TCR² Therapeutics Announces Positive Interim Results from Ongoing Phase 1/2 Trial of Gavo-cel for Treatment Refractory Mesothelin-Expressing Solid Tumors

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- Clinical activity observed in all three mesothelin-expressing tumor types treated

- Gavo-cel disease control rate (DCR) 81% with tumor regression in 15 of 16 evaluable patients

- Overall response rate (ORR) 31% in patients infused with gavo-cel following lymphodepletion

- Meaningful survival benefit at 11.2 months for patients with refractory mesothelioma

- Recommended Phase 2 Dose (RP2D) being refined after identification of the Maximum Tolerated Dose (MTD)

- TCR^2 to host a conference call on Friday, September 17 at 9:00a.m. ET

CAMBRIDGE, Mass., Sept. 17, 2021 (GLOBE NEWSWIRE) -- TCR^2 Therapeutics Inc. (Nasdaq: TCRR), a clinical-stage cell therapy company with a pipeline of novel T cell therapies for patients suffering from cancer, today announced positive interim results from the ongoing Phase 1 portion of the gavo-cel Phase 1/2 clinical trial for mesothelin-expressing solid tumors. A dataset will also be featured in an oral presentation at the European Society for Medical Oncology (ESMO) Congress 2021 on September 17 at 14:20 CEST (8:20am EST) (Presentation #959O) and is part of the official ESMO Press Programme.

As of the June 30, 2021 data cutoff, 17 patients (12 mesothelioma, 4 ovarian cancer and 1 cholangiocarcinoma) had received a single gavo-cel infusion in the dose escalation portion of the gavo-cel Phase 1 clinical trial. The median number of prior lines of therapy was 5, including immune checkpoint inhibitors (n=11) and mesothelin-directed therapies (n=5). Gavo-cel was administered up to dose level 5 (DL5) ($5x10^8/m^2$ following lymphodepletion). Two dose limiting toxicities were reported: one Grade 3 pneumonitis at DL1 that resolved with supportive measures, which permitted the continuation of dose escalation, and one Grade 5 bronchoalveolar hemorrhage at DL5, which along with the development of severe CRS in all 3 patients treated at this dose level, led the Safety Review Team to declare $5x10^8/m^2$ as the MTD. Following identification of the MTD, one patient has received gavo-cel at $3x10^8/m^2$ after lymphodepletion using a split dosing approach to refine the RP2D and an additional patient has been treated at DL3 ($1x10^8/m^2$ following lymphodepletion). In both cases gavo-cel was well tolerated with only Grade 1 non-hematological toxicities being reported.

15 of the 16 patients evaluable for efficacy experienced regression of their target lesions, ranging in magnitude from 5% to 75%. Six patients achieved partial responses (PRs) by target lesion assessment, four of whom (3 with mesothelioma and 1 with ovarian cancer) achieved a PR according to RECIST 1.1 criteria, including one who also achieved a complete metabolic response. One patient with cholangiocarcinoma was also considered to have achieved a PR by investigator assessment, for an ORR of 31%. By independent review assessment, the ORR was 25% with a DCR Rate of 81%. The median overall survival for patients with mesothelioma is 11.2 months, whereas the median progression free survival is 5.9 months.

“The interim gavo-cel data reported today showed continued clinical benefit and a manageable safety profile in a population of patients that previously achieved minimal or no improvement due to the advanced and aggressive state of their cancer,” said principal investigator David Hong, M.D., deputy chair of the Department of Investigational Cancer Therapeutics at The University of Texas MD Anderson Cancer Center. “Patients with treatment refractory cancer have very limited treatment options and will often need hospice and supportive care. We are encouraged by the early survival data from gavo-cel in patients previously treated with checkpoint inhibitors and other therapies.”

“Our ambition with gavo-cel from the start was to redefine treatment for solid tumors with cell therapies. We are excited to present data demonstrating clinical activity in all three mesothelin-expressing solid tumors treated to date and tumor regression in a majority of patients who are treatment refractory after numerous lines of therapy. We are very encouraged by the progression free survival and overall survival observed among patients with refractory mesothelioma treated so far with gavo-cel in the Phase 1 trial,” said Alfonso Quintás-Cardama, M.D., Chief Medical Officer of TCR^2 Therapeutics. “Based on these data and the most recent patient experiencing a very mild safety profile at a cell dose of $3x10^8/m^2$, we believe the identification of the RP2D is close at hand. As we approach the Phase 2 expansion phase, our focus will shift to further optimizing outcomes for patients by studying combinations with immune checkpoint inhibitors, allowing gavo-cel re-treatment and evaluating different mesothelin expression thresholds.”

