resTORbio Announces Positive Topline Results in Phase 2b Trial of RTB101

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-- Statistically significant and clinically meaningful 30.6% reduction in the percentage of patients with one or more laboratory-confirmed respiratory tract infections (RTIs), the primary endpoint of the trial, in the RTB101 10 mg once daily cohort compared to the placebo cohort --

-- Statistically significant 68.4% reduction in the incidence of laboratory-confirmed RTIs in the pre-specified analysis of asthma patients 65 years and older treated with RTB101 10 mg once daily --

-- Statistically significant 66.7% reduction in the incidence of laboratory-confirmed RTIs in the pre-specified analysis of patients 85 years and older treated with RTB101 10 mg once daily --

-- All doses were well-tolerated; RTB101 10 mg once daily had a comparable safety profile to placebo --

-- The Phase 2b trial successfully identified a dose and patient populations with high unmet need for upcoming pivotal trials --

-- Conference call 8:30 AM Eastern Time today --

BOSTON, July 25, 2018 (GLOBE NEWSWIRE) -- resTORbio, Inc. (Nasdaq:TORC) today announced positive topline results from its dose-ranging Phase 2b clinical trial that enrolled 652 elderly patients at increased risk of morbidity and mortality associated with respiratory tract infections (RTIs). In this trial, RTB101, an oral, selective, and potent inhibitor of target of rapamycin complex 1 (TORC1), demonstrated a statistically significant and clinically meaningful reduction in the percentage of patients with one or more laboratory-confirmed RTIs during the 16-week treatment period compared to placebo, the primary endpoint of the study, with the 10 mg once daily dose. Greater TORC1 inhibition with RTB101 10 mg in combination with everolimus 0.1 mg did not meet the primary endpoint, suggesting that that less TORC1 inhibition with RTB101 10 mg once daily may have greater benefit in high-risk elderly patients.

“This Phase 2b has successfully defined a dose, RTB101 10 mg once daily, to be evaluated in future pivotal studies. That dose led to a statistically significant decrease in the incidence of laboratory-confirmed RTIs and was well-tolerated in the high-risk elderly patients enrolled in the Phase 2b study. We have also identified patient populations that were particularly high responders,” said Joan Mannick, M.D., Co-Founder and Chief Medical Officer of resTORbio. “We believe the findings of this trial provide us with a clear path forward for pursuing a pivotal program for RTB101 to reduce the incidence of RTIs in high-risk elderly patients. We look forward to working closely with the U.S. Food and Drug Administration (FDA) and other regulatory agencies on this program.”

“The majority of RTIs requiring hospitalizations in the very elderly and the majority of asthma exacerbations are caused by viruses for which there are currently no approved therapies,” said Professor Sebastian Johnston, Professor of Respiratory Medicine and Allergy at the National Heart and Lung Institute, Imperial College London. “The magnitude of reduction in the incidence of laboratory-confirmed RTIs observed with RTB101 suggests that, if successfully developed and approved, RTB101 may be a new promising treatment for the very elderly and elderly patients with asthma who are at high risk of morbidity and mortality associated with RTIs.”

“The primary endpoint of this Phase 2b study, the percentage of patients with laboratory-confirmed RTIs, was chosen based on feedback from the FDA, and we look forward to discussing these results at our end of Phase 2 meeting with the agency,” said Chen Schor, Co-Founder, President and CEO of resTORbio. “RTIs are the fourth leading cause of hospitalization in patients 65 years and older, and the second leading cause of hospitalization in patients 85 years and older in the U.S. We are committed to helping the millions of elderly patients at high risk of morbidity and mortality due to RTIs.”

The Phase 2b trial was a two-part, randomized, double-blind, placebo-controlled clinical trial conducted during the winter cold and flu season in the southern hemisphere (Part 1) and northern hemisphere (Part 2). Patients enrolled were those at increased risk of morbidity and mortality from RTIs including patients who were: (i) 85 years of age or older, or (ii) 65 years of age or older with asthma, type 2 diabetes mellitus (T2DM), chronic obstructive pulmonary disease (COPD), or current smokers. The doses investigated in Part 1 were RTB101 5 mg and RTB101 10 mg once daily. The doses investigated in Part 2 were RTB101 10 mg once daily, RTB101 10 mg twice daily and RTB101 10 mg in combination with everolimus 0.1 mg once daily.

