Translate Bio Announces Results from Second Interim Data Analysis from Ongoing Phase 1/2 Clinical Trial of MRT5005 in Patients with Cystic Fibrosis (CF)

March 17, 2021

-- First inhaled mRNA therapeutic delivered in multiple doses to the lungs of CF patients is generally safe and well tolerated; no observed pattern of increases in $ppFEV_1$ *--*

-- Data supports advancing mRNA therapeutics for pulmonary diseases; additional translational research ongoing to optimize future clinical development of mRNA cystic fibrosis programs, including MRT5005 and a next-generation CF candidate --

-- Company committed to advancing innovative mRNA therapeutics for all patients with CF; Phase 1/2 clinical trial for MRT5005 ongoing and next-generation CF candidate anticipated to enter IND-enabling studies in 2H 2021 --

-- Conference call today at 4:30 pm ET --

LEXINGTON, Mass. , March 17, 2021 (GLOBE NEWSWIRE) -- Translate Bio (Nasdaq: TBIO), a clinical-stage messenger RNA (mRNA) therapeutics company, today announced results from the second interim analysis from a first-in-human Phase 1/2 clinical trial evaluating the safety and tolerability of single- and multiple-ascending doses of MRT5005 in patients with cystic fibrosis (CF). MRT5005 is designed to address the underlying cause of CF regardless of genetic mutation by delivering mRNA encoding fully functional cystic fibrosis transmembrane conductance regulator (CFTR) protein to cells in the lung through nebulization.

Results from the second interim analysis build on the previously reported single-ascending dose (SAD) data (8, 16 and 24 mg dose groups) with new data from a subsequently added 20 mg SAD group, as well as data from multiple-ascending dose (MAD) groups (five once-weekly doses of 8, 12 and 16 mg) through one month follow-up post treatment.

The topline findings from the analysis of the MAD portion of the clinical trial are summarized as follows:

- In evaluating safety and tolerability, the primary outcome measure, repeat dosing of MRT5005 was generally safe and well tolerated with no serious adverse events; treatment-emergent adverse events (TEAEs) were mild to moderate; transient, mild to moderate symptoms of a febrile reaction such as fever, headache and chills occurred in three patients after the first dose of MRT5005 and did not recur with subsequent dosing in the two patients who continued dosing; the third patient discontinued due to the febrile reaction
- Percent predicted forced expiratory volume in 1 second ($ppFEV_1$), a measure of lung function, was assessed as a safety measure at pre-defined timepoints throughout the trial; there was no pattern of increases in $ppFEV_1$

The Phase 1/2 clinical trial is ongoing, and the Company anticipates reporting the findings from the clinical trial, including an additional MAD dose group (20 mg) and a daily dosing cohort (4 mg once-daily for 5 days), at a future medical meeting. The Company plans to continue with ongoing and additional translational studies with MRT5005 and its next-generation CF candidate to support and optimize future clinical development, including research into dosing, formulation and nebulization. Translate Bio has a next-generation CF discovery program that has generated positive preclinical data supporting planned initiation of investigational new drug (IND)-enabling studies in the second half of 2021.

“We have seen the impact that mRNA is having across the vaccine landscape, and given the novelty of its science, I am hopeful that mRNA may have a similar role in treating pulmonary diseases including cystic fibrosis,” said Steven Rowe, M.D., director of the Gregory Fleming James Cystic Fibrosis Center, professor in the Division of Pulmonary, Allergy and Critical Medicine at University of Alabama, Birmingham, and principal investigator of the Phase 1/2 clinical trial of MRT5005. “While innovative clinical science is often incremental, I believe that with these interim results we have gleaned important insights applicable to mRNA therapeutic development for cystic fibrosis.”

“This is the first time messenger RNA encoding CFTR has been administered to patients with cystic fibrosis through inhaled repeat doses, and I believe, this represents an important building block in our pioneering efforts to develop transformative mRNA therapeutics,” said Ronald Renaud, chief executive officer of Translate Bio. “We are evaluating learnings from this trial along with findings from our ongoing CF translational research, while also advancing our next-generation CF discovery efforts. We will continue to leverage the internal capabilities that we’ve built over the last 12 to 18 months in pulmonary biology and aerosol sciences as well as the valuable partnerships established with leading academic research teams to optimize further development in our CF programs. Our patient communities are of the utmost importance to us, and we are committed to advancing mRNA therapeutics for CF and other pulmonary diseases. This is the first step in an area with significant potential and we look forward to sharing more as we advance our development programs.”

