gavo-cel Continues to Demonstrate Clinical Benefit in Solid Tumors with Additional RECIST Reponses in Ovarian Cancer and Mesothelioma

September 28, 2022

- Completed Phase 1 clinical trial establishes gavo-cel monotherapy as the first anti-mesothelin cell therapy to demonstrate tolerability and clinical benefit
- Second RECIST partial response in ovarian cancer supports broad potential of gavo-cel
- Consistent tumor regression in 28 of 30 (93%) evaluable patients with disease control rate of 77%
- Progression-free survival of 5.6 months and overall survival of 11.2 months suggest durability of benefit in mesothelioma
- Phase 2 portion of trial underway implementing multiple approaches to further improve clinical outcomes
- TCR^2 to host a conference call on Wednesday, September 28, 2022 at 8:00a.m. ET

CAMBRIDGE, Mass., Sept. 28, 2022 (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 solid tumors, today announced positive topline results from the Phase 1 portion of the gavo-cel Phase 1/2 clinical trial for mesothelin-expressing solid tumors, with some patients still being monitored for clinical response or stable disease.

As of the September 9, 2022 data cutoff, 32 patients (including 23 mesothelioma, eight ovarian cancer and one cholangiocarcinoma) had received a single gavo-cel infusion in the Phase 1 portion of the clinical trial. The patients were heavily pretreated with a median of five prior lines of therapy, including immune checkpoint inhibitors in 66% of patients and mesothelin-directed therapies in 19% of patients. Following identification of a dose-limiting toxicity (DLT) at dose level (DL) 5 ($5x10^8$ cells/m^2 following lymphodepletion) in September 2021, the study proceeded to a dose de-escalation portion, first at DL3.5 ($3x10^8$ cells/m^2 following lymphodepletion) using a split-dosing approach, and subsequently at DL3 ($1x10^8$ cells/m^2 following lymphodepletion) which was declared the recommended Phase 2 dose (RP2D). No new DLTs were observed.

gavo-cel demonstrated a disease control rate (DCR) of 77%, which is defined in the Phase 1 portion of the trial as a response or sustained stable disease for at least three months post infusion. As measured by blinded independent central review (BICR), 28 of the 30 (93%) patients evaluable for efficacy experienced tumor regression of their target lesions, ranging in magnitude from 4% to 80%. Eight patients experienced target lesion regression greater than 30%, six of whom (four with mesothelioma and two with ovarian cancer) achieved a partial response (PR) according to RECIST 1.1 criteria, including one patient who also achieved a complete metabolic response. One patient with cholangiocarcinoma was also considered to have achieved a PR by investigator assessment, demonstrating that gavo-cel has induced responses in every tumor type tested to date. The overall response rate (ORR) among patients who received gavo-cel following lymphodepletion chemotherapy was 22% by BICR and 26% by investigator assessment. By BICR, the ORR was 21% among patients with malignant pleural/peritoneal mesothelioma (MPM) and 29% among those with ovarian cancer. The median overall survival (OS) for patients with MPM was 11.2 months, whereas the median progression-free survival (PFS) for patients with MPM was 5.6 months.

“We believe our Phase 1 clinical data already position gavo-cel as a first- and best-in-class anti-mesothelin monotherapy with a near-term opportunity during Phase 2 to further improve the depth and durability of clinical benefit by using it in combination with immune checkpoint inhibitors and redosing strategies. These are remarkable data in the context of solid tumors where there have been significant challenges with current CAR-T therapies. I am particularly excited by this second RECIST response in ovarian cancer as it supports the meaningful clinical activity of gavo-cel in a large patient population. Additionally, we continue to observe consistent tumor regression for heavily pre-treated patients with mesothelioma for whom limited options are available,” said Garry Menzel, Ph.D., President and Chief Executive Officer of TCR^2 Therapeutics. “As a result, we have narrowed our focus in the short-term to our three core programs, gavo-cel, TC-510 and TC-520, so that we can maximize the number of patients with access to our investigational therapies.”

“The results of the Phase 1 trial underscore the potential clinical value of gavo-cel in a very heavily pretreated patient population that are receiving our engineered T cells as their sixth line of therapy on average,” said Alfonso Quintás-Cardama, M.D., Chief Medical Officer of TCR^2 Therapeutics. “gavo-cel has demonstrated a manageable safety profile at the RP2D, induced RECIST responses in every indication studied to date, and has provided a promising survival signal among patients with mesothelioma as well as encouraging preliminary efficacy data in ovarian cancer. These results clearly support the further development of gavo-cel in the Phase 2 portion of the study where we believe that the combination with checkpoint inhibitors and the ability to retreat patients with additional doses of gavo-cel will allow us to increase patients’ exposure to gavo-cel, potentially translating into even higher response rates and improved durability of benefit.”

“We have already dosed a number of patients in combination with checkpoint inhibitors, including patients with ovarian cancer, in the randomized Phase 2 portion of the trial and look forward to providing ongoing progress updates on the various arms of the study as well as following the remaining patients still on the Phase 1 portion. We are clearly delighted that patients with various cancers continue to derive meaningful benefit from gavo-cel,” added Dr. Menzel.

