TScan Therapeutics Presents Preclinical Data at the American Society of Gene and Cell Therapy 25th Annual Meeting

May 19, 2022

Identified lead TCR-T cell therapy candidate, TCR-200-A02, for the treatment of HPV-positive solid tumors, on track for IND submission in 2H22

*TCR directed to a novel C*07:02-restricted epitope of MAGEA1, TSC-204-C07, on track for IND submission in 2H22*

Multiplexing TCRs in vitro *leads to cytotoxicity of target cell lines and cytokine-mediated enhancement of anti-tumor activity of specific TCR cells*

ImmunoBank enables customized multiplexing of TCRs across both targets and HLA restrictions

Hosting virtual KOL event May 19, 2022 at 4:30 p.m. ET to share preclinical data highlights

WALTHAM, Mass., May 19, 2022 (GLOBE NEWSWIRE) -- TScan Therapeutics, Inc. (Nasdaq: TCRX), a clinical-stage biopharmaceutical company focused on the development of T-cell receptor (TCR) engineered T cell therapies (TCR-T) for the treatment of patients with cancer, presented two posters and an oral presentation around TScan's proprietary platform technologies for its solid tumor program at the American Society of Gene and Cell Therapy (ASGCT) 25th Annual Meeting.

"The initial preclinical data on our solid tumor program presented at ASGCT demonstrate the capability of TScan's proprietary platforms to identify novel TCRs. Through ReceptorScan, we identified TSC-200-A02 that targets an HLA-A*02:01 restricted epitope of HPV16-E7 and with TargetScan we identified TSC-204-C07 targeting a novel HLA-C*07:02 restricted epitope of MAGE-A1. We are excited to report initial preclinical results, which showed strong cytoxicity of TSC-200-A02 in HPV+ target cell lines and no off-target activity. When we multiplexed the two TCRs *in vitro*, we were excited to see synergistic cytotoxic activity." said Gavin MacBeath, Ph.D., Chief Scientific Officer.

Dr. MacBeath continued, "We are on track to continue progressing IND-enabling studies for the TSC-200 series and submitting IND applications for TSC-200-A02 and TSC-204-C7 during the second half of this year. These initial preclinical results suggest that multiplexing TCRs has the potential to overcome both tumor antigen heterogeneity and HLA loss-of-heterozygosity (LOH)."

Presentation Highlights:

Poster presentation titled "Discovery of TSC-200-A02: A natural HPV16 E7-specific TCR-T cell therapy candidate for the treatment of HPV-positive solid tumors," presented by Gavin MacBeath, Ph.D.

- Using TScan's proprietary ReceptorScan platform, 453 putative HPV16 E7-specific TCRs were discovered by screening 681 million naïve CD8+ T cells from 15 unique healthy donors and testing each TCR for expression in primary T cells and for its ability to kill cells pulsed with the E7 peptide, using a National Cancer Institute (NCI) HPV TCR as a benchmark.
- ReceptorScan identified a lead TCR, TCR-200-A02, and showed comparable cytotoxicity to the therapeutic TCR from NCI that has previously shown a 50% objective response rate in a Phase 1 clinical trial.
- SafetyScan, an array-based screening technology for off-target reactivity, showed that TCR-200-A02-expressing CD3+ T cells did not cross-react with 108 out of 110 of the most common HLA types in the US population, allowing this TCR-T to be used in the vast majority of patients. Additionally, TCR-200-A02 showed no reactivity to normal cells from healthy HLA-A*02:01+ human donors, indicating no off-tumor reactivity risk.
- Treatment with TCR-200-A02 showed significant inhibition of tumor growth in immunocompromised mice inoculated with HPV positive tumor cell lines.
- TScan has designed a transposon-based vector to deliver TSC-200-A02, along with genes for CD8α/β and a dominant-negative form of TGFβ Receptor II, into both CD4+ and CD8+ T cells. T cells expressing this vector were able to efficiently overcome TGFβ-mediated suppression.
- These results validate the use of ReceptorScan and SafetyScan as a way to rapidly identify naturally occurring, high affinity, and derisked TCRs suitable for clinical development.
- The Company has advanced this TCR-T into IND-enabling studies as TSC-200-A02.

