Translate Bio Presents Preclinical Data Supporting MRT5201 for the Treatment of Ornithine Transcarbamylase (OTC) Deficiency at the Society for Inherited Metabolic Disorders (SIMD) Annual Meeting

April 8, 2019

-- MRT5201 was efficiently delivered to the liver of a mouse model of OTC deficiency --

-- Preclinical data demonstrated a single IV dose of MRT5201 was sufficient to protect against hyperammonemia for up to 4 weeks --

LEXINGTON, Mass., April 08, 2019 (GLOBE NEWSWIRE) -- Translate Bio, Inc. (Nasdaq: TBIO), a clinical-stage messenger RNA (mRNA) therapeutics company developing a new class of potentially transformative medicines to treat diseases caused by protein or gene dysfunction, today announced the presentation of preclinical data for MRT5201, an mRNA therapeutic designed to treat patients with ornithine transcarbamylase (OTC) deficiency, the most common urea cycle disorder. The poster presentation, entitled "Treatment of Ornithine Transcarbamylase Deficiency with a Targeted mRNA Therapeutic (MRT)," includes data demonstrating that a functional OTC mRNA encapsulated in a lipid nanoparticle (LNP) was successfully delivered to the liver in a preclinical mouse model of OTC deficiency via intravenous (IV) administration. These data were featured in a poster presentation at the Society for Inherited Metabolic Disorders (SIMD) Annual Meeting on April 7, 2019 in Bellevue, Washington.

"MRT5201 is designed to treat patients with OTC deficiency by intravenous delivery of mRNA encoding fully functional OTC enzyme to the liver to enable hepatocytes to produce the normal OTC enzyme," said Dr. Ann Barbier, chief medical officer of Translate Bio. "These data demonstrate MRT5201's ability to prevent hyperammonemia in a relevant disease model and support further study of MRT5201 as a possible treatment for OTC deficiency."

Preclinical Study Data
The poster presentation included findings from experiments using MRT5201, an LNP containing a codon-optimized human OTC mRNA, delivered to the liver of a mouse model of OTC deficiency ($OTC^{spf\text{-}ash}$) following IV administration. This mouse model was designed to replicate certain clinical features of OTC deficiency, such as high levels of ammonia in the blood and elevated urinary orotic acid levels. In these experiments, the mice were treated with MRT5201 and then challenged with an intraperitoneal injection of ammonium chloride to mimic a hyperammonemic episode.

The Company observed the following in the preclinical data:

- *Functional human OTC protein expression in the livers of OTC-deficient mice.* After treatment with single escalating IV doses of MRT5201, delivery of human OTC mRNA was observed in a dose-dependent manner resulting in expression of human OTC enzyme. This OTC enzyme was functionally active as demonstrated by reduction of blood ammonia, following an ammonium chloride challenge given 24 hours post dose, to levels that are normal for wild-type mice, as well as normalization of urinary orotic acid levels.
- *Production of durable levels of functional human OTC expression in the livers of OTC-deficient mice.* After treatment with a single IV dose of MRT5201, the OTC-deficient mice were challenged with ammonium chloride at 1, 2, 3 or 4 weeks post dose. MRT-treated mice showed durable levels of functional human OTC protein expression with protection against hyperammonemia and normalization of urinary orotic acid for up to 4 weeks.
- *Efficacy following repeated dosing of MRT5201.* OTC-deficient mice received one to five IV doses of MRT5201 and were given an ammonium chloride challenge every two weeks. Repeated dosing of MRT5201 showed sustained effects of targeted human OTC mRNA treatment in OTC-deficient mice.

The full abstract #20 can be found in the March issue of Molecular Genetics and Metabolism, Volume 126, Issue 3, Pages 209-340.

About MRT5201
MRT5201 is designed to treat patients with OTC deficiency by intravenous delivery of mRNA encoding fully functional OTC enzyme to the liver to enable the hepatocytes, the predominant type of liver cell, to produce the normal OTC enzyme. MRT5201 has been granted orphan drug designation for the treatment of OTC deficiency in the U.S. and EU.

About OTC Deficiency
OTC deficiency is a metabolic liver enzyme disorder that results from a mutation in the OTC gene, and is the most common urea cycle disorder. The OTC enzyme is necessary for preventing the accumulation of ammonia, a normal byproduct of protein breakdown. When the enzyme is defective or absent, high levels of ammonia accumulate in the blood, which can cause serious and irreversible neurological damage. Based on published research, the incidence of OTC deficiency is estimated to be 1 in 56,500 live births in the United States. OTC deficiency is an X-chromosome-linked disease, and females are typically less severely affected than males.

About Translate Bio
Translate Bio is a clinical-stage mRNA therapeutics company developing a new class of potentially transformative medicines to treat diseases caused by protein or gene dysfunction. The Company's MRT platform is designed to develop product candidates that deliver mRNA carrying instructions to produce intracellular, transmembrane and secreted proteins for therapeutic benefit. Translate Bio believes that its MRT platform is applicable to a broad range of diseases caused by insufficient protein production or where production of proteins can modify disease, including diseases that affect the lung, liver, eye, central nervous system and lymphatic system. The Company also believes its MRT platform may be applied to various classes of treatments, such as therapeutic antibodies or vaccines in areas such as infectious disease and oncology. Translate Bio's two lead programs are being developed as treatments for cystic fibrosis (CF) and ornithine transcarbamylase (OTC) deficiency. For more information about the Company, please visit www.translate.bio or on Twitter at @TranslateBio.

Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Such forward-looking statements include, but are not limited to, those regarding: the potential for MRT5201 to treat OTC deficiency, prevent the occurrence of hyperammonemia and deliver mRNA encoding fully functional OTC enzyme to the liver; the benefits and broad applicability of the Company's MRT ™ platform; and Translate Bio's plans, strategies and prospects for its business, including its lead development programs. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Such statements are subject to numerous important factors, risks and uncertainties that may cause actual events or results to differ materially from current expectations and beliefs, including but not limited to: Translate Bio's ability to advance the development of its platform and programs under the timelines it projects, demonstrate the requisite safety and efficacy of its product candidates and replicate in clinical trials any positive findings from preclinical studies; the content and timing of decisions made by the FDA, other regulatory authorities and investigational review boards at clinical trial sites, including as it relates to ongoing and planned clinical trials; Translate Bio's ability to obtain, maintain and enforce necessary patent and other intellectual property protection (for example, two of our patents issued in Europe are under opposition); the availability of significant cash required to fund operations; competitive factors; general economic and market conditions and other important risk factors set forth under the caption "Risk Factors" in Translate Bio's Annual Report on Form 10-K for the year ended December 31, 2018 filed with the Securities and Exchange Commission on March 21, 2019 and in any other subsequent filings made by Translate Bio. Any forward-looking statements contained in this press release speak only as of the date hereof, and Translate Bio specifically disclaims any obligation to update any forward-looking statement, whether as a result of new information, future events or otherwise.

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