June 11, 2018

Study published in Cancer Discovery Indicates that NY-ESO SPEAR T-cells are Long-lived, Self-renewing, and Capable of Persistent Anti-Tumor Effects

Data indicate that self-renewing pools of SPEAR T-cells can produce a continuous supply of effector cells capable of mediating sustained antitumor effects

PHILADELPHIA and OXFORD, United Kingdom, June 11, 2018 (GLOBE NEWSWIRE) -- Adaptimmune Therapeutics plc (Nasdaq:ADAP), a leader in T-cell therapy to treat cancer, today announced that data from the pilot study of NY-ESO SPEAR T-cells in synovial sarcoma will be published in *Cancer Discovery* (an American Association of Cancer Research [AACR] publication). Beyond the clinical data, some of which having been reported previously (most recently at CTOS 2017 [https://bit.ly/2mtk13W]), this peer-reviewed paper provides new insights into SPEAR T-cells and the responses they mediate in patients.

GlaxoSmithKline plc (LSE:GSK) (NYSE:GSK) exercised its option to exclusively license the right to research, develop, and commercialize NY-ESO SPEAR T-cell therapy program in September 2017. Transition of this program to GSK is ongoing.

“Metastatic synovial sarcoma is virtually incurable with standard therapy. NY-ESO SPEAR T-cells can mediate durable antitumor responses in these patients,” said Rafael Amado, Adaptimmune’s Chief Medical Officer. “Data published in *Cancer Discovery* highlight that our persisting SPEAR T-cells comprise a robust, self-regenerating pool of polyfunctional, non-exhausted T-cells capable of antitumor effects despite prolonged exposure to antigen. Our efforts to better understand the characteristics of our SPEAR T-cells post-infusion will continue as we strive to bring the most effective therapies to patients.”

"The results of the study are encouraging," said Dr Sandra D'Angelo, medical oncologist at Memorial Sloan Kettering Cancer Center. "Through this research and these results we are understanding how to better treat synovial sarcoma."

Data from Cohort 1 of the synovial sarcoma pilot study, based on twelve patients treated, included in the peer reviewed paper (data cut off 30 March 2017), is summarized below.

Compelling response data

- Median duration of response of 30.9 weeks (range 13-72 weeks)
- Overall response rate of 50% (6/12 patients), and 60% among the ten patients who received the target dose of at least one billion transduced cells

- There was one confirmed complete response and five confirmed partial responses
- Median time to initial response of 6.2 weeks (range 4-9 weeks)

Encouraging survival data

- Median progression-free survival (PFS) was 15 weeks (range 8-38 weeks)
- The current estimate of the median overall survival is approximately 120 weeks among the twelve patients in Cohort 1 (range 37 weeks-undetermined value, as the upper bound has not been reached)

Characteristics of antitumor responses indicate effects are immune-mediated

- Maximal effects of chemotherapy are typically observed within four weeks of treatment; however, seven patients experienced continued decreases in tumor burden following the four week evaluation point, and maximal antitumor responses occurred in four patients more than three months post-infusion
- There was also demonstration of transient increases in the size of metastatic lesions consistent with lymphocyte-induced inflammation followed by regression as well as trafficking of SPEAR T-cells into the tumor bed, indicating that, unlike currently available immune therapies, these cells can kill cancer cells in previously non-inflamed tumors

Acceptable safety profile

- The majority of adverse events were consistent with those typically experienced by cancer patients undergoing cytotoxic chemotherapy or other cancer immunotherapies.
- There were no fatal serious adverse events in this treatment cohort
- The most common adverse events ≥ grade 3 were lymphopenia (100%), leukopenia (92%), neutropenia (83%), anemia (83%), hypophosphatemia (75%), and thrombocytopenia (67%)
- Five patients experienced cytokine release syndrome (CRS) of grades 1 (n=2), 2 (n=1), and 3 (n=2)
  - CRS occurred within a median of four days post-infusion (range 0-11 days; 1 instance occurred on day of treatment), and the median duration of CRS was ten days (range 8 – 28 days)
- Another safety assessment was monitoring for lentivirus that is used for gene transfer during manufacturing. Polymerase chain reaction (PCR) was performed and all patients were found to be negative for replication-competent lentivirus.
- Clonality assessment was carried out to exclude insertional oncogenesis as a mechanism for persistence, and all analyzed samples showed high levels of SPEAR T-cell polyclonality with the absence of dominant clones indicating that oncogenesis is not a mechanism of persistence

SPEAR T-cells expand significantly in responding patients with long-term persistence and functionality

- SPEAR T-cells were detectable in all patients following infusion, with peak levels measured within the first ten days
- Peak NY-ESO vector copy levels were statistically significantly higher ($p = 0.0411$) in responders compared to non-responders

- Among seven patients for whom monitoring continued beyond 200 days, circulating SPEAR T-cells were readily detectable
- Persisting pools comprised largely central memory and stem cell memory subsets that remained virtually negative for exhaustion markers such as PD-1 and LAG-3 for the duration of the analysis period (up to 6 months)
- $CD8^+$ SPEAR T-cells were isolated from the pre-infusion product and at post-infusion time points, and analyzed for cytokine production in an *in vitro* assay with NY-ESO expressing target cells; cytokine staining showed production of various cytokines by SPEAR T-cells *in vitro* (i.e., IFN-γ, IL-2, or TNF-α; or, combinations thereof) indicating that SPEAR T-cells are polyfunctional both pre- and post-infusion
- SPEAR T-cells from patient 202 were isolated and placed in an*in vitro* killing assay 28 months after infusion and found to kill NY-ESO expressing target cells without addition of exogenous cytokines

Responses in a second solid tumor, myxoid/round cell liposarcoma (MRCLS) with NY-ESO SPEAR T-cells were recently reported, and these data were presented at the American Society of Clinical Oncology (ASCO) Annual Meeting on June 2, 2018.

About Adaptimmune
Adaptimmune is a clinical-stage biopharmaceutical company focused on the development of novel cancer immunotherapy products. The Company's unique SPEAR (Specific Peptide Enhanced Affinity Receptor) T-cell platform enables the engineering of T-cells to target and destroy cancer, including solid tumors. Adaptimmune is currently conducting clinical trials with SPEAR T-cells targeting MAGE-A4, -A10, and AFP across several solid tumor indications. GlaxoSmithKline plc (LSE:GSK) (NYSE:GSK) exercised its option to exclusively license the right to research, develop, and commercialize Adaptimmune's NY-ESO SPEAR T-cell therapy program in September 2017. Transition of this program to GSK is ongoing. The Company is located in Philadelphia, USA and Oxfordshire, U.K. For more information, please visit http://www.adaptimmune.com

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 filed on form 10-Q with the Securities and Exchange Commission (SEC) on May 9, 2018 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. – Director, Investor Relations
T: +1 215 825 9310
M: +1 215 460 8920
Juli.Miller@adaptimmune.com

Source: Adaptimmune Therapeutics plc