Marengo Presents Promising First-in-Human Safety, Tolerability and Clinical Activity Data for its Lead Program, Invikafusp Alfa (STAR0602), at the 2024 SITC Annual Meeting

- *STARt-001 is the first clinical study to evaluate Marengo's novel, selective Vβ TCR agonist technology to promote in vivo expansion and reprogramming of tumor-infiltrating lymphocytes (TILs) in patients with advanced cancers*
- *Invikafusp alfa, a first-in-class, TCR Vβ6/Vβ10 selective dual T cell agonist, as a single agent, demonstrated tumor shrinkage across multiple tumor types with a manageable safety profile in heavily pre-treated, anti-PD-1 resistant patients*
- *Clinical activity of invikafusp alfa observed in cancers with high tumor mutation burden (TMB-H) including confirmed responses in microsatellite stable (MSS) colorectal cancer*

Cambridge, Mass., November 9, 2024 – Marengo Therapeutics, Inc., a clinical-stage biotechnology company pioneering novel approaches for precision T cell activation, today announced encouraging initial Phase 1 clinical data from its lead program, invikafusp alfa (STAR0602), during a late-breaking oral presentation at the Society for Immunotherapy of Cancer (SITC) 39th Annual Meeting taking place in Houston, Texas.

This is the first public disclosure of results from the ongoing STARt-001 Phase 1/2 trial (NCT05592626), evaluating invikafusp alfa as monotherapy in biomarker-enriched (TMB-H, MSI-H/dMMR or virally associated) patients with advanced anti-PD-1 resistant, or refractory solid tumors.

Phase 1 data from STARt-001 trial demonstrate early anti-tumor activity, including initial signals of clinical benefit in heavily pre-treated, anti-PD-1 resistant cancer patients. Invikafusp alfa also showed a manageable safety profile consistent with its novel mechanism of action, further supporting its potential as a treatment option across a range of high tumor mutational burden (TMB-H) cancers or virally associated malignancies.

"Having completed Phase 1 and commenced the Phase 2 dose expansion cohorts of STARt-001, Marengo is thrilled to share initial clinical findings that validate our novel selective dual T cell agonist platform," said Zhen Su, M.D., MBA, Chief Executive Officer of Marengo Therapeutics. "The single agent activity observed in Phase 1, especially in PD-1 resistant cold tumors such as colorectal cancer is a critical milestone, and we look forward to further exploring the potential of STAR0602 to become a next-generation backbone IO therapy across a range of tumor types."

Additional highlights from the Phase 1 findings include:

- Sustained and selective *in vivo* expansion of TCRVβ6/Vβ10 T cells was achieved across all 6 dose levels with up to ~500% peak increase post invikafusp alfa treatment

- Disease Control Rate (PR + SD) was reported in 50% of 28 patients from all dose escalation cohorts with 32% of patients experienced tumor shrinkage across six tumor types
- At the optimal biological dose range (0.08 mg/kg and 0.12 mg/kg), invikafusp alfa had single agent clinical activity with 63% Disease control rate, 50% of patients experienced tumor shrinkage and 25% ORR reported in TMB-H, anti-PD-1 resistant patients
- Safety profile was consistent with the T cell activation/expansion mechanism of action (MOA) without corticosteroid or tocilizumab pretreatment. The most common treatment-related adverse events (TRAEs) were mainly transient grade 1 & 2 CRS during first and second infusion without any grade 4 adverse events (AEs) or immune effector cell-associated neurotoxicity syndrome (ICANS)
- Recommended Phase 2 dose (RP2D) of 0.08 mg/kg was selected for Phase 2 dose expansion studies based on safety, PK/PD data and preliminary anti-tumor activity

"The first-in-human data suggest that this novel approach to selectively activate and expand Vβ T cell subsets may hold promise for treating patients with advanced solid tumors," said Dr. James L. Gulley, Co-Director of the Center for Immuno-Oncology and Clinical Director of the National Cancer Institute. "The observed unique Vβ T cell biology in humans and selective expansion of Vβ6/Vβ10 across a range of solid tumors, combined with the initial anti-tumor activity, particularly in heavily pre-treated anti-PD-1 resistant cancer patients with TMB-H colorectal cancer, are encouraging signs. The differentiated clinical profile supports further investigation of this unique mechanism of action in the next phase of clinical trials for high unmet medical needs in anti-PD-1 resistant tumors."

Taken together, the data presented from the STARt-001 study underscore invikafusp alfa's potential as a novel therapeutic option for patients with advanced, PD-1-resistant solid tumors. Marengo has initiated the Phase 2 dose expansion and expects to share initial results in 2H 2025.

Late-breaking oral presentation details:

- **Title:** A Phase 1/2 study of Invikafusp alfa (STAR0602), a first-in-class TCR β chain-targeted bispecific antibody, as monotherapy in patients with antigen-rich solid tumors resistant to anti-PD(L)1.
- **Conference:** 39th SITC Annual Meeting.
- **Abstract Number:** LBA-1470.
- **Session Title:** Late-Breaking Abstract Session 2.
- **Session Date and Time:** Saturday, November 9, 2024, 11:45 AM - 12:15 PM.
- **Presenter:** James L. Gulley, M.D., Ph.D. (National Cancer Institute, Bethesda, Maryland, USA).

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 Vβ 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 invikafusp alfa (STAR0602)
Invikafusp alfa (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 Vβ 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 and is currently being studied in a Phase 1/2 clinical trial.

About the STARt-001
STARt-001 is a Phase 1/2 clinical trial evaluating the safety, tolerability, and preliminary clinical activity of invikafusp alfa (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 2 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 1800-4-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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