatigue (2 of the 11 pts), pyrexia (2/11), productive cough (2/11), upper respiratory tract infection (2/11) and decreased appetite (2/11). Two grade 3 AEs, ascites, and upper respiratory tract infection, were reported in two different pts. Treatment–related AEs were grade 1 fatigue (1/11) and rash (1/11). Three serious AEs observed in three different pts were grade 3 ascites, grade 3 upper respiratory tract infection and death with unknown cause, and none of them were considered treatment-related. As of 24 Feb 2017, the median follow-up was 4.1 months (range 0.7 – 13.6 months) and 8/11 pts remain on study. The disease control rate (DCR), defined as the proportion of pts who have achieved complete response (CR), partial response (PR) and stable disease (SD) per RECIST v1.1, is 70%. Among 10 evaluable pts, an ongoing confirmed PR was observed in one pt with 75% sum-of-the-longest-diameter (SLD) reduction; SD was observed in 6 pts, including one pt with AFP reduction from 4399 to 5.25 ng/mL and another pt with initial documentation of PR (31% SLD reduction) at the 2nd evaluation awaiting confirmation. This study will enroll about 50 pts with HCC, and data will be updated at time of presentation.

Conclusions: BGB-A317 appears to be tolerable in pts with refractory/relapsed HCC. The preliminary safety profile and anti-tumor activity support continued exploration and development of BGB-A317 in pts

with advanced HCC.