Marengo

Marengo Therapeutics Presents Preclinical Data Supporting Clinical Investigation of its Lead Asset, STAR0602, at the 2022 Society for Immunotherapy of Cancer (SITC) Annual Meeting

- *STAR0602 expands both pre-existing and neoantigen-specific tumor infiltrating Vβ T cell subsets to induce potent anti-tumor activity as monotherapy in PD-1 refractory human and murine tumor models*

- *Comprehensive pharmacology in non-human primates (NHPs) supports the design of a biomarker enriched, tissue-agnostic Phase 1/2 trial with STAR0602 in PD-1 refractory patients, planned to commence in Q4 2022*

Cambridge, Mass. November 10, 2022 – Marengo Therapeutics, Inc., a company pioneering novel therapeutics targeting the T cell receptor Vβ chain (TCR Vβ) to selectively activate the right T cell subsets to fight cancer, today will be presenting preclinical data that characterizes the mechanism of action and confirms robust anti-tumor activity for its novel T cell-activating antibody STAR0602 at the Society for Immunotherapy of Cancer (SITC) 37th Annual Meeting in Boston. The data disclosed also includes extensive characterization pharmacokinetic (PK) and pharmacodynamic (PD) relationships of STAR0602 in NHP studies. These data support the modelling of human pharmacology and inform the design of START-001, a Phase 1/2 clinical trial of STAR0602 monotherapy in a biomarker enriched, tissue agnostic, PD-1 refractory cancer patient population.

"STAR0602 has been shown to promote potent anti-tumor activity through a PD-1 independent mechanism and leads a new IO category of selective immune activators, potentially offering another important treatment option to reach more patients," said Zhen Su, M.D., MBA, Chief Executive Officer of Marengo. "We are pleased to present a compelling body of preclinical data that builds on the initial proof-of-concept data shared during our Plenary Oral presentation at the recent 34th EORTC-NCI-AACR (ENA) Symposium last month."

The data presented at SITC by Marengo scientists and its academic collaborators highlight Marengo's novel TCR Vβ repertoire-targeting antibody platform, which promotes the expansion of polyclonal Vβ T cells with a novel effector memory phenotype.

Presentation details are outlined below.

Title: A novel class of T cell-activating antibody that selectively targets the TCR β chain to promote antitumor activity through activation and expansion of a novel, polyclonal effector memory T cell subset
Abstract Number: 1316
Presenter: Andrew Bayliffe, Ph.D. (Marengo Therapeutics, Cambridge, Massachusetts USA)
Research Highlights: STAR0602 is a first-in-class bifunctional fusion molecule that selectively binds and activates subsets of the germline TCR repertoire. In vitro, STAR0602 promotes a novel T cell phenotype with hallmarks of both effector and central memory cells, and in vivo mSTAR0602 demonstrates potent and durable single-agent anti-tumor activity in several solid tumor models that is dependent on expanded Vβ T cells. The modulation of the tumor

microenvironment (TME), striking increase in TCR diversity, and functional immune memory observed in murine models suggests that STAR0602 could remodel the adaptive immune response to solid tumors that are refractory to checkpoint inhibitor therapy, and thus represents a novel therapeutic strategy for patients.

Title: Preclinical evaluation of STAR0602, a novel, first-in-class anti-TCR Vβ targeted bispecific antibody with potent anti-tumor activity for PD-1 refractory solid tumors
Abstract Number: 1337
Presenter: James Gulley, M.D., Ph.D. (National Cancer Institute, Bethesda, Maryland USA)
Research Highlights: STAR0602 is a first-in-class T cell activator that targets subsets of the germline TCR repertoire that are enriched in TILs. STAR0602 potently expands both naive and antigen-specific human T cells. In PD1 refractory human organoid models with a high TMB, STAR0602 induced potent anti-tumor activity as monotherapy, mediated by selective expansion of Vβ CD8+ memory T cells. This pharmacology was translated into monkeys with IV dosed STAR0602 and supports the design of a novel Phase 1/2 precision-oncology trial with STAR0602 planned to commence in 2022.

Title: An atypical central-memory like phenotype can be induced in human T cells by Innate TCRαβ engagement
Abstract Number: 1392
Presenter: Pierre Vantourout, Ph.D. (Kings College London, London, UK)
Research Highlights: Engaging germline-encoded regions of human TCRVβ consistently activate primary human T cells toward an atypical central memory (TCM)-like phenotype distinct from those most commonly described for anti-CD3 antibody stimulation. The cells show myriad surface markers of chronic stimulation, but are not exhausted, being highly proliferative and strongly expressing cytolytic mediators and IFN-γ. This phenotype can be induced in cells previously driven toward effector memory (TEM) and TEMRA states. The use of TCRβ chain as an innate receptor offers new insight into T cell biology and ways in which such cells might be clinically manipulated.

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About Marengo Therapeutics
Marengo Therapeutics, Inc, an ATP company, is pioneering first-in-class therapeutics that activate the right immune response to promote lifelong protection against cancer. 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 STAR0602
STAR0602, Marengo's lead program, is the first T cell activator generated by the company's STAR platform, a multi-specific fusion protein library that targets specific TCR Vβ variants fused to different co-stimulatory moieties generating potent T cell activators. The unique feature of the Marengo STAR platform is to fine-tune the T cell response in selected T cell subsets to

generate endogenous, highly functional, cancer-killing T cells for solid tumors. STAR0602 is a fusion protein that binds to a specific region of TCR Vβ and delivers a unique activation signal on the same T cell, leading to a selective expansion of the targeted T cell subclones. This molecule has shown remarkable single agent activity in a vast array of preclinical models.

Media Contact:

Darby Pearson
Verge Scientific Communications
dpearson@vergescientific.com