Background Despite recent therapeutic developments for patients with advanced, metastatic, unresectable HER2 positive (HER2+) solid tumors, significant unmet medical needs still exist, especially in tumors other than breast and gastric cancers and in patients with HER2-low expression. The T cell antigen coupler (TAC) technology is a novel approach to modifying T cells, allowing them to recognize and treat HER2+ solid tumors. Mechanistically, the TAC receptor redirects T cells to tumor cells, and upon recognition, co-opts the Natural T cell receptor (TCR) signaling action to yield safe anti-tumor responses. In preclinical studies, TAC T cells led to complete tumor clearance in various human HER2+ mouse models, without any TAC-related toxicities, and results superior to a similar 2nd generation chimeric antigen receptor (CAR) T cell.

In this ongoing clinical trial (NCT04727151), subjects undergo leukapheresis, bridging therapy while their TAC T cells are engineered (if needed), lymphodepletion chemotherapy (LDC), and finally TAC01-HER2 infusion.

Methods Dose escalation in Phase 1 is investigating the safety and tolerability of TAC01-HER2 single doses of 0.08, 0.3 (starting dose), 0.8, 3, 8 x 10^6 cells/kg in adult subjects with HER2+ solid tumors (1+, 2+ or 3+ by immunohistochemistry) who have progressed after ≥2 lines of systemic therapy. Dose limiting toxicities (DLTs) are being assessed up to 28 days after TAC01-HER2 infusion. In Phase 2, dose expansion groups will further evaluate the safety, efficacy, and pharmacokinetics of the optimal TAC01-HER2 dose in HER2+ breast and other HER2+ tumor types, including: lung, pancreatic, colorectal, gastric, endometrial, and ovarian.

As of 20 July 22, eight subjects have been treated in Cohorts 1 and 2, with no DLTs or events of special interest, such as cytokine release syndrome or immune effector cell-associated neurotoxicity syndrome, being observed. Four subjects had 8 serious adverse events; all unrelated to TAC01-HER2 infusion and attributed to LDC or underlying malignancies. Preliminary safety results indicate single TAC01-HER2 treatments in a heavily pre-treated population have been well-tolerated, with the most frequent adverse events (AEs) being cytopenias related to LDC. Continued dose escalation of TAC01-HER2 is ongoing.

Following completion of each dose level, a Data Safety Monitoring Committee has met to review all AEs to approve or deny escalation to the next highest dose level.