Marengo Therapeutics Presents Preclinical Proof-of Concept Data for STAR0602, a First-in-class Selective T cell Activator, at the 34th EORTC-NCI-AACR Symposium 2022

- ***Preclinical data with STAR0602 demonstrates potent, single agent anti-tumor activity in PD-1 refractory solid tumor models***
- ***Distinct mechanism of action through expansion of a subset of Vβ T cells with a novel memory phenotype that promotes durable de novo antitumor immune responses***
- ***STAR0602 slated to initiate Phase 1/2 clinical trial (START-001) in the fourth quarter of 2022***

Cambridge, Mass. October 28, 2022 – Marengo Therapeutics, Inc., a company pioneering novel therapeutics targeting the T cell receptor Vβ chain (TCR Vβ) to selectively activate the right T cell subsets to fight cancer, today presented the first preclinical proof-of-concept data on STAR0602, its novel TCR agonist antibody, during the 34th EORTC-NCI-AACR Symposium on molecular targets and cancer therapeutics (ENA) in Barcelona, Spain. The data presented showed potent anti-tumor activity of STAR0602 in a range of solid tumor models, including those refractory to checkpoint inhibitors like PD-1/PD-L1.

The plenary oral presentation was given by James Gulley, M.D., Ph.D., Co-Director of the Center of Immuno-Oncology (CIO), Deputy Director of the Center for Cancer Research (CCR) at the National Cancer Institute (NCI), and acting Clinical Director, NCI.

"STAR0602 offers an entirely new mechanism of selective T cell activation that increases both the quantity and quality of T cell responses to the tumor via a mechanism that is distinct to checkpoint inhibitors," said Zhen Su, M.D., MBA, Chief Executive Officer of Marengo. "These results strongly suggest our lead asset has the potential to become a next-generation IO backbone treatment against a range of solid tumors representing a novel therapeutic strategy for patients."

"We are pleased to share the first data for our STAR0602 program," added Andrew Bayliffe, Ph.D., Chief Scientific Officer of Marengo. "These studies show that our selective Vβ T cell activators access novel T cell immunology that has the potential to fundamentally remodel the adaptive immune response to solid tumors and install long-term tumor immunity."

Across a range of refractory murine syngeneic solid tumor models, mSTAR0602 (the murine surrogate of STAR0602) monotherapy at moderate dose levels either eradicated tumors or led to substantial regressions – effects that were durable over the long term. mSTAR0602-cured mice also showed long-term protection from tumor re-challenge. This anti-tumor activity was

shown to be dependent on the accumulation of a specific subset of Vβ T cells in tumors that adopt a novel effector memory phenotype and a striking increase in TCR diversity. The expansion of these effector memory Vβ T cells was accompanied by a reduction in exhausted T cells and regulatory T cells. Similar potent expansion of human TILs and tumor killing was observed in primary syngeneic human ex vivo tumor models derived from several patient samples. The anti-tumor activity of STAR0602 in these ex vivo human tumor models was superior to pembrolizumab when tested in parallel at therapeutic concentrations.

Additional presentation details are outlined below:

- Title: STAR0602, a novel TCR agonist antibody, demonstrates potent anti-tumor activity in refractory solid tumor models through the expansion of a novel, polyclonal effector memory T cell subset
    - Abstract Number: ENA22-0183
    - Session Day/Time: Friday, October 28; 12:40 pm, CET
    - Location: Barcelona International Convention Center, Barcelona, Spain
    - Presenter: James Gulley, M.D., Ph.D.
- Research Highlights:
    - Non-human primate and patient organoid studies were conducted to confirm translation of STAR0602 target immunology to support planned human clinical trials.
    - The START-001 clinical study will assess the safety, tolerability, and preliminary clinical activity of STAR0602 as a single agent in patients with advanced antigen-rich solid tumors including PD-1 refractory patients. This open label, multicenter Phase 1/2 study consists of two parts: Phase 1 dose escalation and Phase 2 dose expansion. For more information, please visit clinicaltrials.gov (trial identifier: NCT05592626)

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About Marengo Therapeutics

Marengo Therapeutics, Inc., an ATP company, is pioneering first-in-class therapeutics that activate the right immune response to promote lifelong protection against cancer. With a passionate team of dedicated scientists experienced in immunology and oncology, Marengo's proprietary Selective T Cell Activation Repertoire (STAR) platform leverages an extensive biological understanding of T cell function and receptor signaling to create a world in which everyone's immune system can defeat cancer. To learn more, visit marengotx.com.

About STAR0602

STAR0602 is the company's lead program, the first T cell activator generated by Marengo's STAR platform, a multi-specific fusion protein library that targets specific TCR Vβ variants fused to different co-stimulatory moieties generating potent T cell activators. The unique feature of this

platform is to fine-tune the T cell response in selected T cell subsets to generate endogenous, highly functional, cancer-killing T cells for solid tumors. STAR0602 is a fusion protein that binds to a specific region of TCR Vβ and delivers a unique activation signal on the same T cell, leading to a selective expansion of the targeted T cell subclones. This molecule has shown remarkable single agent activity in a vast array of preclinical models.

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