Background We are developing MiNK-413; a novel allogeneic CAR-iNKT product targeting BCMA and secreting soluble IL-15 for treatment of relapsed/refractory Multiple Myeloma (rrMM). Chimeric Antigen Receptor (CAR)-T cell therapy has revolutionized treatment of rrMM with two autologous products already approved by the FDA. However, current treatments come with significant toxicity, cost, and logistical challenge and many patients relapse, with 60% of relapsed patients still expressing BCMA. To address these, we propose the use of invariant Natural Killer T (iNKT) cells as a platform for BCMA-targeted allogenic cell therapy for rrMM. iNKT cells have potent immunostimulatory activity and intrinsic CD1d- and NK receptor ligand targeted cytotoxicity, and do not cause Graft versus Host Disease due to their invariant T cell receptor. In our native iNKT cell (agentT-797) clinical trials for COVID, solid tumors and Multiple Myeloma we observe excellent tolerability to up to 1 billion cell dosing with minimal treatment-related adverse events, absence of signs of CRS or peripheral neuropathy, and early signs of biological activity. AgentT-797 is administered without prior lymphodepletion, which is an approach we intend to pursue with MiNK-413.

Methods Our proprietary CARDIS™ platform consists of highly diverse (>10¹⁰) scFv library screening followed by library-based direct functional selection in CAR format using mammalian display. Candidates can be further optimized using affinity tuning to ensure optimal and highly selective on-target/on-tumor activity. We developed a manufacturing approach to engineer and specifically expand CAR and soluble IL-15-expressing allogeneic iNKT cells. Lead candidates are assessed in vitro and in vivo for cytotoxicity, cytokine secretion, exhaustion, tumor homing and persistence.

Results Discovery using our CARDIS™ platform generated a fully human, potent, and specific anti-BCMA CAR which forms the basis for MiNK-413. Xenograft in vivo studies demonstrate effective bone marrow homing, and potent cytotoxic activity, with soluble IL-15 prolonging persistence. In vitro data show potent immunomodulatory activity and lack of exhaustion against BCMA+ human hematologic tumor cell lines in vitro and in vivo.

Conclusions Combination of our proprietary CARDIS™ and iNKT platforms enabled rapid discovery and development of MiNK-413, a next generation armored allogeneic BCMA-targeting CAR therapies. MiNK-413 is eligible to target a broader rrMM patient population due to intrinsic iNKT cell properties such as effective bone-marrow homing, high BCMA specific activity augmented by natural CD1d and NK receptor-ligand mediated activity. We believe MiNK-413 will provide additional benefits to rrMM patients beyond currently available treatments.