The following was observed in an analysis of the primary endpoint:

- A 30.6% decrease relative to placebo in the percentage of all patients treated with RTB101 10 mg once daily who developed one or more laboratory-confirmed RTIs (p=0.026)
- A 20.6% decrease relative to placebo in the percentage of all patients treated with RTB101 5 mg once daily who developed one or more laboratory-confirmed RTIs (p=0.108)
- No decrease relative to placebo in the percentage of patients treated with either RTB101 10 mg twice daily or the combination of RTB101 10 mg + everolimus 0.1 mg once daily who developed one or more laboratory-confirmed RTIs, suggesting that less TORC1 inhibition with RTB101 10 mg once daily may have greater benefit in high-risk elderly patients

To better understand the activity observed in the RTB101 10 mg once daily cohort, a pre-specified analysis of each patient subgroup enrolled in the study was conducted. The following decreases in the percentage of patients with laboratory-confirmed RTIs were observed in the RTB101 10 mg once

daily cohort as compared to the placebo cohort:

- A 68.4% decrease in all asthma patients (p=0.0002)
- A 66.7% decrease in all patients 85 years of age and older (p=0.007)
- A 26.9% decrease in all T2DM patients (p=0.020)
- No decrease was observed in either COPD patients or current smokers; a 42.0% decrease in all patients was observed when excluding patients with COPD (p=0.002) and a 43.9% decrease in all patients was observed when excluding current smokers (p=0.001)

All doses were observed to be well-tolerated. Data from the RTB101 10 mg once daily cohort are as follows: Adverse events (AEs) were balanced between the RTB101 10 mg once daily and placebo treatment groups. 4.5% of subjects in the RTB101 10 mg once daily cohort and 7.2% of subjects in the placebo cohort had a serious adverse event, none of which were considered related to study drug. 4.5% of subjects in the RTB101 10 mg once daily cohort and 6.1% of subjects in the placebo cohort discontinued study drug due to an AE. All AEs were mild or moderate except for 11 severe AEs in the RTB101 10 mg once daily cohort and 22 severe AEs in the placebo cohort.

This Phase 2b is the second study in which RTB101 10 mg once daily was observed to be well-tolerated and reduce the incidence of RTIs in the elderly. Together, these studies enrolled more than 900 elderly people.

Conference Call and Webcast Information

resTORbio management will host a conference call today at 8:30 a.m. ET to discuss the results of the Phase 2b trial. To participate in the conference call, please dial (877) 356-9149 (domestic) or (629) 228-0720 (international) and refer to conference ID 3181638. A live webcast of the call can be accessed in the “Investors” section of the Company's website at www.restorbio.com. An archived webcast recording will be available on the resTORbio website beginning approximately two hours after the call.

Phase 2b Trial Design

The purpose of the exploratory dose-finding, randomized, double-blind, placebo-controlled, multi-center Phase 2b clinical trial was to determine if RTB101 alone or in combination with everolimus decreased the incidence of RTIs in high-risk elderly patients, as well as to evaluate safety and tolerability alone or in combination with everolimus, to support dose selection for pivotal trials.

The study enrolled 652 patients at increased risk of morbidity and mortality from RTIs including patients who were: (i) 85 years of age or older, or (ii) 65 years of age or older with asthma, T2DM, COPD, or current smokers. The study consisted of two parts. Part 1 was conducted during the winter cold and flu season in the southern hemisphere and 179 elderly patients were randomized to receive either placebo, RTB101 5 mg or RTB101 10 mg once daily. At the end of Part 1, an interim analysis was conducted by an unblinded data monitoring committee who selected the RTB101 10 mg dose to move forward into Part 2 of the study. Part 2 was conducted during the winter cold and flu season in the northern hemisphere and 473 elderly patients were randomized to receive either placebo, RTB101 10 mg once daily, RTB101 10 mg twice daily, or RTB101 10 mg in combination with everolimus 0.1 mg once daily. All patients were treated with study drug for 16 weeks, and then were followed for an additional eight weeks off study drug.

