Background: GBR 1302 is a HER2xCD3 bispecific antibody engineered to direct T-cells to HER2-expressing tumor cells. This ongoing first-in-human study (NCT02829372) in subjects with HER2-positive cancers aims to evaluate the safety, tolerability, and preliminary efficacy of GBR 1302.

Methods: Adults with HER2-positive (immunohistochemistry 2+ or 3+) solid tumors with no available standard treatment receive GBR 1302 on Day 1 and Day 15 in 28-day treatment cycles at escalating dose levels, starting at 1 ng/kg. The primary endpoint includes determination of the maximum tolerable dose and safety profile of GBR 1302. Secondary and exploratory endpoints include pharmacodynamic (PD) testing for modulation of cellular and cytokine biomarkers.

Results: To date, 19 evaluable subjects for dose-limiting toxicity (DLT) have been treated up to a dose of 750 ng/kg; dose escalation is ongoing. Grade (G) 1 to 2 infusion related reaction (IRR)/cytokine release syndrome (CRS) is the most common treatment emergent adverse event that has been observed in subjects treated at doses ≥100 ng/kg. The majority of subjects were managed with conservative treatment. 2 subjects experienced DLT events: one asymptomatic subject (100 ng/kg) was noted to have reduced left ventricular ejection fraction on routine echocardiogram at 4 weeks, which resolved spontaneously after treatment discontinuation; the second subject (500 ng/kg) experienced G4 IRR/CRS which required ICU care but resolved within 36 hours. Beginning at 30 ng/kg, CD3, CD4, and CD8 positive T-cell populations decreased within 6 hours of administration and recovered to levels at or above baseline by 48 hours. Dose-proportional, transient increases in cytokines (IL-2, IL-6, IL-10, IFN-γ, TNF-α), which peaked at 6 hours and began to normalize within 48 hours, were observed. No subjects have documented radiological response, but 2 subjects (HER2 3+; gastroesophageal adenocarcinoma and HER2 2+; breast adenocarcinoma) have prolonged disease stabilization lasting ≥4 months.

Conclusions: The combination of clinical findings and PD changes suggests T-cell activation with higher doses of GBR 1302. Dose escalation is continuing and updated results will be presented.

Clinical trial identification: NCT02829372.

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Updated safety, PK, PD, and efficacy data will be reported. Initial antitumor activity has been observed. Clinical trial information: NCT02959905; Release date: November 9, 2016.

Conclusions:
Further treatment and analyses are ongoing.

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Disclosure:
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