



TCR² Therapeutics Announces RECIST Responses with First TC-210 Dose Tested in Advanced Mesothelin-Expressing Solid Tumors

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- TC-210 TRuC-T cell monotherapy induced tumor regression in first five patients
- Two RECIST unconfirmed partial responses and two patients with stable disease through six months
- Manageable toxicity profile, with only one patient exhibiting TC-210-related non-hematologic Grade >2 toxicity
- Translational data demonstrated T cell expansion and cytokine production
- TCR² to host conference call tomorrow starting at 8:00am E.T. with live webcast available online

CAMBRIDGE, Mass., July 26, 2020 (GLOBE NEWSWIRE) -- TCR² Therapeutics Inc. (Nasdaq: TCRR), a clinical-stage immunotherapy company with a pipeline of novel T cell therapies for patients suffering from cancer, today announced positive interim data from the first five patients treated in the Phase 1 portion of the TC-210 Phase 1/2 clinical trial for mesothelin-expressing solid tumors. All five patients showed tumor regression including two RECIST unconfirmed partial responses (one of which remains subject to independent central review) and two patients with stable disease through six months. Translational data further demonstrated TRuC-T cell expansion and activation. A manageable toxicity profile was observed with only one patient exhibiting TC-210-related non-hematologic grade >2 toxicity and no evidence of neurotoxicity or on-target, off-tumor toxicity.

"We are delighted that our very first dose of TC-210 induced consistent tumor regression and clinical benefit in heavily pre-treated cancer patients," said Garry Menzel, Ph.D., President and Chief Executive Officer of TCR² Therapeutics. "There are very few options for patients with solid tumors and those expressing mesothelin represent a significant frontier of unmet medical need. While these are early data requiring further study, we are encouraged by the potential of our TRuC-T cells as we continue to enroll and treat patients with the goal of quickly finding a recommended Phase 2 dose for TC-210."

"Based on my prior experience working with both TCR-T and CAR-T cells, including the FDA approval of Kymriah, observing consistent clinical benefit in patients at presumably suboptimal T cell doses is quite meaningful," said Alfonso Quintás-Cardama, M.D., Chief Medical Officer of TCR² Therapeutics. "These early TC-210 data suggest our approach may overcome the challenges faced by many T cell therapies in the hostile solid tumor microenvironment. Our enrolled patients have failed multiple lines of therapy, including standard chemotherapy, checkpoint inhibitors and in some cases other mesothelin-directed approaches, in indications where survival has been historically shorter than six months."

The primary objectives of the Phase 1 portion of the study are to define the safety profile of TC-210 in patients whose tumors overexpress mesothelin and to determine the recommended Phase 2 dose (RP2D). Secondary objectives include overall response rate (ORR) and disease control rate (DCR). Exploratory objectives include the assessment of expansion, tumor infiltration, and persistence of TC-210 T cells.

Summary of trial conduct, baseline characteristics and TC-210 dose:

- **Screening:** Forty-eight percent of patients met the mesothelin expression cut-off as defined per protocol.
- **Manufacturing:** TC-210 T cell products meeting protocol defined specifications have been manufactured successfully for each patient enrolled in the clinical trial.
- **Patient Characteristics:** TC-210 treated patients included four with mesothelioma and one with ovarian cancer with a median age of 61 years (range, 36-74 years). The median number of prior therapies was five (range, 3-9), including immune checkpoint inhibitor therapy (n=3) and the anti-mesothelin ADC anetumab ravtansine (n=1).
- **TC-210 Dose:** All patients received the same TC-210 dose either with or without lymphodepletion. One patient with mesothelioma was enrolled to dose level (DL) 0 (5×10^7 TC-210 T cells/m² without lymphodepletion) whereas four patients (three with mesothelioma and one with ovarian cancer) were enrolled to DL1 (5×10^7 TC-210 T cells/m² following lymphodepletion with fludarabine 30 mg/m²/day x4 and cyclophosphamide 600 mg/m²/day x3).

Key clinical findings from the first five patients treated with TRuC-T cells include:

- **Safety:** TC-210 was generally well tolerated, with no patients experiencing neurotoxicity or on-target, off-tumor toxicities. Three (60%) patients experienced Cytokine Release Syndrome (CRS), which was Grade 1 in two patients and Grade 3 in one patient. The patient experiencing Grade 3 CRS also developed Grade 3 pneumonitis during the first week post infusion that responded to tocilizumab and steroid therapy. This patient died 34 days post treatment due to fungal sepsis, which was deemed unrelated to TC-210. Because of the earlier pneumonitis event, however, the Safety Review Team recommended the expansion of the cohort from three to six patients. None of the subsequent three patients treated at DL1 developed pneumonitis or CRS above Grade 1.
- **Clinical Activity:** All five patients treated with TC-210 T cells have had at least one disease response assessment. The DCR was 100%, with all patients experiencing tumor regression. The median change in the sum of diameters of target

lesions was -42% (range, -17% to -67%). The ORR was 40% (2 unconfirmed PRs) according to RECIST v1.1. TC-210 therapy induced a significant reduction in FDG uptake by PET imaging in two evaluable patients, including one patient who achieved a complete metabolic response (PR by RECIST v1.1).

- **Translational Data:** Peak TC-210 expansion (C_{max}) occurred between days 7 and 22. The median peak TC-210 expansion was 821 copies/ μ g of genomic DNA (range, 520 to 5,901 copies/ μ g). C_{max} increased when TC-210 was administered following lymphodepletion. Cytokine induction post-TC-210 infusion was observed in all evaluable patients suggesting target engagement.

