Allogene Therapeutics Unveils Novel Approach to Generate Engineered AlloCAR T™ Cells to Control Immune Rejection at the Annual Meeting of the Society for Immunotherapy of Cancer

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- Promising Preclinical Data Highlights a Simple One-Step Gene Editing Strategy to Prevent the Rejection of AlloCAR T™ Cells by Host T Cells and NK Cells
    - Cloaking Approach Demonstrates Superiority to B2M Knock Out in a Syngeneic In Vivo Model
- Proprietary Approach Is One of Several Next Generation Technologies Being Pioneered at Allogene to Control Rejection

SOUTH SAN FRANCISCO, Calif., Nov. 10, 2022 (GLOBE NEWSWIRE) -- Allogene Therapeutics, Inc. (Nasdaq: ALLO), a clinical-stage biotechnology company pioneering the development of allogeneic CAR T (AlloCAR T™) products for cancer, today presented pre-clinical data on a novel approach to immune “cloaking” designed to protect AlloCAR T™ cells from rapid host rejection. The technology is designed to prevent AlloCAR T™ cells from being recognized by host T cells without triggering substantial natural killer (NK) cell rejection and while preserving CAR T cell function. The findings were presented today during a poster session at the 37th Annual Meeting of the Society for Immunotherapy of Cancer (SITC).

The development of “off-the-shelf” (allogeneic) CAR T products that utilize cells from healthy donors have the potential to make CAR T therapies scalable and accessible to more patients. The effectiveness of allogeneic CAR T cells requires controlling immune rejection of allogeneic CAR T cells by the patient’s immune cells, namely T and NK cells. Allogene is currently developing ALLO-647, a lymphodepletion agent which targets host immune cells but not AlloCAR T™ cells, to enhance the window of CAR T engraftment, but is also investigating several novel strategies that may enhance the performance of allogeneic CAR T products by controlling immune rejection. This preclinical study evaluated an alternative approach to immune evasion by selectively targeting NLRC5 and RFX5, transcriptional regulators that control expression of HLA molecules. NLRC5 knockout avoids CD8 T cell mediated rejection and RFX5 knockout avoids rejection by both CD8 and CD4 T cells, allowing the possibility to avoid a broader spectrum of T cell-mediated rejection with just one edit, in contrast to alternative approaches that require two edits.

“We believe that novel approaches to cloaking may further increase the efficacy of off-the-shelf CAR T products through avoidance of immune rejection,” said Barbra Sasu, Ph.D. Chief Scientific Officer at Allogene. “As we look to deliver on the promise of AlloCAR T cell products, we are investigating several novel approaches to supplement or potentially even replace our current platform for immune rejection avoidance. The data presented today is promising, showing that knockout of NLRC5 and RFX5 reduced T cell rejection whilst minimizing NK cell rejection and without impacting CAR T cell performance.”

In the study, the survival of “cloaked” cells was assessed in mixed lymphocyte reaction assays with T cells, NK cells, or a combined assay with T and NK cells. The knockout of NLRC5 or RFX5 in allogeneic CAR T cells enhanced survival in the presence of host T cells and elicited only minor NK cell reactivity, thereby effectively mitigating rejection. Importantly, the inactivation of NLRC5 or RFX5 did not impact CAR T cell phenotype or cytotoxic activity. The NLRC5 or RFX5 edited CAR T cells also demonstrated superior persistence and anti-tumor efficacy compared to un-edited CAR T cells or B2M edited CAR T cells in a stringent syngeneic model *in vivo*. These modifications would be designed to be part of an overall editing and gene expression platform to avoid CAR T rejection.

About Allogene Therapeutics
Allogene Therapeutics, with headquarters in South San Francisco, is a clinical-stage biotechnology company pioneering the development of allogeneic chimeric antigen receptor T cell (AlloCAR T™) products for cancer. Led by a management team with significant experience in cell therapy, Allogene is developing a pipeline of “off-the-shelf” CAR T cell candidates with the goal of delivering readily available cell therapy on-demand, more reliably, and at greater scale to more patients. For more information, please visit www.allogene.com and follow @AllogeneTx on Twitter and LinkedIn.

Cautionary Note on Forward-Looking Statements
This press release contains forward-looking statements for purposes of the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. The press release may, in some cases, use terms such as "predicts," "believes," "potential," "proposed," "continue," "estimates," "anticipates," "expects," "plans," "intends," "may," "could," "might," "will," "should" or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements. Forward-looking statements include statements regarding intentions, beliefs, projections, outlook, analyses or current expectations concerning, among other things: the ability to research and develop technologies to protect AlloCAR T™ cells from rapid host rejection; the ability of NLRC5 or RFX5 edited CAR T cells to demonstrate persistence and antitumor efficacy; and the potential benefits of ALLO-647 and AlloCAR T products. Various factors may cause differences between Allogene’s expectations and actual results as discussed in greater detail in Allogene’s filings with the SEC, including without limitation in its Form 10-Q for the quarter ended September 30, 2022. Any forward-looking statements that are made in this press release speak only as of the date of this press release. Allogene assumes no obligation to update the forward-looking statements whether as a result of new information, future events or otherwise, after the date of this press release.

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