

A PHASE 1 DOSE ESCALATION STUDY OF GCC19CART A NOVEL COUPLEDCAR[®] THERAPY FOR SUBJECTS WITH METASTATIC COLORECTAL CANCER

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Background Chimeric antigen receptor (CAR) T-cell therapy has shown remarkable clinical efficacy in hematologic malignancies but limited success in solid tumors. GCC19CART, the first clinical candidate from the CoupledCAR[®] solid tumor platform, is designed to overcome the limitations of conventional CAR T-cells in solid tumor malignancies by pairing solid tumor CAR T-cells with CD19 targeting CAR T-cells to amplify proliferation and activation of the solid tumor CAR T component. GCC19CART targets guanylate cyclase-C (GCC) which is expressed in the metastatic lesions of 70%-80% of subjects with colorectal cancers. A Phase 1 investigator-initiated clinical trial is underway in China for patients with relapsed or refractory metastatic colorectal cancer who have received at least 2 prior lines of therapy. Based on a data cut-off on December 13, 2021, 21 subjects have been enrolled in 2 dose escalation groups at 5 hospitals in China.

Methods Subjects are screened for GCC expression by immunohistochemistry. Eligible subjects undergo leukapheresis, a single dose of lymphodepleting chemotherapy (fludarabine 30mg/m² and cyclophosphamide 300mg/m²) 3 days prior to infusion, and then administration of a single infusion of GCC19CART at one of two preassigned doses: 1x10⁶ or 2x10⁶ CAR T-cells/kg. Endpoints are safety and preliminary evidence of efficacy as determined by CT or PET/CT per RECIST 1.1 or PERCIST 1.0. All responses were confirmed by an independent third-party imaging contract research organization (CRO).

Results 13 subjects have been enrolled to dose level 1 (1x10⁶ cells/kg) and 8 subjects have been enrolled to dose level 2 (2x10⁶ cells/kg). The most common adverse events were cytokine release syndrome (CRS) in 21/21 subjects (Grade 1 19/21 (90.48%) or Grade 2 2/21 (9.52%)) and diarrhea in 21/21 subjects (Grade 1 6/21 (28.57%) Grade 2 5/21 (23.81%) Grade 3 9/21 (42.86%) or Grade 4 1/21 (4.76%)). Neurotoxicity was observed in 2/21 (9.52%) subjects at Grade 3 or 4 and resolved with corticosteroids. The combined overall response rate (ORR) for both dose levels was 28.6% (6/21). For dose level 1, the overall response rate (ORR) per RECIST 1.1 was 15.4% (2/13). Two subjects demonstrated a partial response (PR) while 3 additional subjects had partial metabolic response (PMR) on PET/CT with stable disease (SD) or progressive disease (PD) per RECIST 1.1. For dose level 2, The ORR per RECIST 1.1 was 50% (4/8). 4 subjects demonstrated a PR (3 at month 1, 1 at month 3 after being SD at month 1) and 2 additional subjects had PMR on PET/CT with SD per RECIST 1.1.

Conclusions GCC19CART demonstrated meaningful dose dependent clinical activity and an acceptable safety profile in relapsed or refractory metastatic colorectal cancer. This trial is ongoing and updated data will be presented. A United States based Phase 1 trial of GCC19CART is anticipated for mid-2022.