

Marengo Therapeutics Presents Phase 2 START-001 Results at ESMO 2026 Demonstrating Tissue-Agnostic Single-Agent Activity of Invikafusp Alfa in TMB-H Solid Tumors Mostly Unresponsive to Immune Checkpoint Blockade

- Objective responses observed across eight distinct tumor types, including breast, colorectal, endometrial, gastroesophageal junction, gastric, head and neck, non-small cell lung and bladder cancers
- Tumor shrinkage observed in 56% of evaluable patients, with an 18% objective response rate (ORR) and 60% disease control rate (DCR) across these eight tumor types in a heavily pretreated population
- Clinical and translational findings provide further evidence that selective V β T-cell activation can amplify and expand antitumor immune responses beyond the PD-1 pathway
- Results complement first-in-human START-001 findings simultaneously published today in the peer-reviewed journal *Nature Medicine*

CAMBRIDGE, Mass., October 23, 2026 /PRNewswire/ -- Marengo Therapeutics, Inc., a clinical-stage biotechnology company pioneering precision immunotherapies for oncology and inflammation and immunology (I&I), today announced the presentation of Phase 2 results from the START-001 clinical trial of invikafusp alfa at the European Society for Medical Oncology (ESMO) Congress 2026, taking place October 23–27 in Madrid, Spain.

The oral presentation, titled “START-001: Phase 2 results of invikafusp alfa, a first-in-class T-cell receptor β -chain–targeted bispecific antibody, as monotherapy in patients with TMB-H solid tumors resistant to immune checkpoint blockade,” includes clinical and translational findings from the ongoing Phase 2 study.

START-001 is a Phase 1/2 study evaluating invikafusp alfa, a first-in-class dual T-cell agonist designed to amplify antitumor immunity, as a single agent in patients with unresectable, locally advanced or metastatic tumor mutation burden-high (TMB-H) solid tumors mostly unresponsive to immune checkpoint blockade (ICB). This population includes patients whose tumors progressed following prior checkpoint inhibition, as well as patients with tumor types for which checkpoint inhibitors are not approved or have historically demonstrated limited benefit.

The results showed tissue-agnostic antitumor activity across multiple heavily pretreated tumor types, providing further clinical evidence that selective activation of V β T-cell populations can generate antitumor responses beyond the PD-1 pathway. The findings are consistent with the tissue-agnostic rationale recognized in invikafusp alfa’s second FDA Fast Track Designation, recently granted for TMB-H solid tumors regardless of tissue of origin.

“Patients with tumors that are unresponsive to immune checkpoint blockade continue to face a significant unmet need, whether their disease has progressed following prior checkpoint inhibition or checkpoint therapy is not an established treatment option for their tumor type,” said Elena Garralda, M.D., Ph.D., Director of the Research Unit for Molecular Therapy of Cancer

(UITM) – CaixaResearch at Vall d’Hebron Institute of Oncology and principal investigator of the study. “The Phase 2 results presented at ESMO show a tissue-agnostic efficacy signal with invikafusp alfa across multiple heavily pretreated tumor types. The translational findings also demonstrate selective expansion of Vβ6-positive T-cell clonotypes, along with an increase in tumor-infiltrating lymphocyte clonotypes, supporting the ability of this novel mechanism to generate antitumor immune responses beyond PD-1 biology.”

Highlights from the Phase 2 START-001 oral presentation

- Objective responses were observed across eight distinct tumor types, including breast, colorectal, endometrial, gastroesophageal junction, gastric, head and neck, non-small cell lung and bladder cancers.
- Among 62 evaluable patients with heavily pretreated TMB-H solid tumors across these eight tumor types, tumor shrinkage was observed in 56% of patients, with an 18% ORR and 60% DCR.
- Activity was observed in both ICB-experienced and ICB-naïve patients.
 - ORR and DCR were numerically higher among ICB-experienced patients than among ICB-naïve patients (20% versus 14%, and 68% versus 43%), respectively.
 - Among ICB-experienced patients, responses were observed in tumors with both primary and secondary resistance, with ORRs of 23% and 28%, respectively.
- Translational analyses showed rapid and reproducible polyclonal expansion of Vβ6-positive T-cell clonotypes following the first infusion, accompanied by increased overlap between blood and tumor clonotypes consistent with trafficking of activated T cells into tumors. These findings further support selective Vβ T-cell activation as a mechanism capable of expanding antitumor immune responses beyond the PD-1 pathway.
- In 104 patients evaluated for safety, invikafusp alfa showed a manageable tolerability profile consistent with selective T-cell activation. Cytokine release syndrome was mainly Grades 1 and 2, with no immune effector cell-associated neurotoxicity syndrome and no Grade 5 treatment-related adverse events observed.