Poster presentation titled "Multiplexed TCR-T cell therapy: A strategy to enhance the efficacy of engineered T cell therapy," presented by Gavin

MacBeath, Ph.D.

- Variable inter- and intra-tumoral antigen expression was observed in human melanoma tumor samples as shown by heterogenous antigen expression of PRAME and MAGEC2 that varied from cell to cell within the same tumor.

- Non-small cell lung cancer (NSCLC) samples showed wide prevalence of clonal and partial HLA LOH of the HLA-A*02:01 allele occurring in ~40% of NSCLC samples indicating that these tumors would not have responded to single TCRs targeting HLA-A*02:01 epitopes. Previous studies have indicated that this HLA LOH occurs through deletion of an entire chromosome arm where the HLA genes are located.

- Synergistic cytotoxicity was observed when HPV+ and MAGEA1+ cell lines were grown in the presence of an HPV16 E7-TCR-T and MAGEA1-TCR-T combination.

- MAGEA1-specific TCR-T cells co-cultured with a target cell line with high expression of MAGEA1 synergistically enhanced the cytotoxicity of MAGEC2 TCR-T cells co-cultured with a cell line with moderate MAGEC2 expression. The increased cytotoxicity was driven by cytokines secreted by MAGEA1-targeted T cells, leading to increased activation of MAGEC2-targeted T cells. These data suggest that a multiplexing approach can synergistically address target heterogeneity.

- TScan has devised a screening strategy to select patients for multiplexed TCR therapy. This includes germline HLA genotyping, followed by tumor assessment for target expression and HLA LOH. If LOH is observed, TCRs are chosen that target two different HLAs on the intact chromosome, which cannot be lost. If LOH is not observed, TCRs are chosen that target HLAs on opposite chromosomes to avoid secondary LOH.

- TScan's ImmunoBank enables customized multiplexing of TCRs across both targets and HLAs, which is designed to prevent resistance arising from either target loss or HLA LOH.

- These findings support the hypothesis that multiplexed TCR-T has the potential to overcome antigen heterogeneity not only through independent targeting of different target cells in the same tumor, but also by cytokine-mediated enhancement of each T cell's response.

Oral presentation titled "Discovery of a novel C*07:02-restriced epitope on MAGE-A1 and pre-clinical development of an enhanced TCR-T cell therapy candidate for the treatment of solid tumors," presented by Gavin MacBeath, Ph.D.

- TScan's proprietary technology, TargetScan, allowed for the identification of TCRs and cancer antigens from a head and neck cancer patient who exhibited substantial tumor reduction after only eight weeks of checkpoint therapy.

- Two different expanded T cell clones from the patient's tumor shared a common TCR directed to a novel C*07:02-restricted epitope of MAGEA1 which was a potential driver of the anti-tumor response.

- MAGEA1 is a cancer/testis antigen expressed in various cancers but not normal tissues except for testis which is an immune privileged organ. MAGE-A1 is expressed in ~50% of melanoma and non-small cell lung cancer and high expression is correlated with poor survival.

- TSC-204-C07 displayed strong cytotoxicity and cytokine secretion in response to HLA-C*07:02 positive cell lines that expressed MAGEA1 but not a cell line that lacked MAGEA1 expression, indicating no risk of off-tumor reactivity.

- Our results suggest that TargetScan can identify relevant tumor antigens and TCRs from expanded T cell repertoires of patients exhibiting strong and durable responses to checkpoint therapy, thereby providing suitable TCRs for clinical development.

- The Company has advanced this TCR-T to IND-enabling studies as TSC-204-C07.

A copy of the presentation materials can be accessed on the "Events and Presentations" section of the Company's Investor Relations website at www.ir.tscan.com.