The primary endpoint of the trial was a reduction, as compared to placebo, in the percentage of patients with one or more laboratory-confirmed RTIs during the 16 weeks of study drug treatment. A pre-specified exploratory endpoint was a reduction, as compared to placebo, in the percentage of patients with one or more laboratory-confirmed RTIs in each of the patient subgroups (≥ 85 years of age, ≥ 65 years of age with asthma, COPD, T2DM, or current smokers).

Additional information about the study [NCT03373903] can be obtained at www.ClinicalTrials.gov.

About Respiratory Tract Infections

The reduced ability of the aging immune system to effectively detect and fight infections results in increased susceptibility of the elderly to RTIs. In the U.S., RTIs are the fourth leading cause of hospitalizations and seventh leading cause of death in people age 65 years and older. Additionally, the majority of asthma exacerbations are caused by RTIs, and the majority of RTIs are caused by viruses for which there are no currently approved therapies.

A survey was conducted by resTORbio of 100 physicians in the U.S. that treat approximately 25,000 patients aged 65 years or older monthly. Depending on their specialty, the physicians surveyed estimated that they would prescribe a therapeutic that reduced the incidence of laboratory-confirmed RTIs by 25% to approximately 30-50% of their high-risk elderly patients. Data from market surveys may not predict actual prescribing behavior should RTB101 receive regulatory approval.

About RTB101

RTB101 is an oral, selective, and potent inhibitor of TORC1. RTB101 inhibits the phosphorylation of multiple targets downstream of TORC1. Inhibition of TORC1 has been observed to extend lifespan and healthspan in aging preclinical species and to enhance immune, cardiac and neurologic functions, suggesting potential benefits in several aging-related diseases.

About resTORbio

resTORbio, Inc. is a clinical stage biopharmaceutical company targeting TORC1 and other biological pathways that regulate aging to develop innovative medicines with the potential to extend healthy lifespan. resTORbio’s lead program is selectively targeting TORC1, an evolutionarily conserved pathway that contributes to the decline in function of multiple organ systems, including the immune, cardiovascular and central nervous systems.

Forward Looking Statements

This press release contains forward-looking statements that are made pursuant to the safe harbor provisions of the federal securities laws. Investors are cautioned that statements in this press release which are not strictly historical statements, including, without limitation, express or implied statements or guidance regarding our plans to develop and commercialize RTB101 alone or in combination with everolimus, including the therapeutic potential and clinical benefits thereof, and the potential patient populations that may be addressed by our product candidates, our ongoing and future clinical trials for RTB101 alone or in combination with everolimus, including the timing of the initiation and anticipated results of these trials, as well as the intended regulatory path for our product candidates and interactions with regulatory authorities, constitute forward-looking statements identified by words like “believe,” “expect,” “may,” “will,” “should,” “seek,” “anticipate,” or “could” and similar expressions. Such forward-looking statements are subject to a number of risks and uncertainties that could cause actual results to differ materially from those anticipated, including, without limitation, risks associated with: the delay of any planned clinical trials and/or development of RTB101, either alone or in combination with everolimus; our ability to successfully demonstrate the efficacy and safety of our lead product candidate; the clinical results for our lead product candidate which may not support further development of additional indications; and obtaining, maintaining and protecting our intellectual property; as well as those risks more fully discussed in the section entitled “Risk Factors” in the Annual Report on Form 10-K filed by resTORbio, Inc. with the Securities and Exchange Commission, as well as discussions of potential risks, uncertainties, and other important factors in our subsequent filings with the Securities and Exchange Commission. In addition, any forward-looking statements represent our views only as of today and should not be relied upon as representing its views as of any subsequent date. resTORbio explicitly disclaims any obligation to update any forward-looking statements.

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