“These Phase 2 results demonstrate the breadth of invikafusp alfa’s single-agent activity across biologically distinct, heavily pretreated tumor types and represent an important efficacy signal for this first-in-class mechanism,” said Zhen Su, M.D., M.B.A., President and Chief Executive Officer of Marengo Therapeutics. “START-001 was designed as a signal-seeking basket study to evaluate this novel biology across a heterogeneous group of tumors. The activity observed across eight tumor types is now informing a focused, evidence-led development strategy in populations where the biological rationale and unmet need are strongest.”

The tissue-agnostic results presented at ESMO point to the potential breadth of Vβ-directed immunotherapy. Invikafusp alfa was designed to amplify antitumor immunity and is well suited to complement standard-of-care therapies, with the potential for synergistic antitumor activity.

Marengo's combination strategy aims to build greater depth in prioritized indications by pairing invikafusp alfa with these therapies while also supporting its long-term vision for invikafusp alfa as a potential immuno-oncology backbone that can be tailored to the right tumor, the right patient and the right therapeutic solution.

Additionally, results from the Phase 1 dose-escalation and initial Phase 2 expansion of STARt-001 were published today in *Nature Medicine*. The publication represents the first clinical report of a V β -directed dual T-cell agonist and establishes first-in-human proof that selected germline-encoded V β T-cell populations can be therapeutically activated and expanded in patients with advanced cancer.

The *Nature Medicine* publication and ESMO presentation collectively provide compelling evidence for invikafusp alfa and Marengo's broader V β -directed immunotherapy strategy.

Marengo is advancing invikafusp alfa through a focused clinical strategy spanning biomarker-selected single-agent development and rational combinations in prioritized tumor settings. The company will present interim Phase 2 results from STARt-002, the first clinical study combining a V β 6-selective T-cell agonist with an antibody-drug conjugate in triple-negative and HR-positive/HER2-negative metastatic breast cancer at the Society for Immunotherapy of Cancer 2026 Annual Meeting.

Further analyses from STARt-001 are also ongoing, with a more complete clinical dataset expected in 2027.

About Invikafusp Alfa (STAR0602)

Invikafusp alfa (STAR0602), the lead candidate from Marengo's STAR™ platform, is a first-in-class, bispecific dual T-cell agonist. It is designed to selectively activate a common V β T-cell subset shared across most cancers by combining a non-clonal mode of TCR activation with a T-cell co-stimulatory signal in a single molecule. This approach promotes the expansion of clonally diverse, effector memory V β T cells, enhancing antitumor immunity and enabling durable tumor clearance. Invikafusp alfa was designed to restore and amplify antitumor immunity in patients who have progressed on, or are insensitive to, prior immune checkpoint blockade. Invikafusp alfa has been granted two Fast Track Designations from the U.S. Food and Drug Administration; the first for the treatment of TMB-H colorectal cancer (granted January 2025) and the second designation, which expands invikafusp alfa's Fast Track status to TMB-H solid tumors regardless of their tissue of origin (granted October 2026).

About the STARt-001 Clinical Study

STARt-001 is a global Phase 1/2 trial evaluating invikafusp alfa monotherapy in patients with advanced, antigen-rich solid tumors that are unresponsive to immune checkpoint blockade, including tumors that progressed on prior PD-1-directed therapy. The Phase 2 portion uses biomarker-enriched cohorts, including TMB-H and MSI-H, to assess activity across multiple tumor types and help identify patients most likely to benefit. For more information, visit

ClinicalTrials.gov ([NCT05592626](https://clinicaltrials.gov/ct2/show/study/NCT05592626)). STARt-001 Phase 2 expansion is ongoing to further investigate invikafusp alfa for the treatment of ICB-resistant 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.

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