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Adaptimmune Announces Clinical Responses across Five Solid Tumor Indications with an Overall Response Rate of 36% and Promising Early Durability from its Next-Generation SURPASS Trial

- Confirmed complete response in ovarian cancer, and confirmed partial responses in ovarian, head and neck, esophagogastric junction, bladder, and synovial sarcoma cancers -

- Majority of patients experienced antitumor activity with a disease control rate of 86% -

- ADP-A2M4CD8 cell therapy shows improved tumor cell killing and engagement of the broader immune system to fight cancer -

PHILADELPHIA and OXFORD, U.K., Sept. 13, 2021 (GLOBE NEWSWIRE) -- Adaptimmune Therapeutics plc (Nasdaq: ADAP), a leader in cell therapy to treat cancer, announced updated data from its Phase 1 SURPASS trial in multiple solid tumors to be presented in a digital poster at the upcoming European Society for Medical Oncology (ESMO) annual meeting. The poster will be displayed on the ESMO congress web site on Thursday, September 16th. The Company has also released a video of Adrian Rawcliffe, Adaptimmune's Chief Executive Officer (CEO), and Elliot Norry, Adaptimmune's Chief Medical Officer, describing these data in more detail that can be accessed here: https://bit.ly/38ZQCGt.

"It is no longer a question of whether our SPEAR T-cells are effective against a range of MAGE-A4 expressing tumors — they undoubtedly are. Now, our focus is on turning them into approved therapies. This begins with ongoing recruitment in this SURPASS trial for people with lung, bladder, gastroesophageal, head and neck, and now ovarian cancer, and continues with the recently initiated SURPASS 2 trial in esophageal and EGJ cancers," said Adrian Rawcliffe, Adaptimmune's CEO. "These data bring us closer to identifying further indications to take into late-stage development and confirm our expertise in developing and enhancing cell therapies. ADP-A2M4CD8 does exactly what we designed it to do — kill cancer cells and more effectively engage the broader immune system to deliver improved potency and clinical benefit."

Dr. David Hong, Professor, Deputy Chairman in the Department of Investigational Cancer Therapeutics (Phase I Program) at The University of Texas MD Anderson Cancer Center said, "We are encouraged by these promising early data from the SURPASS trial. Having previously seen strong responses with afami-cel, this next-generation cell therapy appears safe and demonstrated antitumor activity for a majority of patients across many cancer indications."

Topline results from the Phase 1 SURPASS trial (data cut-off August 2, 2021)
Emerging efficacy and durability data are promising with responses in five solid tumor indications

- As of the data cut-off date, 25 patients had received the next-generation cell therapy, ADP-A2M4CD8, in the Phase 1 SURPASS trial, 22 patients were evaluable for efficacy with at least one post-baseline scan meeting the ≥4-week duration for evaluation of stable disease
- All patients had advanced metastatic disease and had received multiple prior regimens of systemic therapy (median: 3; range 1-6)
- The overall response rate was 36% and the disease control rate was 86%
- There was a complete response reported in a patient with ovarian cancer, which remains ongoing at 6 months post-infusion (data on file at Adaptimmune)
- Initial durability is encouraging. As of the data cut-off, 11 patients remain on study. Of the 8 responders, 5 remain in response with some remaining progression free >24 weeks

Best Overall Response (n=22)*	**Overall, n (%)**	**Cancer Indication (n=1 unless otherwise noted)**
Complete response (CR)	1 (4.5)	Ovarian
Partial response (PR)	7 (31.8)	Ovarian (2); head and neck (2)**; esophagogastric junction (EGJ)**; bladder; synovial sarcoma
Stable disease (SD)	11 (50.0)	Ovarian cancer (3); EGJ (2); esophageal (2); lung cancer, MRCLS, melanoma,
Progressive disease (PD)	3 (13.6)	EGJ, lung, ovarian
Overall response rate (CR, PR)	8 (36.4)	
Disease control rate (CR, PR, SD)	19 (86.4)	

* Of 25 patients who received ADP-A2M4CD8, 3 were not evaluable at the time of data cut-off: 2 patients (ovarian or esophageal cancers) did not have post-baseline scans; 1 patient (EGJ) had a post-baseline scan that did not meet the ≥4-week duration for evaluation of stable disease
** One PR in head and neck cancer and one PR in EGJ cancer were reported previously at SITC 2020

