Marengo Late-Breaking Oral Presentation Highlights Single-Agent, Pan Tumor Activity of Invikafusp Alfa Across PD-1-Resistant Cancers in Phase 2 Clinical Trial at SITC 2025

- ***20% ORR and 80% DCR observed as monotherapy in TMB-H tumors across seven major solid tumor types, including colorectal, lung, breast, gastric, gastroesophageal junction (GEJ), head and neck, and bladder cancers***

- ***Clinical activity was consistent across all subgroups and independent of prior PD-1 treatment, with 59% of patients experiencing target-lesion tumor shrinkage***

Cambridge, Mass., November 7, 2025 – Marengo Therapeutics, Inc., a clinical-stage biotechnology company pioneering precision immunotherapies for oncology and inflammation & immunology (I&I), today announced updated interim results from the ongoing Phase 2 expansion of its lead program, Invikafusp alfa (STAR0602).

The data were presented in a late-breaking clinical oral presentation at the Society for Immunotherapy of Cancer (SITC) 2025 Annual Meeting. This marks Invikafusp alfa's fifth major oral presentation, underscoring continued external interest and excitement around the rapid progression of Marengo's lead program.

"The expanded, pan-tumor single-agent activity of Invikafusp alfa in PD-1 resistant TMB-H cancers across seven major solid tumor indications reinforces our vision for developing a next-generation immuno-oncology (IO) backbone therapy," said Zhen Su, M.D., MBA, Chief Executive Officer of Marengo Therapeutics. "Paired tumor biopsy analyses provide compelling evidence that we are selectively activating and reprogramming Vβ6⁺ T cells within the TIL compartment — a critical mechanism that translates into meaningful clinical benefit. These results validate our first-in-class precision dual T cell activation platform and support our bold mission to overcome PD-1 resistance."

As of the July 15, 2025 data cutoff, 57 patients with TMB-H advanced solid tumors were enrolled across 20 histologies and 46 patients were efficacy-evaluable. Key findings are outlined below.

- Pan tumor monotherapy activity in PD-1-resistant TMB-H patients:
  - 20% ORR and 80% DCR observed across seven major tumor types — colorectal, gastric, lung, breast, GEJ, head and neck, and bladder cancers
  - Responses by indication include gastrointestinal (GI) tumors (28% ORR, 78% DCR), colorectal cancer (CRC) (33% ORR, 67% DCR), and non-small cell lung cancer (NSCLC) (20% ORR, 80% DCR)
  - Target tumor shrinkage, with 59% of patients experiencing target-lesion regression
  - Anti-tumor activity observed in both immune checkpoint blockade (ICB)-naïve and ICB-experienced patients, across both primary and secondary PD-1-resistant tumors
  - Activity in both microsatellite stable (MSS) and microsatellite instability (MSI)-H Tumors, including clinical benefit observed across a range of TMB levels, irrespective of MSI status

- A safety profile consistent with the selective T cell activation mechanism of action, treatment-related adverse events (AEs) were transient and manageable with supportive care
- Mechanistic activity validated in paired biopsies and blood samples, with evidence of:
    - Selective Vβ6⁺ T cell expansion consistent with peripheral expansion and intratumoral enrichment of Vβ6⁺ T cells observed following treatment
    - In vivo TIL reprogramming with robust upregulation of TCR signaling, cytotoxicity, and chemokine expression post-treatment, indicating enhanced immune activation within the tumor microenvironment
    - Downregulation of immune-suppressive factors and upregulation of activation and cytotoxic markers among patients who experienced tumor shrinkage

Invikafusp alfa is a first-in-class bispecific dual T cell agonist designed to selectively activate and expand Vβ6⁺/Vβ10⁺ T-cell subsets — which represent highest prevalent of tumor-infiltrating lymphocytes (TILs) — to restore and amplify anti-tumor immunity in patients who have progressed on or are insensitive to ICB.

Marengo is advancing a post–PD-1, biomarker-enriched development strategy for Invikafusp alfa, continuing the Phase 2 monotherapy expansion in TMB-H and MSI-H/dMMR solid tumors to further characterize depth and durability of response across priority indications.

To reach broader, frontline patient populations beyond the TMB-H setting, the company is also conducting a Phase 2 combination study with Trodelvy® (a TROP2-directed antibody-drug conjugate) in triple-negative breast cancer (TNBC) and HR⁺/HER2⁻ breast cancer to evaluate synergy in ADC + IO combination settings. In parallel, Marengo continues to advance regulatory interactions, including recent receipt of U.S. FDA Fast Track designation for Invikafusp alfa in TMB-H metastatic colorectal cancer (mCRC).

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 global 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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