The primary objectives of the Phase 1 portion of the trial are to evaluate 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-eight percent of patients met the mesothelin expression cutoff as defined per protocol.
- **Patient Characteristics**: Thirty-two patients received gavo-cel including 23 with mesothelioma, eight with ovarian cancer and one with cholangiocarcinoma, with a median age of 63 years (range, 28-84 years). The median number of prior therapies was five (range 1-13), including immune checkpoint inhibitor therapy in 66% of patients and mesothelin directed therapy in 19% of patients.
- **gavo-cel Dose**: The 32 patients disclosed to date have received gavo-cel at the following DL:
    - **DL 0:** $5x10^7$ cells/m^2 without lymphodepletion – one mesothelioma
    - **DL 1:** $5x10^7$ cells/m^2 following lymphodepletion – seven mesothelioma and one ovarian cancer
    - **DL 2:** $1x10^8$ cells/m^2 without lymphodepletion – one mesothelioma
    - **DL 3:** $1x10^8$ cells/m^2 following lymphodepletion – six mesothelioma, one cholangiocarcinoma and six ovarian cancer
    - **DL 3.5:** $3x10^8$ cells/m^2 following lymphodepletion - four mesothelioma and one ovarian cancer
    - **DL 4:** $5x10^8$ cells/m^2 without lymphodepletion – one mesothelioma
    - **DL 5:** $5x10^8$ cells/m^2 following lymphodepletion – three mesothelioma

Key topline clinical findings from patients treated with gavo-cel:

- **Safety Data**: gavo-cel was generally well tolerated with a manageable adverse event profile up to DL5. Over the course of the Phase 1 clinical trial, two DLTs were observed: one case of Grade 3 pneumonitis at DL1 that resolved with anti-cytokine therapy, and one case of Grade 5 bronchioalveolar hemorrhage at DL5. All three patients treated at DL5 experienced severe cytokine release syndrome (CRS) which resulted in the Safety Review Team recommending de-escalation. The most frequent Grade 3 or higher non-hematological toxicity among patients treated at the RP2D was CRS, which was reported in 15% of patients.
- **Clinical Activity**: Thirty patients were evaluable for response. DCR was 77%. Tumor regression was observed in 28 (93%) patients. Eight patients experienced target lesion regression greater than 30%, including six patients who achieved a PR by RECIST criteria (four with MPM and two with ovarian cancer). The ORR by RECIST criteria among patients infused with gavo-cel following lymphodepletion chemotherapy was 22% by BICR, which includes one patient who achieved a complete metabolic response, and 26% by investigator assessment, which includes an additional PR reported in a patient with metastatic cholangiocarcinoma.
- **Survival:** Among patients with mesothelioma, median OS and PFS were 11.2 months and 5.6 months, respectively, which compare favorably with the published outcomes of patients with relapsed refractory MPM treated in the second-line setting with standard therapy. Among patients with ovarian cancer, median OS and PFS were 8.1 months and 5.8 months, respectively.
- **Translational Data**: Peak gavo-cel expansion (C_{max}) occurred between days 7 and 23. C_{max} markedly increased when gavo-cel was administered following lymphodepletion. Cytokine induction post gavo-cel infusion was observed in all evaluable patients, which is indicative of mesothelin target engagement. Post infusion, expression of PD-1 was observed to be upregulated on circulating gavo-cel T cells. Detection of gavo-cel in tumors and malignant effusions showed higher expansion and longer persistence in these tissues as compared to peripheral blood.

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”; previously known as TC-210), TCR^2s 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 (MPM). The Phase 1 dose escalation portion of the clinical trial utilized a modified 3+3 design with four increasing gavo-cel doses. At each dose, gavo-cel was tested in two separate dose levels: first without lymphodepletion and then following lymphodepleting chemotherapy.

In the Phase 2 portion of the clinical trial, patients will receive gavo-cel at the recommended Phase 2 dose ($1x10^8$ cells/m^2 following lymphodepletion). A total of 75 patients will be treated in the MPM cohort and a total of 20 patients will be treated in each one of the following indications: ovarian, NSCLC and cholangiocarcinoma. In the MPM cohort, patients will be randomized to receive either single agent gavo-cel, gavo-cel in combination with OPDIVO® (nivolumab), or gavo-cel in combination with OPDIVO and YERVOY® (ipilimumab). Patients enrolled in the ovarian cancer, NSCLC or cholangiocarcinoma cohorts will all receive gavo-cel in combination with OPDIVO.

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 81,000 annually in the United States alone.

TCR^2 Therapeutics Conference Call and Webcast

TCR^2 Therapeutics will host a conference call and webcast on Wednesday, September 28, 2022 at 8:00am E.T. In order to participate in the conference call, please register at https://bit.ly/3BTJ9Z7. Participants can register via this link up to ten minutes prior to start time. 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 TCR2 Therapeutics

TCR^2 Therapeutics Inc. is a clinical-stage cell therapy company developing a pipeline of novel T cell therapies for patients suffering from solid tumors. The Company is focused on the discovery and development of product candidates against novel and complex targets utilizing its proprietary T cell receptor (TCR) Fusion Construct T cells (TRuC®-T cells). The TRuC platform is designed to specifically recognize and kill cancer cells by harnessing signaling from the entire TCR, independent of human leukocyte antigens (HLA). 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, TC-510 and TCR^{2}s other product candidates, including potential improvements in efficacy, safety and durability in the Phase 2 portion of the gavo-cel trial, expectations regarding future growth and prospects, future clinical development plans and anticipated timing of data updates, 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 and topline 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; TCR2's ability to maintain sufficient manufacturing capabilities to support its research, development and commercialization efforts, including TCR2's ability to secure additional manufacturing facilities; TCR ^{2}s ability to enroll patients in its clinical trials; whether TCR2's cash resources will be sufficient to fund TCR2's foreseeable and unforeseeable operating expenses and capital expenditure requirements, the impact of the COVID-19 pandemic on TCR2's ongoing operations; and other risks set forth under the caption "Risk Factors" in TCR2'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 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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Source: TCR2 Therapeutics