729 **A FIRST-IN-HUMAN, OPEN-LABEL, MULTICENTER, PHASE 1/2A, DOSE ESCALATION AND EXPANSION STUDY OF GI-102, A NOVEL IMMUNOCYTOKINE COMBINING CD80-IL2V3, IN PATIENTS WITH ADVANCED OR METASTATIC SOLID TUMORS**

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Background GI-102 (CD80-IL2v3) is a novel immunocytokine, designed to direct IL-2v to tumor and immune cells. IL-2v3 of GI-102 is designed to abolish the affinity to IL-2Rα thereby maximizing expansion of cytotoxic T and NK cells but not Treg cells. CD80 portion of GI-102 further inhibits Treg cell function. The complementary mechanisms of action of GI-102 via blocking CTLA-4 with IL-2 activity can promote cancer immunity cycle. In Cynomolgus monkeys, intravenous administration of GI-102 resulted in robust expansion of total lymphocytes, CD8+ T and NK cells (21.5-fold, 39.6-fold and 22-fold at GI-102 2.5 mg/kg, respectively) without significant toxicities. In addition, GI-102 elicited anti-tumor activity when used as a single agent or in combination with different agents in various in vivo models. Given the promising preclinical pharmacodynamic profile and anti-cancer activity, we hypothesize that GI-102 may exert anti-tumor activity as a single agent in cancers without effective therapeutic options.

Methods NCT05824975 is an ongoing phase 1/2a, first-in-human study of GI-102 in solid tumors. It composes two parts: dose escalation and expansion phases. Approximately 92 patients with advanced or metastatic solid tumors are planned to be enrolled. Patients assigned to dose escalation phase will receive escalating doses of intravenous GI-102 every three weeks (Q3W). Pharmacokinetic (PK) and/or pharmacodynamic (PD) modeling and simulations utilized to select the effective dose range for GI-102, to determine the dose level of desirable expansion of peripheral immune cells. In the lowest (0.06 mg/kg) and the highest (0.45 mg/kg) dose cohorts, simulated lymphocyte expansion is 2.7 and 4.7-fold from baseline, providing sufficient immune cell expansion level for anti-cancer activity. The dose escalation phase will enroll up to 52 patients with conventional 3+3 design to determine maximum tolerated dose (MTD) and/or tentative RP2D. Each cohort in dose escalation phase may be extended to enroll additional patients, potentially enriched in certain tumor types and/or characteristics to confirm safety, PK and/or PD data. Once RP2D is determined, additional 40 patients including 10 renal cell carcinoma and 10 melanoma patients will be enrolled in dose expansion phase to more fully inform the safety, tolerability and anti-cancer activity of GI-102. The primary objective of this study is to assess the safety and tolerability of GI-102 to define the MTD and/or RP2D in dose escalation phase and to assess the anti-tumor activity of GI-102 in dose expansion phase.

Results This study is currently enrolling patients with advanced/metastatic solid tumors.

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