“Based on the first and second interim analyses, we believe we have a achieved a safety profile that supports repeat dosing of inhaled mRNA and further advancement of the pulmonary platform for chronic dosing,” said Ann Barbier, M.D., Ph.D., chief medical officer of Translate Bio. “Participating in clinical trials, especially those evaluating first-of-a-kind therapeutics, is an act of service, commitment to innovation and optimism that does not go unnoticed by the team at Translate Bio. We are grateful to the patients who are helping to advance novel treatments for debilitating diseases.”

Phase 1/2 Clinical Trial Design and Results: Single-Ascending Dose (SAD) Groups

- **Study Design and Baseline Characteristics Summary:** In the SAD part of the clinical trial, 16 adult patients with CF were enrolled and received either MRT5005 or placebo (3:1 randomization) at dose levels of 8, 16, 20 or 24 mg. Fifteen

patients had at least one copy of the F508del mutation and one patient did not have a F508del mutation and was considered non-amenable to CFTR modulator treatment. Nine of the 16 patients were taking either Symdeko® or Orkambi®.

- **Safety, Tolerability and Pharmacokinetic Summary – 20 mg SAD Cohort:** The safety profile of the 20 mg SAD group was generally consistent with that previously reported for the 8, 16 and 24 mg dose groups. The majority of TEAEs were considered mild to moderate. One patient experienced symptoms suggestive of a hypersensitivity reaction, which resolved with medical treatment by Day 2 and the patient was discharged as planned. There was one serious adverse event (SAE), a pulmonary exacerbation on Day 23 (or 22 days post dose). All three patients receiving MRT5005 had variable but detectable levels of mRNA in the blood at one or more time points. No patients had detectable levels of lipid in the blood.
- **Lung Function (ppFEV$_1$) Summary – 20 mg SAD Cohort:** ppFEV$_1$ was assessed at pre-defined timepoints throughout the trial. Marked increases in ppFEV$_1$ were not observed.
- **Immunogenicity Summary:** Evaluation of immunogenicity markers showed no clear pattern of anti-CFTR antibodies, anti-PEG antibodies or T-cell sensitization to CFTR.

Phase 1/2 Clinical Trial Design and Results: Multiple-Ascending Dose (MAD) Groups

- **Study Design and Baseline Characteristics Summary:** The three dose levels (8, 12 and 16 mg) in the MAD groups enrolled 14 patients in total; two patients were replaced after receiving only a single dose (one in the placebo group discontinued due to a COVID-related site closure, and one in the 16 mg dose group discontinued after a febrile reaction). As a result, 12 patients received five doses, except one patient in the 12 mg dose group who was not able to receive their 5th dose due to a COVID-19-related site closure. Of the 14 patients, 10 had at least one copy of the F508del mutation and two of the 14 patients are considered non-amenable to CFTR modulator treatment. Seven of the 14 patients were taking either Symdeko® or Orkambi®.
- **Safety, Tolerability and Pharmacokinetic Summary:** Through one month post last dose, the safety profile of the MAD groups was consistent with that seen in the SAD part of the trial. There were no SAEs reported. The most common adverse events were cough and headache. All TEAEs were considered mild to moderate. As mentioned above, one patient in the 16 mg group discontinued after the first dose due to a febrile reaction. Two additional patients (one receiving 12 mg and one receiving 16 mg) experienced a transient, mild to moderate suspected febrile reaction, after the first dose but not after subsequent doses. Five patients, all in the 12 and 16 mg groups, had detectable levels of mRNA and/or lipid in the blood with no signs of accumulation.
- **Lung Function (ppFEV$_1$) Summary:** In the MAD part of the clinical trial, ppFEV$_1$ was measured before and after each dose and again the day after dosing. ppFEV$_1$ was also measured one week, 2 weeks and 4 weeks after the last dose. There was no pattern of increases in ppFEV$_1$.
- **Immunogenicity Summary:** No clear pattern of new or increasing levels of immunogenicity markers (anti-CFTR antibodies, anti-PEG antibodies or T-cell sensitization to CFTR) was observed during repeat dosing with MRT5005.

About MRT5005

MRT5005 is the first clinical-stage mRNA product candidate designed to address the underlying cause of CF by delivering mRNA encoding fully functional cystic fibrosis transmembrane conductance regulator (CFTR) protein to the lung epithelial cells through nebulization. MRT5005 is being developed to treat all patients with CF, regardless of the underlying genetic mutation, including those with limited or no CFTR protein. The U.S. Food and Drug Administration (FDA) has granted MRT5005 Orphan Drug, Fast Track and Rare Pediatric Disease designation.

