Marengo Therapeutics Announces Publication Describing STAR0602, a Novel, TCR-Targeting Cancer Immunotherapy, in *Science Translational Medicine*

- **Marengo's first pan-tumor Vβ T cell activator, STAR0602, expands Vβ6 T cells that drive potent, single agent anti-tumor activity via a distinct mechanism to anti-PD1 therapies**
- **A phase I/II clinical study investigation of STAR0602 as a single agent in PD-1 refractory/resistant solid tumors is ongoing**

Cambridge, Mass. December 6, 2023 – Marengo Therapeutics, Inc., a clinical-stage biotech company pioneering a new way to activate T cells by targeting germline-encoded alleles in the β chain of the T cell receptor (TCR) to selectively activate the right T cell subsets to fight cancer, today announced that its lead program, STAR0602, is the subject of an article published in the latest edition of *Science Translational Medicine*.

The publication, titled *"A T cell receptor β chain-directed antibody fusion molecule activates and expands subsets of T cells to promote antitumor activity,"* highlights the potent and durable anti-tumor activity of STAR0602 across a broad range of PD1-refractory murine and human solid tumor models via a mechanism that is distinct to checkpoint inhibitors and cytokine therapies. Lead authors on the publication are Jonathan Hsu, M.Sc., Principal Scientist at Marengo, and Renee Donahue, from the National Cancer Institute (NCI), part of the National Institutes of Health (NIH).
Link to Publication: https://www.science.org/doi/epdf/10.1126/scitranslmed.adi0258

"The comprehensive data reported in our *Science Translational Medicine* publication underscore the potential of Marengo's broad STAR platform to target and activate subsets of T cells expressing different beta chain TCRs," said Andrew Bayliffe, Ph.D., Chief Scientific Officer of Marengo. "Our studies of STAR0602 show Vβ T cells expand to create a new, much more fit population of tumor-infiltrating T cells that recognize a broader set of tumor antigens or epitopes, and we are excited for the continuation of our clinical trial and the potential for STAR0602 to help patients with checkpoint inhibitor-resistant tumors."

Through a novel bi-specific antibody-fusion molecule design, STAR0602 achieves dual boosting of T cells through the TCR and costimulatory receptors that leads to profound activation, expansion and reprogramming of Vβ6 T cells representing a specific subset of the total T cell pool. STAR0602-expanded Vβ6 T cells acquire a novel effector memory phenotype with a highly expanded TCR repertoire suggesting reinvigoration and diversification of tumor antigen-specific T cell responses.

"The biology elicited by STAR0602 through engaging the TCR in this novel way seems quite different to canonical routes of TCR activation, including anti-CD3 antibodies. The atypical memory T cell phenotype observed in preclinical models dosed with STAR0602 also seem to be quite distinct and serve to illustrate that there may be many different routes to boosting anti-tumor T cell responses," said John Wherry, Ph.D., Chair of the Department of Systems

Pharmacology and Translational Therapeutics in the Perelman School of Medicine at the University of Pennsylvania (UPenn), Director of the UPenn Institute for Immunology, and Co-Chair of Marengo's Scientific Advisory Board.

In large animal studies, dosing of STAR0602 was associated with less release of proinflammatory cytokines and cytokine-related toxicities, suggesting the potential for a potent treatment option with lower risk of cytokine-related adverse effects.

"As clinicians, we have mostly immune checkpoint inhibitors and some experimental CAR-Ts to treat solid tumor patients, but only a subset of them respond, and some who respond initially then relapse." said James Gulley, M.D., Ph.D., Co-Director of the Center for Immuno-Oncology at the NCI and Clinical Director, NCI. "Having a new strategy to activate the immune system for these patients is important and currently an unmet need. STAR0602 may offer a new way to selectively activate a subset of T cells with potent antitumor activity, with the added potential to avoid the toxicity associated with activating all T cells. This unique modality of T cell activation holds significant promise for patients."

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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