ADP-A2M4CD8 demonstrated an acceptable safety profile

- Eighteen (72%) patients experienced cytokine release syndrome (CRS) related to T-cell infusion, most of which were lower grade: Grade 1 or 2 (n=14); Grade 3 (n=4)
- The most common serious adverse event (SAE) of any grade (> 30% of patients) was CRS
- Four (16%) patients experienced immune effector cell-associated neurotoxicity syndrome (ICANS) related to T-cell infusion: Grade 1 (n=1); Grade 2 (n=1); Grade 3

(n=2)
- Five (20%) patients experienced prolonged cytopenia at Week 4
- One patient experienced a fatal (Grade 5) SAE of pancytopenia (previously reported in the Company's 10K Report filed with the Securities and Exchange Commission on February 25, 2021)

ADP-A2M4CD8 was designed to be more potent than the first-generation product

- Adaptimmune's Specific Peptide Enhanced Affinity Receptor (SPEAR) T-cell therapies are a mix of CD8+ ("killer") and CD4+ ("helper") T-cells engineered with a T-cell receptor (TCR) designed with Adaptimmune's proprietary affinity enhancement technology to recognize a cancer target
- ADP-A2M4CD8 is a next-generation T-cell therapy engineered to target MAGE-A4 positive tumors, and to express a CD8α co-receptor
- ADP-A2M4CD8 uses the same engineered T-cell receptor that recognizes MAGE-A4 as Adaptimmune's first-generation T-cell therapy, afami-cel, which has shown compelling results in synovial sarcoma and myxoid/round cell liposarcoma (presented at ASCO 2021)
- Co-expression of CD8α adds CD8+ killer cell capability to CD4+ helper T-cells, while maintaining or enhancing the CD4+ helper function (i.e., producing the inflammatory cytokines IFN-γ and IL-2)

Initial translational data confirm that ADP-A2M4D8 is more potent and better engages the immune system, compared to the first-generation product

- Patient manufactured product and serum samples from the first-generation Phase 1 afami-cel trial and the next-generation SURPASS trial were compared
- *In vitro* tumor cell killing assays confirm that the next-generation product results in greater tumor cell killing by CD4+ SPEAR T-cells
- Analyses of patient serum samples demonstrate increases in a subset of 22 measured serum cytokines confirming increased helper function of the next-generation CD4+ T-cells and engagement of the broader immune system
- Additional serum analyses showed increased serum IL-12 in the SURPASS trial versus the first-generation Phase 1 trial, which is also consistent with engagement of the broader immune system, including dendritic cells, as IL-12 is not known to be produced by T-cells

Conclusions from the Phase 1 SURPASS Trial Data at ESMO

- Initial efficacy and durability data are encouraging with responses across five different solid tumors including a complete response in a patient with ovarian cancer ongoing at 6 months
- The safety profile of the next-generation ADP-A2M4CD8 cell therapy was acceptable
- Data confirm preclinical observations that the enhanced TCR interaction in ADP-A2M4CD8 results in a more potent product
- Safety and efficacy, including duration of response, will continue to be evaluated in the ongoing SURPASS trial, which is enrolling eligible patients with gastroesophageal, head and neck, lung, bladder, and ovarian cancers
- A Phase 2 trial, SURPASS-2, has initiated for patients with esophageal and EGJ cancers

Overview of Phase 1 SURPASS trial design

- This is a Phase 1, open-label, dose escalation clinical trial designed to evaluate the safety and antitumor activity of ADP-A2M4CD8 in patients with MAGE-A4+ tumors in the context of HLA-A*02
- This is a first-in-human dose-escalation trial using a modified 3+3 design, with 2 dose cohorts plus an expansion cohort
- The number of transduced cells ranged from $0.8x10^9$ to $1.2x10^9$ (Cohort 1 complete), $1.2x10^9$ to $6.0x10^9$ (Cohort 2 complete), and $1.2x10^9$ to $10.0x10^9$ (Expansion)
- Dose-limiting toxicities are adjudicated by a Safety Review Committee, regardless of the investigator's attribution
- Responses are assessed per RECIST v1.1

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 August 9, 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, Corporate Affairs and Communications
T: +44 1235 430 583
M: +44 7718 453 176
Sebastien.Desprez@adaptimmune.com

Investor Relations:

Juli P. Miller, Ph.D. — VP, Investor Relations
T: +1 215 825 9310
M: +1 215 460 8920
Juli.Miller@adaptimmune.com

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