



Translate Bio Announces Interim Results from Phase 1/2 Clinical Trial of MRT5005 in Patients with Cystic Fibrosis

July 31, 2019

-- MRT5005 was generally well tolerated at low and mid-dose levels; no serious adverse events reported at any dose level --

-- Marked increases in ppFEV₁ (percent predicted forced expiratory volume in one second) observed after single dose of MRT5005, primarily at mid-dose --

-- Findings support exploration of two additional dose cohorts --

-- MRT5005 is the first mRNA therapeutic administered to patients for the treatment of a genetic disease --

-- Conference call today at 8:00 am ET --

LEXINGTON, Mass., July 31, 2019 (GLOBE NEWSWIRE) -- Translate Bio (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 interim results from a first-in-human Phase 1/2 clinical trial evaluating 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. Today's results, the first clinical investigation of an inhaled mRNA therapeutic, summarize the single ascending dose (SAD) portion of the clinical trial in 12 patients through one-month follow up post treatment. The multiple ascending dose (MAD) portion of the trial is ongoing with data expected in 2020.

"Effectively delivering the desired mRNA sequence is an essential step to producing functional CFTR proteins. While some variability in ppFEV₁ from day to day in CF patients is expected in a trial of this size, we believe that the observed improvements in ppFEV₁ from baseline and the timecourse of the effect support a CFTR-related mechanism and may suggest that MRT5005 can enable the production of functional protein," 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. "These early promising data warrant continued evaluation of MRT5005 to optimize the dosing regimen and assess the effect with repeated administration. If future data confirms this early positive signal, MRT5005 has the potential to provide clinically meaningful benefit for people with CF independent of CFTR genotype."

"Despite significant advances in the treatment of patients with CF, there remains a critical unmet need for patients whose genetic mutations are considered non-amenable to CFTR modulators," said Ann Barbier, M.D., Ph.D., chief medical officer of Translate Bio. "mRNA therapy represents a potential new approach to treating CF, and we look forward to sharing the results from the multiple-ascending dose part of the trial next year."

Dr. Barbier continued, "On behalf of the team at Translate Bio, I would also like to extend our most sincere gratitude to the investigators, the Cystic Fibrosis Foundation, and most importantly, the patients who are participating and have participated in this clinical trial."

"These encouraging interim results represent a milestone in the mRNA development landscape as this is the first time an mRNA therapeutic has been evaluated for its potential to treat a genetic disease," said Ronald Renaud, chief executive officer of Translate Bio. "Also, as the first inhaled mRNA therapeutic, these data indicate the potential of mRNA therapeutics for the treatment of lung diseases, and support the planned expansion of our earlier-stage programs based on this pulmonary delivery platform."

Phase 1/2 Clinical Trial Results

Study Design and Baseline Characteristics Summary

The interim results summarize data from 12 adult patients with CF who received a single dose of either MRT5005 or placebo (3:1 randomization). Patients who received MRT5005 were assigned to one of three dose groups (8, 16 or 24 mg). Of the 12 patients, 11 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. Seven of the 12 patients were taking an approved CFTR modulator through screening, dosing and follow-up.

Safety, Tolerability and Pharmacokinetic Summary

The most common adverse events through Day 29 were cough and headache. There were no treatment-emergent serious adverse events (SAEs). All treatment-emergent adverse events (TEAEs) were considered mild to moderate. Five patients, 3 of whom were in the 24 mg dose group, experienced transient, mild to moderate febrile reactions deemed related to study drug. These events occurred approximately 4-10 hours post dosing, and were characterized by fever and symptoms such as headache, fatigue, chills or nausea, which were treated with medicines such as acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs), or an anti-emetic. Symptoms resolved within 24 hours, and all patients were discharged from the study center on Day 2 as planned. In these five patients, low levels of mRNA and/or lipid were detected in the blood.

Characteristics through Day 29	MRT5005	MRT5005	MRT5005	Pooled
	8 mg (N=3)	16 mg (N=3)	24 mg (N=3)	Placebo (N=3)
Overall Number of TEAEs reported	28	25	33	11
Not related	11	9	10	9
Related	17	16	23	2
Number of Serious TEAEs reported	0	0	0	0
Number of TEAEs leading to discontinuation	0	0	0	0
Number of TEAEs resulting in death	0	0	0	0

Number of TEAEs classified as pulmonary exacerbation	0	0	2*	0
Number of TEAEs by Severity				
Mild	23	24	21	11
Moderate	5	1	12	0
Severe	0	0	0	0

