TransCode Therapeutics Announces Positive Pre-Clinical Glioblastoma Results with Lead Therapeutic Candidate, TTX-MC138

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Further Supports TTX-MC138 Application in Brain Cancer

BOSTON, Sept. 25, 2023 (GLOBE NEWSWIRE) -- TransCode Therapeutics, Inc. (NASDAQ: RNAZ), the RNA oncology company committed to more effectively treating cancer using RNA therapeutics, announced today positive results with its lead therapeutic candidate, TTX-MC138, in murine models bearing human glioblastoma multiforme (GBM) tumors. In this study, the therapeutic candidate was delivered to brain tumors and effectively engaged its target.

GBM is the most common and aggressive form of brain cancer. Its prognosis is poor despite advances in standard-of-care therapy. The 5-year survival rate has remained essentially unchanged over the past 30 years. TransCode believes there is an urgent need to develop more effective therapies. In the study reported by TransCode, mice implanted with tumors derived from human GBM patients were treated with TTX-MC138 and imaged by magnetic resonance imaging (MRI) to determine delivery of the therapeutic candidate to the tumors. In addition, the pharmacodynamic activity of TTX-MC138 was determined by measuring inhibition of the therapeutic target, miRNA-10b, using qRT-PCR. TTX-MC138 was injected intravenously and accumulated efficiently in the tumors. Importantly, the therapeutic candidate showed lasting activity and significantly inhibited miRNA-10b, known to be a driver of tumor progression in glioblastoma.

TTX-MC138 consists of an iron oxide nanocarrier conjugated to a nucleic acid designed to inhibit the oncogenic RNA, microRNA-10b. MiRNA-10b is described as the master regulator of cancer progression in a number of advanced solid tumors. TransCode believes that TTX-MC138 could be used as a treatment for many of these cancers. Administration of TTX-MC138 has resulted in complete regression of metastatic disease in numerous mouse models of pancreatic and breast cancer. In addition, TTX-MC138 was successfully delivered and demonstrated efficacy in spontaneous feline mammary carcinoma.

TransCode's Chief Technology Officer, Zdravka Medarova, commented, "We believe that the latest data obtained in GBM further support the application of TTX-MC138 for the treatment of cancer. Given the lethal nature of this disease and the paucity of therapeutic options for patients with GBM, a therapeutic candidate with a novel mechanism of action, such as TTX-MC138, could have a dramatic impact on patient outcomes considering the evidence obtained to date of disease regressions by this therapeutic candidate in various cancers".

"We believe that successful *in vivo* delivery of TTX-MC138 in GBM tumors derived from human tissue supports earlier evidence that therapeutic candidates using the TTX platform have the potential to accumulate in tumor tissue, engaging RNA targets beyond the liver", added Michael Dudley, Chief Executive Officer of TransCode.

The study was led by Dr. Anna Moore, Professor and Director of the Precision Health Program at Michigan State University, and a scientific co-founder of TransCode.

TransCode's first-in-human clinical trial with TTX-MC138 is open for enrollment and has dosed it' first patient. In this clinical trial, up to 12 patients will be given a single microdose of radiolabeled TTX-MC138 followed by noninvasive PET-MRI and other testing. The trial is intended to quantify the amount of TTX-MC138 delivered to metastatic lesions and the pharmacokinetics of the therapeutic candidate in cancer patients. The trial could yield important data regarding TTX-MC138 delivery to clinical metastases that could inform dose selection, dosing frequency, and patient selection to expedite the path to success in later stage clinical trials. This trial is not intended to evaluate therapeutic efficacy.

About TransCode Therapeutics

TransCode is an RNA oncology company created on the belief that cancer can be more effectively treated using RNA therapeutics. Using its iron oxide nanoparticle delivery platform, the Company has created a portfolio 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 dramatically improve clinical outcomes in a range of cancers, including breast, pancreatic, ovarian and colon cancer, glioblastomas, and others. Another of the Company's drug candidates, TTX-siPDL1, focuses on treating tumors by targeting a protein called Programmed death-ligand 1 (PD-L1). TransCode also has three cancer-agnostic programs: TTX-RIGA, an RNA–based agonist of the retinoic acid-inducible gene 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 preclinical studies of TTX-MC138 in breast cancer 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 first-in-human study of TTX-MC138, and whether this study will demonstrate proof-of-mechanism, and statements concerning TransCode's portfolio of drug candidates 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 to inform potential 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, 2022, 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.

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