April 16, 2018

Adaptimmune Presents MAGE-A4 and MAGE-A10 pre-clinical data at American Association for Cancer Research (AACR) Annual Meeting

- Preclinical testing raises no safety concerns for MAGE A4 -
- Refined preclinical testing strategy expected to further mitigate risk of unexpected off-target toxicity -

PHILADELPHIA, Pa. and OXFORD, United Kingdom, April 16, 2018 (GLOBE NEWSWIRE) -- Adaptimmune Therapeutics plc (Nasdaq:ADAP), a leader in T-cell therapy to treat cancer, presented two posters summarizing preclinical research with its MAGE-A4 and MAGE-A10 SPEAR T-cells at the annual AACR meeting at McCormick Place in Chicago, Illinois.

The MAGE-A4 poster presented the discovery process and extensive preclinical validation work performed by Adaptimmune to characterize the specificity, affinity, and potency of MAGE-A4 SPEAR T-cells. The T-cell receptor (TCR) engineered to target MAGE-A4 was found to be specific for MAGE-A4 with an appropriate affinity and avidity, and there were no safety concerns identified preclinically. Further, the examination of more than 500 non-small lung cancer (NSCLC) tumor samples stained by MD Anderson Cancer Center scientists through its strategic collaboration with Adaptimmune revealed that the MAGE-A4 antigen is expressed in approximately 51% of squamous cell carcinomas of the lung, 8% of adenocarcinomas, and in 24% of all NSCLC cases. In addition, numerous other tumors express MAGE-A4 at variable levels. Details about the selection and affinity enhancement of MAGE-A10 SPEAR T-cells were also presented. The refined methods used to test this SPEAR T-cell candidate are expected to further mitigate risk of unexpected off-target toxicities.

“Our proprietary preclinical development and validation program for our SPEAR T-cells, developed over more than 10 years, enables us to generate TCRs that have the right level of specificity, affinity, and overall avidity for cancer cells expressing specific targets, while minimizing the risk of off-target toxicity,” said Rafael Amado, Adaptimmune’s Chief Medical Officer. “MAGE-A4 and MAGE-A10 are in clinical trials in a variety of solid tumors, and we expect to deliver data on the benefit:risk profile of these products throughout the second half of 2018.”

Session, date, time, and location (for both posters):

- **Date:** Monday, Apr 16, 2018
- **Time:** 1:00 PM - 5:00 PM (CDT)
- **Location:** McCormick Place South, Exhibit Hall A, Poster Section 24

Poster 1 – MAGE-A4

• **Title:** Affinity-enhanced T-cell receptor (TCR) for adoptive T-cell therapy targeting MAGE-A4
• **Poster Board Number:** 21
• **Permanent Abstract Number:** 2562
• **Objectives:**

- Determine the frequency of MAGE-A4 expression in non-small cell lung cancer (NSCLC) to identify patients most likely to benefit from SPEAR T-cell therapy
- Perform preclinical testing for specificity, potency, and safety of MAGE-A4 SPEAR T-cells

• **Methods:**

- *MAGE-A4 expression in NSCLC:* 534 resected NSCLC cases (stage I to IV) with clinicopathological information including overall survival and recurrence were analyzed for MAGE-A4 expression by immunohistochemistry (IHC)
- *Preclinical testing for specificity, potency, and safety of MAGE-A4 SPEAR T-cells*
  − Potency/efficacy testing of MAGE-A4 SPEAR T-cells by antigen driven proliferation, cytokine release, and cytotoxicity assays
  − *In vitro* testing against panels of primary normal cells from multiple organ systems in 2-D, 3-D, and induced pluripotent stem cell culture formats to identify cross-reactivities in more physiologically relevant cultures
  − Molecular mapping of the TCR peptide-major histocompatibility complex (MHC) binding preferences to identify potential cross-reactive peptides, verification of identified peptides by loading candidates on antigen-presenting cells, and expression of source proteins in antigen-presenting cells to confirm lack of candidate peptide processing and presentation

• **Conclusions:**

- MAGE-A4 expression was observed in ~24% of all NSCLC cases, with higher frequency observed in squamous cell carcinoma (SCC) (51%) versus adenocarcinoma (8%)
- Extensive in vitro preclinical safety assessment and identified no major safety concerns for MAGE-A4 SPEAR T-cell reactivity
- This MAGE-A4 SPEAR T-cell is being evaluated in a clinical trial in patients with in bladder, melanoma, head & neck, ovarian, NSCLC, esophageal, and gastric cancers

Poster 2 – MAGE-A10

• **Title:** Selection of affinity-enhanced T-cell receptors for adoptive T-cell therapy targeting MAGE-A10
• **Poster Board Number:** 23
• **Permanent Abstract Number:** 2564
• **Objectives:** Generate and systematically test affinity-enhanced TCRs that recognize an HLA-A*02 restricted epitope from MAGE-A10 cancer/testis antigens
• Develop an extensive *in vitro* testing strategy to characterize and reduce the risk of TCR cross-reactivity, including a novel approach for generating peptide specificity profiles for candidate TCRs – the peptide X-scan
• **Methods:**

- Twenty-one parental TCRs recognizing the HLA-A*0201-restricted MAGE-A10 peptide GLYDGMEHL254-262 (MAGE-A10254-262) epitope were characterized using surface plasmon resonance (SPR)
- Ten parental TCRs were cloned into a lentiviral vector and transduced into primary human T-cells, and screened for recognition of natively processed antigen using MAGE-A10–positive and –negative cell lines and primary cells as targets
- Three parental TCRs selected for affinity enhancement, and the complementarity-determining regions (CDRs) of their α- and β-chains were mutated, and resulting TCRs tested for affinity and specificity

• **Conclusions:**

- Adaptimmune developed an affinity-enhanced TCR with high specificity and potency against cells expressing HLA-A*0201 and the cancer antigen MAGE-A10
  − After generating TCR mutants with diverse germline and CDR loop sequences, the optimal candidate for preclinical testing was identified by applying a novel comprehensive specificity screen (X-scan)
  − Together with other key developments in preclinical safety and potency assessments, this strategy is expected to mitigate the risk of unexpected off-target crossreactivity and resulting clinical toxicities
- The MAGE-A10 SPEAR T-cell that was selected is being evaluated in clinical trials in NSCLC, and a triple tumor study in bladder, melanoma, and head & neck cancers

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 Annual Report filed on for 10-K with the Securities and Exchange Commission (SEC) on March 15, 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.

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Source: Adaptimmune Therapeutics plc