TransCode Therapeutics Reports Positive Preclinical Results with its Immunotherapy Candidate, TTX-RIGA, in Melanoma

January 31, 2023

Study provides additional support for further advancement of TTX-RIGA

BOSTON, Jan. 31, 2023 (GLOBE NEWSWIRE) -- ***TransCode Therapeutics, Inc.*** (Nasdaq: RNAZ), an RNA oncology company committed to more effectively treating cancer using RNA therapeutics, today reported successful preclinical proof-of-mechanism studies with its immunotherapy candidate, TTX-RIGA, in melanoma.

TTX-RIGA, a novel immunotherapeutic candidate for the treatment of cancer, is designed to work by binding to an intracellular receptor called RIG-I (retinoic acid-inducible gene I). This is expected to result in targeted activation of innate immunity in the tumor microenvironment. Recent developments in the use of pattern recognition receptors (PRRs) such as RIG-I aim to harness the innate power of the immune system for cancer therapy. TransCode believes that understanding how to recruit PRRs, such as RIG-I, in a tumor-selective manner is critical for its adoption in the clinic.

Similar immunotherapeutics of others have been shown to induce complete tumor regressions in animals and have triggered immunity against the tumor. However, those immunotherapeutics are often administered directly into the tumor to avoid the toxicity resulting from activation of an adverse immune response against healthy tissues. This mode of administration has not proven clinically effective due to limited access to the tumor cells, especially in the context of disseminated metastatic cancer.

TransCode seeks to address this challenge by developing a strategy for tumor-selective activation of an immune response specific to cancer cells using systemic administration with its proprietary nanoparticle delivery system, TTX. TransCode anticipates that Immune activation will not be triggered in healthy tissues that do not express the target, but rather will be selectively activated in tumors and metastases that do express the target.

In preclinical studies, TransCode's delivery of TTX-RIGA inside tumors and metastases generated an RNA-based agonist of the RIG-I gene, targeting activation of innate immunity in the tumor microenvironment in multiple solid tumors, holding promise for the development of a novel class of immunotherapeutics for cancer treatment.

The publication entitled "*Template-Directed RIG-I Agonist Assembly for Targeted Cancer*" was published at BioRxiv (https://www.biorxiv.org/content/10.1101/2022.12.08.519592v1.full). "The agonist comprises a single stranded RNA oligonucleotide modified with a 5'-triphosphate complementary to an endogenous microRNA enriched in tumor cells. The template-directed strategy we are employing moves us closer to making RIG-I a clinically relevant target in oncology because it achieves targeted activation of innate immunity in the tumor microenvironment in the context of systemic agonist injection," commented Zdravka Medarova, PhD, co-founder and CTO of TransCode. "As with prior studies, we believe the data from this preclinical study further support advancement of TTX-RIGA into animal studies slated to begin in February 2023. The opportunity for systemic, yet tumor-selective activation of innate immunity using the template-directed model could represent an important step towards effective application of RIG-I and other PRR-agonists for cancer therapy in the clinical setting."

"We believe that demonstrating successful preclinical results with TTX-RIGA is an important step in the preclinical development process and further de-risks our pipeline that includes multiple RNA approaches including RNAi, PRR, mRNA vaccines and gene editing with CRISPR, all of which utilize our proprietary delivery platform," added Michael Dudley, co-founder, president and CEO of TransCode.

Dudley added, "Additionally, as we have previously indicated, we received written authorization from FDA allowing us to proceed with our Phase 0 first-in-human (FIH) clinical trial with our lead candidate, TTX-MC138, in cancer patients with advanced solid tumors. We intend to proceed with patient enrollment as soon as possible." TTX-MC138 targets microRNA-10b, believed to drive metastatic disease. TTX-MC138 has been validated preclinically in multiple cancer models including metastatic breast cancer and pancreatic cancer and has previously been shown to induce durable regression of metastatic disease in murine models of disseminated breast cancer and pancreatic cancer.

About TransCode Therapeutics

TransCode is an RNA oncology company created on the belief that cancer can be effectively treated using RNA therapeutics. The Company has created a platform of drug candidates designed to target a variety of tumor types with the objective of significantly improving patient outcomes. The Company's lead therapeutic candidate, TTX-MC138, is focused on treating metastatic cancer, which is believed to cause approximately 90% of all cancer deaths totaling over nine million per year worldwide. The Company believes that TTX-MC138 has the potential to produce regression without recurrence in a range of cancers, including breast, pancreatic, ovarian and colon cancer, glioblastomas and others. Two of the Company's other drug candidates, TTX-siPDL1 and TTX-siLIN28B, focus on treating tumors by targeting PD-L1 and LIN28B, respectively. TransCode also has three cancer-agnostic programs: TTX-RIGA, an RNA–based agonist of the retinoic acid-inducible gene I, or RIG-I, designed to drive an immune response in the tumor microenvironment; TTX-CRISPR, a CRISPR/Cas9–based therapy platform for the repair or elimination of cancer-causing genes inside tumor cells; and TTX-mRNA, an mRNA-based platform for the development of cancer vaccines designed to activate cytotoxic immune responses against tumor cells.

Forward-Looking Statements

This release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, including, without limitation, statements concerning the results of a preclinical study of TTX-RIGA in melanoma and other tumor types, statements concerning expected clinical results of TransCode's therapeutic candidates, statements concerning the results of RNA research, statements concerning the potential for treating cancer with RNA therapeutics, statements concerning the timing and outcome of expected regulatory filings and clinical trials, including the

planned first-in-human study of TTX-MC138, statements concerning the timing and outcome of this study, including whether this study will demonstrate proof-of-mechanism, and statements concerning TransCode's development programs and TTX technology platform generally. Of note, a Phase 0 clinical trial is an exploratory study, conducted under an exploratory Investigational New Drug (eIND) application. Exploratory IND studies usually involve very limited human exposure to a therapeutic candidate to evaluate mechanism of action in order to inform potential clinical evaluation in future clinical studies, but otherwise have no therapeutic intent. Any forward-looking statements in this press release are based on management's current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to: the risk associated with drug discovery and development; the risk that the results of our planned clinical trials will not be consistent with our pre-clinical studies or expectations; risks associated with the timing and outcome of TransCode's planned regulatory submissions; risks associated with TransCode's planned clinical trials for its product candidates; risks associated with obtaining, maintaining and protecting intellectual property; risks associated with TransCode's ability to enforce its patents against infringers and defend its patent portfolio against challenges from third parties; the risk of competition from other companies developing products for similar uses; risks associated with TransCode's financial condition and its need to obtain additional funding to support its business activities, including TransCode's ability to continue as a going concern; risks associated with TransCode's dependence on third parties; and risks associated with the COVID-19 coronavirus. For a discussion of these and other risks and uncertainties, and other important factors, any of which could cause TransCode's actual results to differ from those contained in or implied by the forward-looking statements, see the section entitled "Risk Factors" in TransCode's Annual Report on Form 10-K for the year ended December 31, 2021, as well as discussions of potential risks, uncertainties and other important factors in any subsequent TransCode filings with the Securities and Exchange Commission. All information in this press release is as of the date of the release; TransCode undertakes no duty to update this information unless required by law.

For more information, please contact:

TransCode Therapeutics, Inc.
Alan Freidman, VP Investor Relations
alan.freidman@transcodetherapeutics.com