About the MRT5005 Phase 1/2 Clinical Trial

The randomized, double-blind, placebo-controlled Phase 1/2 clinical trial of MRT5005 is designed to enroll at least 40 adult patients with CF who have two Class I and/or Class II mutations. The primary endpoint of the trial is safety and tolerability of single and multiple escalating doses of MRT5005 administered by nebulization. Percent predicted forced expiratory volume in one second (ppFEV1) is also measured at pre-defined timepoints throughout the trial. The Phase 1/2 clinical trial of MRT5005 for the treatment of CF is being conducted in collaboration with the Cystic Fibrosis Foundation Therapeutics Development Network and the Emily's Entourage Patient Registry. For more information about the Phase 1/2 clinical trial, visit https://clinicaltrials.gov/ct2/show/NCT03375047.

About Cystic Fibrosis

Cystic fibrosis is the most common fatal inherited disease in the United States, affecting more than 30,000 patients in the U.S. and more than 70,000 patients worldwide. CF is caused by genetic mutations that result in dysfunctional or absent CFTR protein. This defect causes mucus buildup in the lungs, pancreas and other organs. Mortality is primarily driven by a progressive decline in lung function. According to the Cystic Fibrosis Foundation, the median age at death for patients with CF was 32.4 years in 2019. There is no cure for CF. Currently marketed CFTR modulators are effective only in patients with specific mutations, and patients still experience pulmonary exacerbations and a progressive decline in lung function, which represents a significant unmet need.

Conference Call Information

Translate Bio will host a conference call and webcast today at 4:30 PM ET to discuss the second interim results from the single-ascending and multiple ascending dose portions of its Phase 1/2 clinical trial of MRT5005 in patients with CF. The live webcast can be accessed on the investor page of Translate Bio's website at https://investors.translate.bio/investors/news-and-events. The conference call can be accessed by dialing (877) 377-8524 (toll-free domestic) or (629) 228-0742 (international) and using the conference ID 3383727. A replay of the webcast will be available on Translate Bio's website approximately two hours after the completion of the event and will be archived for up to 30 days.

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, or to prevent infectious diseases by generating protective immunity. Translate Bio is primarily focused on applying its technology to treat pulmonary diseases with a lead pulmonary candidate being evaluated as an inhaled treatment for cystic fibrosis (CF) in a Phase 1/2 clinical trial. Additional pulmonary diseases are being evaluated in discovery-stage research programs that utilize a proprietary lung delivery platform. Translate Bio also believes its technology may apply broadly to a wide range of diseases, including diseases that affect the liver. Additionally, the platform may be applied to various classes of treatments, such as therapeutic antibodies or protein degradation. Translate Bio is also pursuing the development of mRNA vaccines for infectious diseases under a collaboration with Sanofi Pasteur. 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 MRT5005 to address the underlying cause of CF; the anticipated reporting of findings from the Phase 1/2 clinical trial of MRT5005, including an additional MAD dose group and a daily dosing cohort; Translate Bio's plans to continue to dose patients in its Phase 1/2 clinical trial of MRT5005 and the expected patient enrollment size; Translate Bio's plans to continue with ongoing and additional translational studies with MRT5005 and its next-generation CF candidate to support and optimize future clinical development; Translate Bio's plans to initiate IND-enabling studies of its next-generation CF candidate in the second half of 2021; the potential of Translate Bio to develop transformative mRNA therapeutics; the potential of mRNA therapeutics for the treatment of genetic disease, including diseases of the lung; Translate Bio's belief that an acceptable safety profile can be achieved with repeat administration of an mRNA therapeutic; 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: the current and potential future impacts of the COVID-19 pandemic on Translate Bio's business, financial condition, operations and liquidity; 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 or early-stage clinical trials; Translate Bio's ability to enroll patients in its ongoing clinical trial of MRT5005; whether interim data from the Phase 1/2 clinical trial of MRT5005 will be predictive of the final results of that trial; the content and timing of decisions made by the FDA, other regulatory authorities and investigational review boards at clinical trial sites, including decisions 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; 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, 2020 filed with the Securities and Exchange Commission ("SEC") on March 1, 2021 and in any other subsequent filings made with the SEC 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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