Marengo Therapeutics and Kings College London Announce Publication in *Science Advances* Highlighting the Discovery of a New Approach to T Cell Activation

- **Antibodies to germline-encoded TCR β-chain alleles drive T cells to distinct memory-like effector states and reveal the potential to modulate the germline T cell repertoire.**

- **Innate engagement of the TCR β-chain promotes clinically beneficial T cell phenotypes through an approach different from conventional anti-CD3ε antibodies.**

Cambridge, Mass. December 7, 2023 – Marengo Therapeutics, Inc., a clinical-stage biotech company pioneering a new way to activate T cells by targeting germline-encoded alleles in the Vβ chain of the T cell receptor (TCR) to selectively activate the right T cell subsets to fight cancer, today announced a publication in *Science Advances* describing the novel immunological effects of its foundational anti-Vβ chain TCR targeting antibodies on human T cells. This unique approach underpins Marengo's therapeutic T cell platform, which has broad application across a range of diseases. The publication describes observations and insights gained through a collaboration between Marengo scientists and the Kings College London-based lab of Adrian Hayday, Ph.D. FmedSci, FRS.

"Professor Hayday and his team are true pioneers in advancing the field of innate TCR biology, particularly in the area of gamma delta T cells," said Andrew Bayliffe, Ph.D., Chief Scientific Officer of Marengo. "Through this collaboration, we have extended the concept of innate TCR engagement to αβ T cells. The resulting learnings will be crucial as we progress our platform and pipeline of broad Vβ T cell therapeutics."

The publication, titled "Innate TCRβ-chain Engagement Drives Human T cells Toward Distinct Memory-like Effector Phenotypes with Immunotherapeutic Potentials," highlights the distinct binding modes of Marengo's Vβ chain-targeting antibodies and their effects on differentiation states of human T cells. Using a battery of immunophenotyping and molecular approaches, researchers in Professor Hayday's Immunobiology Lab at King's College London revealed a unique signature induced in subsets of human T cells treated with Vβ chain-targeting antibodies.

Link to publication: https://www.science.org/doi/10.1126/sciadv.adj6174

This population of cells show hallmarks of both proliferative memory T cells, and effector T cells that are highly distinct to states induced by other non-clonal TCR activators such as anti-CD3ε antibodies and Vβ chain-targeting bacterial superantigens. Further mechanistic investigations revealed diverse transcriptional changes associated with the changes in T cell phenotype that suggest a fundamental reprogramming of T cell differentiation by Vβ chain-targeting antibodies.

"We undertook these studies to tackle a previously unanswered question; namely, will TCRαβ respond in a distinct and interesting way to stimulating by an atypical mode, that we term 'innate'.

We have discovered that the answer is clearly yes, and we are understandably delighted for cancer patients that this innate response mode may prove therapeutically beneficial," said Professor Hayday.

This publication follows on the heels of a paper published November 29 in the journal *Science Translational Medicine*, which further underscores the potential of Marengo's lead asset STAR0602 and the company's STAR platform to target and activate subsets of T cells expressing different β chain TCRs.

About Marengo Therapeutics

Marengo Therapeutics, Inc, a clinical-stage biotech company, develops novel TCR-targeting antibodies that selectively modulate common and disease-specific T cell subsets of the germline TCR repertoire to provide lifelong protection against cancer and other diseases. 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 STAR™ Platform

Marengo's STAR™ Platform is a multi-specific antibody-fusion platform derived from Marengo's proprietary library of antibodies targeting germline-encoded variable (V)β regions of the TCR fused to different T cell co-stimulatory moieties. Combining a novel non-clonal mode of TCR activation with a T cell co-stimulator in the same molecule, promotes a distinct mechanism of action that promotes durable anti-tumor Vβ T cell responses.

About STAR0602

STAR0602 is Marengo's lead program, the first T cell activator generated from Marengo's STAR platform; a library of antibodies targeting non-clonal variable (V)β regions of the TCR fused to different co-stimulatory moieties. STAR0602 selectively targets a common Vβ T cell subset present in all cancers and, by combining a novel non-clonal mode of TCR activation with a T cell co-stimulator in the same molecule, promotes expansion of a new population of clonally enriched, effector memory Vβ T cells that turbo-charge tumor immune responses and promote durable clearance of tumors. STAR0602 has undergone extensive preclinical testing, which demonstrates potent anti-tumor activity in both mouse and human ex vivo tumor models attributed to a distinct mechanism of action from existing cancer immunotherapies.

About the START-001 Clinical Study

START-001 is a Phase 1/2 clinical trial evaluating the safety, tolerability, and preliminary clinical activity of STAR0602 as a single agent in biomarker selected patients with advanced antigen-rich solid tumors including PD-1 refractory and rare tumors. This open-label, multi-center trial consists

of two parts: Phase 1 dose escalation and Phase 2 dose expansion. For more information, please visit clinicaltrials.gov (trial identifier: NCT05592626).

For patients interested in enrolling in this study at NCI, please contact NCI's toll-free number 1-800-4-Cancer (1-800-422-6237) (TTY: 1-800-332-8615) and/or the website https://trials.cancer.gov and/or email NCIMO_referrals@mail.nih.gov.

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