* Occurred at Day 25 and Day 27

Lung Function (ppFEV₁) Summary

A primary measure of lung function, ppFEV₁, was assessed at pre-defined timepoints throughout the trial. Patients in the pooled placebo group and the 8 mg dose group did not show a marked improvement in ppFEV₁. In the eight day period after dosing, the three patients in the 16 mg dose group demonstrated maximal ppFEV₁ increases of 11.1%, 13.6% and 22.2%, for a mean maximum increase from baseline (+/- standard deviation) of 15.7% (5.8). Of the three patients in the 16 mg dose group, two were on a stable CFTR modulator treatment regimen for at least 28 days, while the third had a genotype that is considered non-amenable to CFTR modulator treatments. Of the three patients in the 24 mg dose group, through Day 8, one patient experienced a maximum increase in ppFEV₁ from baseline of 21.4%, while two patients did not show a marked increase in ppFEV₁.

	Mean Baseline ppFEV ₁ % (SD)	Absolute Change from Baseline Mean ppFEV ₁ % (SD)				Maximum Change from Baseline through Day 8 Mean ppFEV ₁ % (SD)
		Day 1 *	Day 2	Day 3	Day 8	
8 mg	53.3 (7.2)	3.7 (0.9)	2.8 (1.8)	3.4 (2.3)	-1.2 (3.0)	4.4 (0.7)
16 mg	72.0 (6.6)	7.2 (7.3)	11.2 (10.3)	11.4 (5.1)	9.2 (1.8)	15.7 (5.8)
24 mg	79.2 (7.1)	2.5 (0.4)	8.6 (11.2)	6.6 (4.8)	2.3 (3.2)	9.7 (10.2)
Pooled Placebo	60.5 (18.5)	2.0 (3.8)	0.4 (2.4)	-0.2 (1.4)	-0.6 (4.0)	3.2 (2.7)

*8 hours post dose

The Company anticipates presenting additional details from this interim data set at the North American Cystic Fibrosis Conference taking place October 31-November 2, 2019.

Phase 1/2 Clinical Trial Design

Based on the analysis of the SAD (Part A) interim results, the Company has proposed certain protocol changes in this ongoing Phase 1/2 clinical trial. In the SAD portion of the trial, the Company plans to amend the clinical trial protocol to include an additional 20 mg single dose cohort of four patients. In the MAD portion of the trial (Part B), the Company plans to amend the clinical trial protocol to add 12 and 20 mg dose cohorts with four patients each, the latter dosing cohort contingent on successful completion of the 20 mg single dose cohort and an acceptable safety profile in the lower MAD dose cohorts. The Company no longer plans to evaluate a 24 mg dose group in the MAD portion of the trial. The originally planned Part C of the clinical trial, which included bronchoscopies, is expected to be redesigned as a Part B expansion to instead focus on the enrollment of additional patients at dose levels of interest. As required, the Company plans to submit these protocol changes to the FDA. The Company expects to report results from the additional 20 mg SAD cohort and the ongoing MAD portion of the trial in 2020.

The randomized, double-blind, placebo-controlled Phase 1/2 clinical trial of MRT5005 was designed to enroll at least 32 adult patients with CF who have two Class I and/or Class II mutations. After accounting for the planned protocol amendments, the Company expects to enroll up to 40 adult patients with CF. The primary endpoint of the trial is to assess the safety and tolerability of single and multiple escalating doses of MRT5005 administered by nebulization. Percent predicted forced expiratory volume in one second (ppFEV₁), which is a well-defined and accepted endpoint measuring lung function, is also being 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.

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 designed to treat all patients with CF, regardless of the underlying genetic mutation, including those with limited or no CFTR protein. MRT5005 has been granted Orphan Drug Designation in the U.S. and EU for the treatment of CF.

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 30.6 years in 2017. There is no cure for CF. CFTR modulators that are currently marketed or in clinical development have effect 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 8:00 AM ET to discuss the interim results from the single-ascending dose portion of 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 2659949. 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. 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, and central nervous 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 MRT5005 to address the underlying cause of CF, Translate Bio's plans to continue to dose patients in its MAD portion of its Phase 1/2 clinical trial of MRT5005 and the expected patient enrollment size; the anticipated availability of the clinical data regarding MRT5005 in 2020; Translate Bio's plans to amend the protocol of its Phase 1/2 clinical trial of MRT5005; the potential of mRNA therapeutics for the treatment of genetic disease, including diseases of the lung; Translate Bio's plans to report additional details on the interim data set from its Phase 1/2 clinical trial of MRT5005; 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 later-stage 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; 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 U.S. Food and Drug Administration, other regulatory authorities and investigational review boards at clinical trial sites; 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 Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2019 and in any other subsequent filings made with the Securities and Exchange Commission 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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Source: Translate Bio, Inc.