Marengo Presents Expanded Clinical Monotherapy Activity of Invikafusp Alfa in Multiple PD-1 Resistant Tumors as a Clinical Plenary Oral at AACR 2025

- ***Invikafusp alfa demonstrates initial durable disease control, tumor regression, and objective responses in both primary and secondary PD-1 resistant tumors including CRC and NSCLC***

- ***Promising early monotherapy efficacy signal across all three major CRC subtypes with 30% ORR in the initial 10 TMB-H CRC patients treated at effective dose range further validates accelerated development plan with FDA fast track designation granted***

- ***New objective response reported in PD-1 negative TMB-H NSCLC post Keytruda + chemo combo further underscore pan-tumor potential and support focused expansion strategies***

Cambridge, Mass., April 29, 2025 – Marengo Therapeutics, Inc., a clinical-stage biotechnology company pioneering novel approaches for precision immunotherapy, today announced new clinical and translational data from the ongoing STARt-001 Phase 1/2 trial of invikafusp alfa (STAR0602), presented as a clinical plenary oral session at the American Association for Cancer Research (AACR) Annual Meeting 2025.

The presentation highlights strong evidence of meaningful clinical activity, robust immune activation *in vivo*, and a well-characterized safety profile, further supporting the momentum behind the ongoing Phase 2 study as well as the value proposition for developing invikafusp as monotherapy in PD1 resistant TMB-H cancers.

“Today’s data represent a major step forward for Marengo and for the field of IO to advance a new class of cancer immunotherapy: Immune Activation Inducers (IAI),” said Zhen Su, M.D., M.B.A., Chief Executive Officer of Marengo Therapeutics. “Invikafusp alfa’s ability to selectively activate and expand a key T cell subset to drive meaningful anti-tumor responses across a range of PD-1 resistant tumors gives us confidence in our precision T cell activation approach. The emerging clinical signals in both colorectal and lung cancers further underscore invikafusp’s pan-tumor potential and justify our focused expansion into these high-need indications.”

“Colorectal cancer is less sensitive to immunotherapy except in a very small percentage of MSI-H tumors. The field has seen few, if any, immunotherapy agents achieve single-agent activity in PD-1 resistant colorectal cancer,” said Josep Tabernero, M.D., Director of Vall d'Hebron Institute of Oncology (VHIO). “The clinical signals observed with invikafusp alfa in both CRC and other tumor types are highly encouraging and warrant further clinical investigation to fully realize the clinical potential of this novel T cell agonist approach.”

Invikafusp alfa is Marengo’s first-in-class dual T cell agonist, designed with a bi-specific antibody format to selectively engage and activate the Vβ6 and Vβ10 subsets of T cells in vivo, promoting durable anti-tumor immunity.

Updated Findings from the STARt-001 Clinical Plenary Presentation:

- **Clinically meaningful anti-tumor activity** as monotherapy in anti-PD(L)1-resistant tumors at the recommended Phase 2 dose (RP2D) of 0.08 mg/kg:
    - **61% disease control rate** in heavily pretreated, PD-1 resistant tumors dosed at 0.08 or 0.12 mg/kg
    - **52% tumor regression rate** observed across multiple tumor types, including colorectal cancer (CRC), non-small cell lung cancer (NSCLC), cervical, squamous cell carcinoma of the head and neck (SCCHN), and melanoma
    - **Objective responses in colorectal cancer and NSCLC:**
        - 3 responders out of 10 TMB-high metastatic CRC patients (across RAS wild-type, RAS mutant, and MSI-H subtypes)
        - 1 additional responder with 73% tumor regression out of 2 anti-PD(L)1-resistant TMB-high NSCLC patients

- **Mechanism of Action and Translational Insights:**
    - Invikafusp promoted potent, selective expansion of peripheral CD8+ Vβ6/Vβ10 T cells, which acquired a novel "memory-like effector" phenotype in both blood and tumor tissue
    - Expanded and activated Vβ T cells in post treatment tumor tissues consistent with enhanced anti-tumor function

- **Safety Profile:**
    - Consistent with a selective T cell activation mechanism
    - Adverse events were generally transient and manageable with supportive care

Based on these early clinical and preclinical findings, the U.S. Food and Drug Administration has granted Fast Track Designation to invikafusp alfa for the treatment of patients with TMB-high colorectal cancer.

The Phase 2 portion of the STARt-002 trial is actively enrolling patients across multiple tumor types, including TMB-H metastatic colorectal cancer, MSI-H and TMB-H tissue-agnostic solid tumors.

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 autoimmune diseases. With a passionate team of dedicated scientists experienced in immunology and oncology, and three proprietary platforms: Selective T Cell Activation Repertoire (STAR), Trispecific T Cell Engager (Tri-STAR) and T cell Depletor (MSTAR), Marengo is working to selectively target the right T cells in the right patients to create a world in which everyone's immune system can defeat cancer and autoimmune diseases. To learn more, visit marengotx.com.

About the 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 the lead candidate from Marengo's STAR™ platform. It is designed to selectively activate a common Vβ T cell subset found in all cancers by combining a non-clonal mode of TCR activation with a T cell co-stimulatory signal in a single molecule. This innovative approach promotes the expansion of clonally diverse, effector memory Vβ T cells, enhancing anti-tumor immunity and enabling durable tumor clearance. Extensive preclinical studies demonstrate STAR0602's potent anti-tumor activity in both mouse and human ex vivo models via a novel mechanism of action.

About the STARt-001 Clinical Study
STARt-001 is a Phase 1/2 clinical trial evaluating the safety, tolerability, and preliminary efficacy of invikafusp alfa as a monotherapy in biomarker-selected patients with advanced antigen-rich solid tumors, including PD-1 refractory and rare tumor types. The trial consists of two parts: Phase 1 dose escalation and Phase 2 dose expansion. For more information, visit clinicaltrials.gov (Identifier: NCT05592626).

Patients interested in participating in this study at the National Cancer Institute (NCI) can contact NCI's toll-free number: 1-800-4-CANCER (1-800-422-6237) (TTY: 1-800-332-8615), visit the website at https://trials.cancer.gov, or email NCIMO_referrals@mail.nih.gov.

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