TCR² Announces RECIST Response in Ovarian Cancer from Ongoing Phase 1/2 Trial of TC-210 in Treatment Refractory Mesothelin-Expressing Solid Tumors

December 13, 2020

- TC-210 induced tumor regression in all of the first eight patients

- Ovarian cancer patient achieved confirmed RECIST partial response (PR)

- Overall response rate (ORR) 50% in patients infused with TC-210 and lymphodepletion

- Continued manageable toxicity profile

- Phase 1 trial amended to accelerate treatment

- TCR^2 to host conference call Monday, December 14 starting at 8:00am E.T. live webcast available

CAMBRIDGE, Mass., Dec. 13, 2020 (GLOBE NEWSWIRE) -- TCR^2 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 ongoing Phase 1 portion of the TC-210 (gavocabtagene autoleucel or "gavo-cel") Phase 1/2 clinical trial for mesothelin-expressing solid tumors. As of the November 24, 2020 data cutoff, three PRs according to RECIST 1.1 criteria have been recorded among the first eight patients treated on study, with our first ovarian cancer patient having achieved a confirmed PR up to month six. In addition, the first patient treated at a higher gavo-cel dose ($1x10^8/m^2$) without lymphodepletion achieved stable disease through two months without any significant toxicities, which has allowed patients to start treatment at that dose with the addition of lymphodepletion. The toxicity profile remains manageable with only two patients to date exhibiting gavo-cel-related non-hematologic grade >2 toxicity and no evidence of neurotoxicity or on-target, off-tumor toxicity. Translational data further demonstrated TRuC-T cell expansion and cytokine induction in all patients.

"Although the focus of any Phase 1 trial is safety, the consistency in tumor regression and RECIST responses we have observed with gavo-cel as a single agent supports our belief in the advantages of TRuC-T cells over other cell therapies and the potential for a fundamentally new approach in the treatment of solid tumors," said Garry Menzel, Ph.D., President and Chief Executive Officer of TCR^2 Therapeutics. "The HLA independence of our technology allows us to treat a broad population of patients with mesothelin surface expression while leveraging the full T cell receptor complex to drive enhanced trafficking, on-target killing and persistence in the hostile solid tumor microenvironment. Most important, we are delivering clinical and survival benefit to those patients with heavily pre-treated mesothelioma or ovarian cancer."

"The ability of gavo-cel to benefit patients who have become treatment refractory after having failed multiple lines of therapy, including immune checkpoint inhibitors and anti-mesothelin therapy, combined with its manageable safety profile is remarkable. The changes announced today to the Phase 1 trial design, reducing the intra-cohort safety observation periods to 14 days from 28 days, enable us to more rapidly identify the recommended Phase 2 dose and initiate the Phase 2 expansion trial where we will evaluate the efficacy of gavo-cel in four solid tumor indications. Importantly, in the Phase 2 we will explore the impact of gavo-cel retreatment and its combination with checkpoint inhibitor therapy which could further improve on the clinical benefit observed to date," said Alfonso Quintás-Cardama, M.D., Chief Medical Officer of TCR^2 Therapeutics.

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

Summary of trial conduct, baseline characteristics and gavo-cel dose:

- **Safety Protocol:** The new clinical trial protocol amendment allows the intra-cohort safety observation periods to be reduced to 14 days from 28 days, allowing the testing of a gavo-cel dose over a minimum of 56 days compared to the previous 84 days.
- **Screening:** Forty-five percent of patients met the mesothelin expression cut-off as defined per protocol.
- **Manufacturing:** Products meeting protocol defined specifications for gavo-cel have been manufactured successfully for each patient from whom apheresis material was sent into production.
- **Patient Characteristics**: Eight patients received gavo-cel including seven with mesothelioma and one with ovarian cancer with a median age of 65 years (range, 36-84 years). The median number of prior therapies was 5.5 (range, 3-9), including immune checkpoint inhibitor therapy (n=6) and anti-mesothelin therapies (n=3).
- **Gavo-cel Dose**: The eight patients disclosed to date have received gavo-cel at the following dose level (DL):
  - **DL 0:** $5x10^7$ cells/m^2 without lymphodepletion – 1 mesothelioma
  - **DL 1:** $5x10^7$ cells/m^2 following lymphodepletion – 5 mesothelioma and 1 ovarian cancer
  - **DL 2:** $1x10^8$ cells/m^2 without lymphodepletion – 1 mesothelioma

Key clinical findings from the first eight patients treated with gavo-cel:

- **Safety**: Gavo-cel was generally well tolerated, with no patients experiencing neurotoxicity or on-target, off-tumor toxicities. Two (25%) patients experienced Cytokine Release Syndrome (CRS) grade 3, which was successfully managed with tocilizumab and corticosteroids.
- **Clinical Activity**: All eight patients have had at least one disease response assessment. The DCR was 100%, with all patients experiencing tumor regression. The median decrease in the sum of diameters of target lesions was 43% (range, 5% to 75%). The ORR was 38% (2 confirmed and 1 unconfirmed PRs) according to RECIST v1.1 criteria, including one patient who achieved a complete metabolic response.
- **Translational Data**: Peak gavo-cel expansion (C_{max}) occurred between days 7 and 23. C_{max} increased when gavo-cel was administered following lymphodepletion. The median peak gavo-cel expansion was 811.9 copies/µg of genomic DNA (range, 520 to 5,901 copies/µg). Cytokine induction post-gavo-cel infusion was observed in all evaluable patients, which is indicative of mesothelin 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 gavocabtagene autoleucel (“gavo-cel”; TC-210), TCR ^{2}s 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 gavo-cel doses. At each dose, gavo-cel 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 gavo-cel 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 gavo-cel as single agent and 12 patients to receive gavo-cel 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 patient population up to 80,000 annually in the United States alone.

TCR^2 Therapeutics Conference Call and Webcast

TCR^2 Therapeutics will host a conference call and webcast on Monday, December 14th at 8:00am E.T. The webcast and presentation will be made available on the TCR^2 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 TCR^2 Therapeutics

TCR^2 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. TCR^{2}s 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, gavo-cel, 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 TCR^2, 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 gavo-cel, 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; TCR^{2}s ability to maintain sufficient manufacturing capabilities to support its research, development and commercialization efforts, whether TCR^2's cash resources will be sufficient to fund TCR^2's foreseeable and unforeseeable operating expenses and capital expenditure

requirements, the impact of the COVID-19 pandemic on TCR^{2}s ongoing operations; and other risks set forth under the caption "Risk Factors" in TCR^{2}s 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 TCR^2 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 TCR^2 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.

Investor and Media Contact:

Carl Mauch
Director, Investor Relations and Corporate Communications
TCR^2 Therapeutics Inc.
(617) 949-5667
carl.mauch@tcr2.com

Source: TCR2 Therapeutics