

$\mathsf{THERAPEUTICS}^{\scriptscriptstyle\mathsf{TM}}$

TransCode Therapeutics Reports Positive Preclinical Results with its Lead Candidate, TTX-MC138, in Glioblastoma

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Study provides support for further evaluation of TransCode's lead therapeutic candidate, TTX-MC138, in clinical trials

BOSTON, June 06, 2023 (GLOBE NEWSWIRE) -- TransCode Therapeutics, Inc. (NASDAQ: RNAZ), a leading clinical-stage oncology company committed to using its proprietary delivery system platform to defeat cancer, today announced acceptance for publication by *Frontiers in Molecular Biosciences* of a preclinical study using TransCode's lead therapeutic candidate, TTX-MC138, in glioblastoma multiforme (GBM).

The findings of this study support further development of TTX-MC138 for the treatment of GBM by identifying a potentially successful combination treatment protocol using TTX-MC138 with temozolomide (TMZ), currently the standard-of-care therapeutic. Treatment of human glioblastoma cells implanted in animals with the TTX-MC138 analogue, MN-anti-miR10b, inhibited tumor cell growth and induced cell death. When combined with a sub-therapeutic dose of TMZ in a sequence-specific protocol, MN-anti-miR10b enhanced the cell-killing ability of TMZ resulting in highly successful inhibition of tumor cell survival and invasiveness. GBM is the most common and aggressive form of brain tumors. The prognosis for patients with GBM is poor despite advances in standard-of-care therapy. The 5-year survival rate has remained unchanged over the past 30 years. There is an urgent unmet need to develop more effective therapies.

TTX-MC138 is designed to inhibit the oncogenic RNA, microRNA-10b, 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. In a preclinical model of pancreatic adenocarcinoma, administration of TTX-MC138 as monotherapy resulted in complete responses, manifested as regression without recurrence, in 40% of treated animals. This study comes on the heels of preclinical studies in breast cancer demonstrating complete regressions of metastatic disease. In addition to murine models of cancer, TTX-MC138 was successfully delivered and demonstrated preliminary efficacy in a case study of spontaneous feline mammary carcinoma.

Frontiers in Molecular Biosciences is a leading journal in its field with more than 22,000 citations and 11 million views across 3,200 articles. The study to appear in Frontiers in Molecular Biosciences was led by Dr. Anna Moore, Professor and Director of the Precision Health Program at Michigan State University, in collaboration with Dr. Zdravka Medarova, Chief Technology Officer at TransCode Therapeutics. Both Drs. Moore and Medarova are scientific co-founders of TransCode.

"We believe that demonstrating additional successful preclinical results with TTX-MC138 is an important step in the development process. Studies such as this 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.

TransCode Therapeutics recently received IRB approval for a first-in-human clinical trial with TTX-MC138 in patients with advanced solid cancers. In this clinical trial, up to 12 patients will be given a single dose of radiolabeled TTX-MC138 followed by noninvasive positron emission tomographymagnetic resonance imaging (PET-MRI). 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 critical data regarding therapeutic dose, timing, and potential safety that could inform later stage clinical trials and further advance TTX-MC138 as a therapeutic candidate against glioblastoma and other advanced malignancies. This trial is not intended to demonstrate any therapeutic effect.

About TransCode Therapeutics

TransCode is an RNA oncology company created on the belief that cancer can be more 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 dramatically improve clinical outcomes 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 canceragnostic 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 a preclinical study of TTX-MC138 in GBM 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, 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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