May 11, 2021

First Preclinical Data from Adaptimmune's Mesothelin HiT Program at ASGCT Demonstrate Antigen-specific Tumor Cell Killing in vitro and Complete Tumor Regression in an Animal Model

- Preclinical data validate that human T-cells expressing a TCR targeting mesothelin, independent of HLA recognition, can kill human tumor cells -

- HiT works as well, or better than, a TRuC construct targeting mesothelin in preclinical studies -

PHILADELPHIA and OXFORDSHIRE, United Kingdom, May 11, 2021 (GLOBE NEWSWIRE) -- Adaptimmune Therapeutics plc (Nasdaq:ADAP), a leader in cell therapy to treat cancer, reported preclinical data from its HiT targeting mesothelin, being co-developed with Astellas, during a poster presentation at the American Society for Cell and Gene Therapy (ASGCT) meeting today.

"These data are very exciting because our HLA-independent TCR targeting mesothelin induced complete regression in a mouse tumor xenograft model and also outperformed a TRuC construct that we developed in-house," said Karen Miller, SVP, Pipeline Research. "The natural signaling machinery of the TCR, as well as our proprietary TCR engineering and affinity optimization expertise, offer distinct advantages over cell therapies that rely on antibody moieties to engage antigen. We are evaluating further HiT targets, as we deliver against our 2-2-5-2 strategic plan to bring new cell therapy products forward for clinical development and launch."

Adaptimmune has developed a T-cell receptor (TCR) that can directly bind to the cell surface protein mesothelin, independent of HLA, using the Company's proprietary naïve phage display libraries and affinity optimization techniques. The HLA-independent TCR or HiT platform enables the Company to target extracellular proteins, such as those utilized by CAR or TRuC T-cell therapies. Data from the ASGCT presentation are summarized below.

Adaptimmune's HiTs are CD8 and HLA-independent and kill mesothelin expressing human tumor cells

- Human T-cells expressing the mesothelin-targeted HiT kill human tumor cell lines and primary human lung tumor cells expressing mesothelin
- Data demonstrate that the mesothelin HiT is not dependent on CD8 to kill target cells, and CD4 cells expressing the HiT are cytotoxic towards tumor cells
- A TRuC construct was developed by Adaptimmune as a comparator for these experiments, which also killed mesothelin target cells independently of CD8

Adaptimmune's HiTs are not neutralized by free mesothelin, but the TRuC construct is

- Data from additional in vitro experiments clearly show that Adaptimmune's HiT is not neutralized by soluble mesothelin, unlike the TRuC construct
- It has been described that CAR-T and similar therapies, which rely on high affinity antibody moieties to engage antigen, can be neutralized by soluble target protein, inhibiting their function[1]
- This is particularly important for many tumor targets that are both cell-surface bound and secreted, as is the case with mesothelin

Adaptimmune's HiT T-cells targeting mesothelin induce complete tumor regression in a mouse xenograft tumor model and outperform a comparator TRuC construct

- Immunodeficient mice were implanted with human pancreatic Capan-2 mesothelin-expressing tumor cells
- Mice with pre-established tumors received HiT T-cells or TRuC comparator T-cells by a single IV injection
- Data showed a strong, dose-dependent, and persistent tumor regression with HiT T-cells
- TRuC T-cells only inhibited tumor growth at comparative doses to those used with the HiT T-cells

About Adaptimmune
Adaptimmune is a clinical-stage biopharmaceutical company focused on the development of novel cancer immunotherapy products for people with cancer. The Company's unique SPEAR (Specific Peptide Enhanced Affinity Receptor) T-cell platform enables the engineering of T-cells to target and destroy cancer across multiple solid tumors.

Forward-Looking Statements
This release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 (PSLRA). These forward-looking statements involve certain risks and uncertainties. Such risks and uncertainties could cause our actual results to differ materially from those indicated by such forward-looking statements, and include, without limitation: the success, cost and timing of our product development activities and clinical trials and our ability to successfully advance our TCR therapeutic candidates through the regulatory and commercialization processes. For a further description of the risks and uncertainties that could cause our actual results to differ materially from those expressed in these forward-looking statements, as well as risks relating to our business in general, we refer you to our Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on May 6, 2021 and our other SEC filings. The forward-looking statements contained in this press release speak only as of the date the statements were made and we do not undertake any obligation to update such forward-looking statements to reflect subsequent events or circumstances.

Adaptimmune Contacts:

Media Relations:

Sébastien Desprez — VP, Communications and Investor Relations
T: +44 1235 430 583

M: +44 7718 453 176
Sebastien.Desprez@adaptimmune.com

Investor Relations:

Juli P. Miller, Ph.D. — Senior Director, Investor Relations
T: +1 215 825 9310
M: +1 215 460 8920

---

[1] Pont MJ, Hill T, Cole GO, et al. γ-Secretase inhibition increases efficacy of BCMA-specific chimeric antigen receptor T cells in multiple myeloma. Blood. 2019;134(19):1585-1597.

Source: Adaptimmune Therapeutics plc