# First-of-its-kind Engineered Macrophage Cell Therapy Platform Shows Ability to Reduce Tumor Burden and Activate Anti-Tumor Immunity, Improving Overall Survival in Pre-Clinical Cancer Models

March 23, 2020

*Study highlights previously untapped potential of genetically engineered macrophages in immunotherapy for solid tumors*

PHILADELPHIA, March 23, 2020 /PRNewswire/ -- Carisma Therapeutics Inc., a biopharmaceutical company focused on discovering and developing innovative immunotherapies, today announced that *Nature Biotechnology* has published a study from the Perelman School of Medicine at the University of Pennsylvania demonstrating Carisma's foundational technology evaluating the potential of human chimeric antigen receptor macrophages (CAR-M) for cancer immunotherapy. The preclinical findings, outlined in "Human Chimeric Antigen Receptor Macrophages for Cancer Immunotherapy," indicate that CAR-M therapy could overcome the key challenges that cell therapies have encountered with solid tumors – limited trafficking to the tumor site, an immunosuppressive tumor microenvironment, and the heterogeneous expression of tumor-associated antigens.

The Penn team hypothesized that CAR macrophages could overcome these barriers because of the macrophage's innate ability to infiltrate solid tumors, eat away at cancer by phagocytosing cells, and activate the adaptive immune system. Carisma engineered human macrophages to express an anti-human epidermal growth factor receptor 2 (HER2) CAR, which, when tested in a variety of humanized mouse models of cancer, reduced tumor burden and significantly improved overall survival.

"This is the first time that human macrophages have been engineered to express CARs and have successfully been shown to infiltrate tumors, influence the surrounding tumor microenvironment, reduce tumor burden through phagocytosis and increase overall survival in animal models of solid tumors," said study co-author Michael Klichinsky, PharmD, PhD, Co-Inventor of the CAR-M technology and Scientific Co-Founder and Vice President of Discovery of Carisma Therapeutics. "Our findings also leave open the possibility for combination therapy in the future with other agents that play a role in cell death pathways or T-cell-based immunity."

The introduction of CARs to macrophages through an efficient and robust adenoviral vector transduction method conferred a pro-inflammatory (M1) macrophage phenotype, which rendered the CAR-M capable of remodeling the tumor microenvironment. Importantly, CAR-Ms maintained anti-tumor activity even in the presence of anti-inflammatory factors such as immunosuppressive cytokines or cells, and demonstrated the ability to convert M2 pro-tumor macrophages to an anti-tumor M1 phenotype.

"We are greatly encouraged by the results we have seen in this study, particularly that CAR-Ms are able to co-stimulate and present ingested tumor antigens to T-cells, potentially inducing a T-cell anti-tumor response," said study co-author Saar Gill, MD, PhD, Scientific Co-Founder of Carisma Therapeutics, Assistant Professor of Hematology-Oncology in Penn's Abramson Cancer Center. "This supports our focus on macrophages as possible game-changers in the field of adoptive cellular therapy."

Carisma is working toward a future IND filing and developing operational plans with key partners to initiate a Phase I clinical trial evaluating CT-0508, a HER2 targeted CAR-M.

"These results demonstrate a previously untapped approach in harnessing our immune systems to tackle cancer," said Steven Kelly, President and Chief Executive Officer at Carisma Therapeutics. "This is novel science with a potentially profound impact, and we're excited to see this unfold and ultimately play a meaningful role in the way patients and their providers determine treatment plans for historically hard-to-treat cancers, especially solid tumors."

**About Carisma Therapeutics Inc.**

Carisma Therapeutics Inc. is a biopharmaceutical company developing a differentiated and proprietary cell therapy platform focused on engineered macrophages, cells that play a crucial role in both the innate and adaptive immune response. The first applications of the platform, developed in collaboration with the University of Pennsylvania, are autologous chimeric antigen receptor macrophages (CAR-M) for the treatment of solid tumors. Carisma Therapeutics is headquartered in Philadelphia, PA.

For more information, please visit www.carismatx.com.

**Media Contact:**
Christina Khoury-Folkens
612-806-0757
ckhoury@w2ogroup.com

SOURCE Carisma Therapeutics Inc.