Virtual KOL Event

The Company is hosting a virtual KOL event today, Thursday, May 19, 2022, at 4:30 p.m. ET, featuring Kai Wucherpfennig, M.D., Ph.D. Chair, Cancer Immunology and Virology and Director, Center for Cancer Immunology Research at the Dana-Farber Cancer Institute, Professor of Neurology, Brigham and Women's Hospital and Harvard Medical School, and Associate Member, Broad Institute of MIT and Harvard. The event will provide an in-depth review of the oral and poster presentations related to solid tumor TCR-T therapy candidates, TSC-200-A02 for HPV16, and TSC-204-C07 for MAGE-A1, as well as TScan's approach to potentially overcome antigen heterogeneity and HLA loss with multiplexed TCR-T. Following the prepared remarks, the call will be opened for a live question and answer session. To submit a question, please reach out to questions@lifesciadvisors.com.

Registration for the live event can be found here. A replay will be available on the "Events and Presentations" section of the Company's website at ir.tscan.com.

About TScan Therapeutics, Inc.

TScan is a clinical-stage biopharmaceutical company focused on the development of T cell receptor (TCR) engineered T cell therapies (TCR-T) for the treatment of patients with cancer. The Company's lead leukemia TCR-T therapy candidates, TSC-100 and TSC-101, are in development for the treatment of patients with hematologic malignancies to eliminate residual leukemia and prevent relapse after hematopoietic stem cell transplantation. The Company is also developing multiplexed TCR-T therapy candidates for the treatment of various solid tumors. The Company has developed and continues to build its ImmunoBank, the Company's bank of therapeutic TCRs that recognize diverse targets and are associated with multiple HLA types in order to provide customized multiplexed TCR-T therapies for patients with various types of solid tumors.

Forward-Looking Statements

This release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, including, but not limited to, express or implied statements regarding current and future research and development plans or expectations, the structure, timing and success of the Company's planned preclinical development, submission of INDs, and clinical trials, the potential benefits of any of the Company's proprietary platforms or current or future product candidates in treating patients, and the Company's goals, strategy, business plans and focus, among other things. TScan intends such forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 21E of the Securities Exchange Act of 1934 and the Private Securities Litigation Reform Act of 1995. In some cases, you can identify forward-looking statements by terms such as, but not limited to, "may," "might," "will," "objective," "intend," "should," "could," "can," "would," "expect," "believe," "anticipate," "project," "target," "design," "estimate," "predict," "potential," "plan," "on track," or similar expressions or the negative of those terms. Such forward-looking statements are based upon current expectations that involve risks, changes in circumstances, assumptions, and uncertainties. The express or implied forward-looking statements included in this release are only predictions and are subject to a number of risks, uncertainties and assumptions, including, without limitation: the beneficial characteristics, safety, efficacy, therapeutic effects and potential advantages of TScan's TCR-T therapy candidates; TScan's expectations regarding its preclinical studies being predictive of clinical trial results; the timing of the initiation, progress and expected results of TScan's preclinical studies, clinical trials and its research and development programs; TScan's plans relating to developing and commercializing its TCR-T therapy candidates, if approved, including sales strategy; estimates of the size of the addressable market for TScan's TCR-T therapy candidates; TScan's manufacturing capabilities and the scalable nature of its manufacturing process; TScan's estimates regarding expenses, future milestone payments and revenue, capital requirements and needs for additional financing; TScan's expectations regarding competition; TScan's anticipated growth strategies; TScan's ability to attract or retain key personnel; TScan's ability to establish and maintain development partnerships and collaborations; TScan's expectations regarding federal, state and foreign regulatory requirements; TScan's ability to obtain and maintain intellectual property protection for its proprietary platform technology and our product candidates; the sufficiency of TScan's existing capital resources to fund its future operating expenses and capital expenditure requirements; and the effect of the COVID-19 pandemic, including mitigation efforts and political, economic, legal and social effects, on any of the foregoing or other aspects of TScan's business or operations; and other factors that are described in the "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" sections of TScan's Annual Report on Form 10-K for the year ended December 31, 2021, filed with the SEC on March 9, 2022 and any other filings that TScan has made or may make with the SEC in the future. Any forward-looking statements contained in this release represent TScan's views only as of the date hereof and should not be relied upon as representing its views as of any subsequent date. Except as required by law, TScan explicitly disclaims any obligation to update any forward-looking statements.

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