Randomized Double-blind Placebo-Controlled Phase 2 Study of Bemarituzumab Combined with Modified FOLFOX6 (mFOLFOX6) in 1st Line (1L) Treatment of Advanced Gastric/Gastroesophageal Junction Adenocarcinoma (FIGHT)

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Background: Bemarituzumab (bema), a first-in-class humanized IgG1 monoclonal antibody, selectively binds to FGFR2b, inhibits ligand binding and mediates antibody-dependent cell-mediated cytotoxicity. A phase 1 study of bema monotherapy in solid tumors had no dose-limiting toxicities and a confirmed objective response rate (ORR) of 18% in patients (pts) with refractory FGFR2b+ gastric cancer (GC).

Methods: The FIGHT study (NCT03343301) is a global, randomized, double-blind, placebo-controlled phase 2 trial. Pts with unresectable locally advanced or metastatic GC that was not HER2+ were eligible if their tumor was positive for FGFR2b overexpression by centrally performed immunohistochemistry (IHC) or for *FGFR2* amplification by circulating tumor DNA (ctDNA). Pts were treated with mFOLFOX6 and randomized 1:1 to bema 15mg/kg or placebo (pbo) every 2 weeks with 1 additional 7.5mg/kg bema/pbo dose on day 8. Treatment was continued until disease progression, intolerable toxicity, or death. The primary endpoint was investigator-assessed progression-free survival (PFS) and key secondary endpoints include overall survival (OS), overall response rate (ORR), and frequency of adverse events. Statistical significance (2-sided α of 0.2) was tested sequentially for PFS, OS and ORR.

Results: Of 910 1L GC pts whose tumors were evaluated 275 (30%) were FGFR2b+. Of 155 pts randomized, 77 to bema+mFOLFOX6 and 78 to pbo+mFOLFOX6, 149 were FGFR2b+ by IHC and 26 by ctDNA. The primary endpoint was met with an improvement in median PFS of 9.5 mo (bema) vs 7.4 mo (pbo) (hazard ratio [HR], 0.68; 95% confidence interval [CI], 0.44-1.04; p=0.07). The secondary endpoint of OS was met; median not reached in the bema arm vs 12.9 mo for pbo (HR, 0.58, 95% CI, 0.35-0.95; p=0.03). Among patients with measurable disease, ORR improved from 40% (pbo) to 53% (bema). Improved efficacy was observed across all 3 endpoints (PFS, OS, ORR) with increasing levels of overexpression of FGFR2b on tumor cells. Grade ≥3 AEs were reported in 83% of pts in the bema arm vs 74% pts in the pbo arm with serious AEs in 32% and 36% respectively. Stomatitis was higher in the bema arm (31.6% vs 13.0%) and corneal AEs were more common in the bema arm (67% vs 10%). There were no reported AEs of retinal detachment or hyperphosphatemia in the bema arm.

Conclusion: Approximately 30% of 1L pts with advanced GC not HER2+, were identified to be FGFR2b+, primarily by IHC. In this randomized, placebo controlled, double-blind phase 2 study, the addition of bema to mFOLFOX6 led to clinically meaningful and statistically significant improvements in PFS, OS and

ORR. An increase in corneal AEs and stomatitis was associated with bema. These results support a prospective randomized phase 3 study in GC and the evaluation of bema in other FGFR2b+ tumor types.