The primary objectives of the Phase 1 portion of the trial are to define the safety profile of gavo-cel in patients whose tumors overexpress mesothelin and to determine the RP2D. Secondary objectives include ORR and 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:

- **Screening:** Forty-six percent of patients met the mesothelin expression cut-off as defined per protocol.
- **Patient Characteristics**: 17 patients received gavo-cel including 12 with mesothelioma, 4 with ovarian cancer and 1 with cholangiocarcinoma with a median age of 57 years (range, 31-84 years). The median number of prior therapies was 5 (range, 1-9), including immune checkpoint inhibitor therapy (n=11) and anti-mesothelin therapies (n=5).
- **Gavo-cel Dose**: The seventeen 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 patient
  - **DL 1:** $5x10^7$ cells/m^2 following lymphodepletion – 5 mesothelioma patients and 1 ovarian cancer patient
  - **DL 2:** $1x10^8$ cells/m^2 without lymphodepletion – 1 mesothelioma patient
  - **DL 3:** $1x10^8$ cells/m^2 following lymphodepletion – 1 mesothelioma patient, 1 cholangiocarcinoma patient, and 3 ovarian cancer patients
  - **DL 4:** $5x10^8$ cells/m^2 without lymphodepletion – 1 mesothelioma patient
  - **DL 5:** $5x10^8$ cells/m^2 following lymphodepletion – 3 mesothelioma patients

Key clinical findings from patients treated with gavo-cel:

- **Safety**: gavo-cel was generally well tolerated with a manageable adverse event profile with no patients experiencing on-target, off-tumor toxicities. Two DLTs were observed: one case of Grade 3 pneumonitis at DL1 that resolved with anti-cytokine therapy, and one case of Grade 5 bronchoalveolar hemorrhage at DL5. Furthermore, all three patients treated at DL5 experienced Grade ≥3 CRS which resulted in $5x10^8$ cells/m^2 following lymphodepletion being declared the MTD.
- **Clinical Activity**: 16 patients were evaluable for response. Tumor regression was observed in 15 (94%) patients with a DCR of 81%. Six patients achieved partial responses (PRs) by target lesion assessment, four of whom (3 with mesothelioma and 1 with ovarian cancer) achieved a PR according to RECIST 1.1 criteria. The ORR by RECISTv1.1 criteria among patients infused with gavo-cel following lymphodepletion chemotherapy was 31% by independent review assessment, including one patient who achieved a complete metabolic response, and 38% by investigator assessment, which included a PR in a patient with metastatic cholangiocarcinoma.
- **Translational Data**: Peak gavo-cel expansion (C_{max}) increased when gavo-cel was administered following lymphodepletion in a dose dependent fashion. Cytokine elevations post-gavo-cel infusion were 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 either mesothelin expressing non-small cell lung cancer (NSCLC), ovarian cancer, cholangiocarcinoma, or 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.

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 Friday, September 17 at 9:00am E.T. In order to participate in the conference call, please dial 866-220-8062 (domestic) or 470-495-9169 (international) and refer to confirmation number 1597681. The webcast and presentation will be made available on the TCR^2 Therapeutics website in the Investors section under Events at 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 cell therapy company developing a pipeline of novel T cell therapies for patients suffering from cancer. 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 TCR^{2}s expectations for the Phase 1/2 clinical trials of gavo-cel and TC-110; TCR ^{2}s expectations for the safety and efficacy of its product candidates and enhancements, including gavo-cel and TC-110, compared to current T-cell therapy approaches; TCR^{2}s expectations regarding the timing of determining an RP2D for gavo-cel and TCR^{2}s expectations regarding the estimated patient populations and related market opportunities in gavo-cel's and TC-110's targeted indications.

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 a trial; the possibility that positive results from preclinical studies and correlative studies may not necessarily be predictive of the results of TCR^{2}s planned clinical trials, including the Phase 1/2 clinical trials of gavo-cel and TC-110; the risk that the results from the Phase 1/2 clinical trials of gavo-cel and TC-110 will not support further development and marketing approval; the risk that TCR^{2}may be unable to gain approval of gavo-cel, TC-110 and its other product candidates on a timely basis, if at all; the risk that TCR^2 has over-estimated the potential patient population for its product candidates, if approved; the risk that the current COVID-19 pandemic will impact TCR^{2}s clinical trials and other 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.

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