A PHASE 1/2 STUDY INVESTIGATING THE SAFETY AND EFFICACY OF AUTOLOGOUS TAC T CELLS IN SUBJECTS WITH UNRESECTABLE, LOCALLY ADVANCED OR METASTATIC CLAUDIN 18.2+ SOLID TUMORS

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Background CLDN18.2 is a tight junction protein found in differentiated gastric epithelial cells which can become abnormally or ectopically expressed in a number of solid tumor indications. This exposure profile illustrates the potential of CLDN18.2 as a candidate for targeted therapy. To date, there are no approved therapeutic agents directed against this target.

The T cell antigen coupler (TAC) technology is an approach to modifying T cells ex vivo, which allows recognition and cytotoxicity of tumor cells by co-opting the natural T cell receptor. TAC T cells demonstrate a safer profile than chimeric antigen receptor T cells. TAC01-CLDN18.2 is an autologous T-cell product comprising T cells expressing CLDN18.2 TAC.

Methods This is a first-in-human study (NCT05862324) to investigate the safety and preliminary anti-tumor activity of TAC01-CLDN18.2 in CLDN18.2+/HER2- solid tumors. Subjects will undergo leukapheresis and may receive bridging anticancer therapy, if deemed necessary by the Investigator, during cell manufacturing. Prior to TAC01-CLDN18.2 infusion, subjects will undergo low-intensity lymphodepletion chemotherapy.

In phase I dose escalation, TAC01-CLDN18.2 will be administered at increasing doses (Cohorts 1–3) in adult subjects after ≥2 lines of therapy using the classic 3+3 dose escalation study design. Subjects with pancreatic ductal adenocarcinoma (PDAC) may have been treated with 1 line of prior therapy. CLDN18.2 expression levels will be determined centrally using a clinical trial assay validated across relevant indications. Dose limiting toxicities will be assessed up to 28 days from TAC01-CLDN18.2 infusion. A second dose may be administered, according to preidentified clinical and safety criteria.

In Phase II, dose expansion groups will further evaluate the efficacy, safety, and pharmacokinetics of the optimal TAC01-CLDN18.2 dose, with the option of redosing. Indications will include gastric and esophageal adenocarcinoma (group A), PDAC (group B) and ovarian and non-small cell lung cancer (group C) in subjects after ≥2 and <4 lines of prior therapy (subjects with PDAC may have been exposed to 1 therapy). Definitions of eligible CLDN18.2 expression levels will be based on retrospective analysis of data from Phase 1 in association with clinical efficacy. A Simon 2-stage design will be used to enroll ≤57 subjects in Group A and ≤22 subjects in Group C. Group B will be exploratory and will enroll ≤10 subjects with an opportunity of cohort enrichment based on clinical efficacy data.

Trial Registration www.clinicaltrials.gov NCT05862324

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