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# Two Confirmed Responses and Five out of Six Patients with Initial Tumor Reductions from Early Dose Cohorts of SURPASS Trial, Presented at SITC

- Data support continued development of ADP-A2M4CD8 -

- On track to start Phase 2 trial in gastroesophageal cancers in the first half of 2021 -

PHILADELPHIA, Pa. and OXFORDSHIRE, UK., Nov. 09, 2020 (GLOBE NEWSWIRE) -- Adaptimmune Therapeutics plc (Nasdaq: ADAP), a leader in cell therapy to treat cancer, presented data from the dose escalation cohorts of its Phase 1 SURPASS trial using ADP-A2M4CD8 in a poster at the Society for the Immunotherapy of Cancer ("SITC") Conference.

In these cohorts of heavily pre-treated patients with advanced cancers (n=6), three were treated with target doses of 1 billion SPEAR T-cells, and three with target doses of 5 billion. Most adverse events were consistent with those typically experienced by cancer patients undergoing cytotoxic chemotherapy or cancer immunotherapy.

"We have seen responses in two out of six patients treated in the safety cohorts of the SURPASS trial as well as antitumor activity in five of them. The responses and antitumor activity we have seen with our next-generation ADP-A2M4CD8 SPEAR T-cells, across a range of solid tumors, support our belief that this is a highly active product," said Ad Rawcliffe, Adaptimmune's Chief Executive Officer. "Based on these data, we will initiate the Phase 2 trial in gastroesophageal cancers in the first half of 2021 and look forward to identifying additional indications to take into late-stage development."

There were two confirmed partial responses (PRs): one in a patient with esophagogastric junction (EGJ) cancer, previously reported, and one in a patient with head and neck cancer, reported as unconfirmed in May. The four other patients had best overall responses of stable disease (SD). Overall, five out of six patients treated had initial tumor shrinkage.

*In vitro* translational data using the manufactured products from patients in the SURPASS trial indicate that co-expression of the CD8α co-receptor on $CD4^+$ ADP-A2M4 SPEAR T-cells enables them to kill MAGE-A4 expressing target cells with equal potency as $CD8^+$ SPEAR T-cells targeting MAGE-A4. These data, combined with the responses and antitumor activity observed at low doses, indicate that ADPA2M4D8 may be a more potent product than the first-generation ADPA2M4 SPEAR T-cells.

Best Overall Response (BOR) and maximum changes from baseline in target lesions in Cohorts 1 and 2

| Indication | Dose x $10^9$ | BOR | Tumor reduction |
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| | | | |
|---|---|---|---|
| Head and neck | 4.6 | PR | -63.16% |
| EGJ | 1.2 | PR | -51.52% |
| EGJ | 1.0 | SD | -34.07% |
| Ovarian | 1.1 | SD | -16.13% |
| Esophageal | 6.0 | SD | -13.37% |
| MRCLS | 5.7 | SD | +1.35% |

As of data cut-off: October 1, 2020

At SITC, Adaptimmune also presented a poster entitled “Inhibition of AKT signaling during expansion of TCR-engineered T-cells from patient leukocyte material generates SPEAR T-cells with enhanced functional potential in vitro.” These preclinical data indicate that AKT inhibition during the manufacture of SPEAR T-cells results in a more consistent expansion and phenotype of the final product. This process is currently being used for manufacture of ADP-A2M4CD8 for the SURPASS trial.

The Company also presented two posters summarizing data for the two completed Phase 1 trials with ADP-A2M10 (a previously terminated program).

**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 SEC on November 5, 2020, 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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**SITC Abstract**

**Title:** Initial safety, efficacy, and product attributes from the SURPASS trial with ADPA2M4CD8, a SPEAR T-cell therapy incorporating an affinity optimized TCR targeting MAGE-A4 and a CD8α co-receptor

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***Abstract Body*:**

**Background:** The ongoing SURPASS trial (NCT04044859) evaluates safety and efficacy of next-generation ADP-A2M4CD8 SPEAR T-cells co-expressing the CD8α co-receptor with the engineered MAGE-A4$^{c1032}$ Tcell receptor (TCR).

**Methods:** First-in-human trial in HLA-A*02 positive patients (pts) with advanced cancers expressing MAGE-A4 antigen by immunohistochemistry. Eligible pts undergo apheresis, Tcells are isolated, transduced with a Lentiviral vector containing the MAGE-A4$^{c1032}$ TCR and CD8α coreceptor, and expanded. Expansion, transduction level, cellular composition and function of the manufactured product (MP) are assessed *in vitro*. Prior to infusion, pts receive lymphodepletion with fludarabine 30 mg/m$^2$/day for 4 days and cyclophosphamide 600 mg/m$^2$/day for 3 days.

**Results:** As of 16 July 2020, 5 pts (1 with MRCLS, 2 with esophagogastric junction [EGJ] cancers, 1 with ovarian cancer, and 1 with head and neck cancer) were treated with ADP-A2M4 CD8 (range ~1 to 5.7 billion transduced cells). No DLTs or SAEs have been reported. To date, 1 pt with EGJ cancer had a partial response (PR per RECIST) and has had progression-free survival >6 months. One pt with head and neck cancer also had a PR. All other pts have had best overall response of stable disease.

MP expanded by an average of 15.3fold during manufacturing (range 5.9 to 25.6-fold). On average, 43% of Tcells in the MP expressed the TCR (range 23 to 63%). The fraction of CD4$^+$ cells in the final MP varied (range 45 to 84%). Coexpression of the MAGE-A4 TCR and CD8α in CD4$^+$ T-cells in the patient MP enabled CD4$^+$ T-cells to kill tumor target cells

directly *in vitro*. MAGE-A4 expression in tumor biopsies varied (H-score range 55 to 300). Transduced T-cells were detected in peripheral blood of all pts. IFNgamma increased transiently in the serum of 1 pt who responded.

**Conclusions**: ADP-A2M4CD8 SPEAR T-cells have shown an acceptable safety profile and pts with EGJ cancer and head and neck cancer have demonstrated evidence of antitumor activity. Translational data and early clinical results indicate that co-expression of the CD8α co-receptor on $CD4^+$ SPEAR T-cells may increase the potency of the product by conferring additional killing activity to the helper T-cell subset. This dose escalation trial is ongoing and updated clinical and translational data will be presented.


Source: Adaptimmune Therapeutics plc