About the Phase 1/2 Clinical Trial in Advanced Mesothelin-Expressing Solid Tumors

The Phase 1/2 clinical trial (NCT03907852) is evaluating the safety and efficacy of TC-210, TCR²s T-cell receptor fusion construct directed against mesothelin. The trial is enrolling patients with mesothelin expressing NSCLC, ovarian cancer, cholangiocarcinoma, and malignant pleural/peritoneal mesothelioma. The Phase 1 dose escalation portion of the clinical trial utilizes a modified 3+3 design with four increasing TC-210 T cell doses. At each dose, TC-210 will be tested in two separate dose levels: first without lymphodepletion and then following lymphodepleting chemotherapy. The Phase 1 portion of the clinical trial is ongoing.

In the Phase 2 portion of the clinical trial, approximately 50 patients are planned to receive TC-210 at the RP2D in four distinct cohorts according to their cancer diagnosis: NSCLC, ovarian cancer, malignant pleural/peritoneal mesothelioma and cholangiocarcinoma. Each cohort will include ten patients, except the NSCLC cohort which will include 20 patients with eight patients to receive TC-210 as single agent and 12 patients to receive TC-210 in combination with a programmed cell death 1 (PD-1) blocking antibody.

About Mesothelin-Expressing Solid Tumors

Mesothelin is a cell-surface glycoprotein highly expressed in a wide range of solid tumors, including malignant pleural/peritoneal mesothelioma, ovarian cancer, cholangiocarcinoma, breast cancer, pancreatic cancer and others. Overexpression of mesothelin is associated with poorer prognosis in some cancers due to its active role in both malignant transformation and tumor aggressiveness by promoting cancer cell proliferation, invasion, and metastasis. Of the wide range of solid tumors expressing mesothelin, non-small cell lung cancer, ovarian cancer, mesothelioma and cholangiocarcinoma represent a significant patient population up to 80,000 in the United States alone.

TCR² Therapeutics Conference Call and Webcast

TCR² Therapeutics will host a conference call and webcast on Monday, July 27th at 8:00am E.T. The webcast and presentation will be made available on the TCR² Therapeutics website in the Investors section under Events at <http://investors.tcr2.com/events>. Following the live audio webcast, a replay will be available on the Company's website for approximately 30 days.

About TCR² Therapeutics

TCR² Therapeutics Inc. is a clinical-stage immunotherapy company developing a pipeline of novel T cell therapies for patients suffering from solid tumors or hematological malignancies. TCR²s proprietary T cell receptor (TCR) Fusion Construct T cells (TRuC[®]-T cells) specifically recognize and kill cancer cells by harnessing signaling from the entire TCR, independent of human leukocyte antigens (HLA). In preclinical studies, TRuC-T cells have demonstrated superior anti-tumor activity compared to chimeric antigen receptor T cells (CAR-T cells), while secreting lower levels of cytokine release. The Company's lead TRuC-T cell product candidate targeting solid tumors, TC-210, is currently being studied in a Phase 1/2 clinical trial to treat patients with mesothelin-positive non-small cell lung cancer (NSCLC), ovarian cancer, malignant pleural/peritoneal mesothelioma, and cholangiocarcinoma. The Company's lead TRuC-T cell product candidate targeting hematological malignancies, TC-110, is currently being studied in a Phase 1/2 clinical trial to treat patients with CD19-positive adult acute lymphoblastic leukemia (aALL) and with aggressive or indolent non-Hodgkin lymphoma (NHL). For more information about TCR², please visit www.tcr2.com.

Forward-looking Statements

This press release contains forward-looking statements and information within the meaning of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. The use of words such as "may," "will," "could," "should," "expects," "intends," "plans," "anticipates," "believes," "estimates," "predicts," "projects," "seeks," "endeavor," "potential," "continue" or the negative of such words or other similar expressions can be used to identify forward-looking statements. These forward-looking statements include, but are not limited to, express or implied statements regarding the therapeutic potential of TC-210, future clinical development plans, the development of the Company's TRuC-T cells, their potential characteristics, applications and clinical utility, and the potential therapeutic applications of the Company's TRuC-T cell platform.

The expressed or implied forward-looking statements included in this press release are only predictions and are subject to a number of risks, uncertainties and assumptions, including, without limitation: uncertainties inherent in clinical studies and in the availability and timing of data from ongoing clinical studies; whether interim results from a clinical trial will be predictive of the final results of the trial; whether results from preclinical studies or earlier clinical studies will be predictive of the results of future trials; the expected timing of submissions for regulatory approval or review by governmental authorities, including review under accelerated approval processes; orphan drug designation eligibility; regulatory approvals to conduct trials or to market products; TCR²s ability to maintain sufficient manufacturing capabilities to support its research, development and commercialization efforts, whether TCR²s cash resources will be sufficient to fund TCR²s foreseeable and unforeseeable operating expenses and capital expenditure requirements, the impact of the COVID-19 pandemic on TCR²s ongoing operations; and other risks set forth under the caption "Risk Factors" in TCR²s most recent Annual Report on Form 10-K, most recent Quarterly Report on Form 10-Q and its other filings with the Securities and Exchange Commission. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed in this press release may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements. You should not rely upon forward-looking statements as predictions of future events. Although TCR² believes that the expectations reflected in the forward-looking statements are reasonable, it cannot guarantee that the future results, levels of activity, performance or events and circumstances reflected in the forward-looking statements will be achieved or occur.

Moreover, except as required by law, neither TCR² nor any other person assumes responsibility for the accuracy and completeness of the forward-looking statements included in this press release. Any forward-looking statement included in this press release speaks only as of the date on which it was made. We undertake no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events or otherwise, except as required by law.

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