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UNITED THERAPEUTICS ANNOUNCES *INCREASE* STUDY OF TYVASO® MEETS PRIMARY AND ALL SECONDARY ENDPOINTS

~First pivotal clinical trial to demonstrate a benefit in PH-ILD ~
~ NDA supplement to be filed by mid-year ~

Silver Spring, MD and Research Triangle Park, NC, February 24, 2020: United Therapeutics Corporation (NASDAQ: UTHR) today announced that preliminary analysis indicates that the *INCREASE* clinical study of Tyvaso® (treprostinil) Inhalation Solution in patients suffering from World Health Organization (WHO) Group 3 pulmonary hypertension associated with interstitial lung disease (PH-ILD) has met its primary efficacy endpoint of demonstrating improvement in six-minute walk distance (6MWD).

Tyvaso increased six-minute walk distance by 21 meters versus placebo (p=0.0043, Hodges-Lehmann estimate) after 16 weeks of treatment. Benefits of Tyvaso were observed across several key subgroups, including etiology of PH-ILD, disease severity, age, gender, baseline hemodynamics, and dose.

Significant improvements were also observed in each of the study's secondary endpoints including reduction in the cardiac biomarker NT-proBNP, time to first clinical worsening event, change in peak 6MWD at Week 12, and change in trough 6MWD at week 15. Treatment with Tyvaso of up to 12 breaths per session, four times daily, in the *INCREASE* study was well tolerated and the safety profile was consistent with previous Tyvaso studies in PAH and known prostacyclin-related adverse events (see the discussion of adverse events below under "About Tyvaso").

"Patients with both interstitial lung disease and pulmonary hypertension have worse clinical trajectories and earlier death than patients with interstitial lung disease alone. There are currently no approved therapies for these patients and so there is a tremendous unmet need," said Aaron Waxman, M.D., Ph.D., Director of the Pulmonary Vascular Disease Program at Brigham and Women's Hospital and the chair of the *INCREASE* Study Steering Committee. "This is the largest clinical trial in this population, and the first to demonstrate a clear benefit. As a clinician, I look forward to soon having an approved treatment to offer these patients with this life-threatening disease."

"I am pleased to announce the successful outcome of the *INCREASE* phase III trial of Tyvaso in a unique kind of pulmonary hypertension, a variant that has no approved therapy," said Martine Rothblatt, Ph.D., Chairman and Chief Executive Officer of United Therapeutics. "Some 30,000 Americans suffer from this disease, called WHO Group 3 Pulmonary Hypertension. It is a tremendous testament to our head of product development, Dr. Leigh Peterson, that her team used the unique characteristics of our inhaled medicine to achieve a highly statistically

significant proof of efficacy while seeming to avoid the safety issues that have plagued systemic therapeutics."

"The results of the *INCREASE* study present a powerful message of efficacy in the interstitial lung disease patient population," said Gil Golden, M.D., Ph.D., Chief Medical Officer of United Therapeutics. "I congratulate the patients and families who participated in this study, along with our principal investigators who produced a clear outcome that we think could change the lives of ten times the number of patients who are on Tyvaso today. This is what we mean at United Therapeutics when we say we 'identify the corridors of indifference and run like hell down them.'"

United Therapeutics plans to submit the results to the U.S. Food and Drug Administration by mid-year in support of an efficacy supplement that is expected to result in revised labeling that reflects the outcome of the *INCREASE* study.

About *INCREASE*

INCREASE was a phase III, multicenter, randomized, double-blinded, placebo-controlled, 16-week, parallel group study of Tyvaso in patients with pulmonary hypertension associated with interstitial lung disease. Enrollment into the study was completed in August 2019 with a total of 326 patients. Patients were randomized in a 1:1 Tyvaso (n=163) or placebo (n=163).

The primary endpoint primary endpoint was to evaluate the change in 6-minute walk distance (6MWD) measured at peak exposure from Baseline to Week 16.

Secondary objectives of the study included:

- Change in plasma concentration of N-terminal pro-brain natriuretic peptide (NT-proBNP) from Baseline to Week 16
- Time to clinical worsening calculated as the time from randomization until one of the following criteria are met:
    - Hospitalization due to a cardiopulmonary indication
    - Decrease in 6MWD >15% from Baseline directly related to disease under study, at two consecutive visits, and at least 24 hours apart
    - Death (all causes)
    - Lung transplantation
- Change in peak 6MWD from Baseline to Week 12
- Change in trough 6MWD from Baseline to Week 15

Exploratory objectives of the study evaluated changes in peak 6MWD at Week 4 and Week 8, changes in quality of life as measured by the St. George's Respiratory Questionnaire (SGRQ) and change in distance saturation product (DSP). Further exploratory analysis will also be performed on biomarkers and pharmacogenomics from this study.

Detailed study results will be made available through scientific disclosure at upcoming medical conferences and in peer-reviewed publications.

About TYVASO® (treprostinil) Inhalation Solution

What is TYVASO?

TYVASO (treprostinil) is a prescription medicine used in adults to treat pulmonary arterial hypertension (PAH; WHO Group I), which is high blood pressure in the arteries of your lungs. TYVASO can improve the ability to exercise. Your ability to exercise decreases four hours after taking TYVASO. It is not known if TYVASO is safe and effective in children under 18 years of age.

IMPORTANT SAFETY INFORMATION

Before you take TYVASO, tell your healthcare provider about all of your medical conditions, including if you:

- Have lung disease, such as asthma or chronic obstructive pulmonary disease (COPD)
- Have a lung infection
- Have liver or kidney problems
- Have low blood pressure
- Have bleeding problems
- Are pregnant or plan to become pregnant. It is not known if TYVASO will harm your unborn baby
- Are breast-feeding or plan to breast-feed. It is not known if TYVASO passes into your breast milk. Talk to your healthcare provider about the best way to feed your baby during treatment with TYVASO.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. TYVASO and other medicines may affect each other.

Especially tell your healthcare provider if you take:

- Medicines used to treat high blood pressure or heart disease
- Medicines that decrease blood clotting (anticoagulants)
- Water pills (diuretics)
- Gemfibrozil (Lopid) or rifampin (Rimactane, Rifadin, Rifamate, Rifater)

What are the possible side effects of TYVASO?

TYVASO can cause **serious side effects**, including:

- **Low blood pressure** (symptomatic hypotension)**.** If you have low blood pressure, TYVASO may lower your blood pressure more.
- **Bleeding problems.** TYVASO may increase the risk of bleeding, especially in people who take blood thinners (anticoagulants).

The **most common side effects** of TYVASO are cough, headache, throat irritation and pain, nausea, reddening of the face and neck (flushing), fainting or loss of consciousness, dizziness, and diarrhea. These are not all the possible side effects of TYVASO. Call your doctor for medical advice about side effects.

You may report side effects to the FDA at www.fda.gov/MedWatch or call 1-800-FDA-1088.

The risk information provided here is not comprehensive. To learn more about Tyvaso, talk with your healthcare provider. Please see Full Prescribing Information, Patient Product Information, and the TD-100 and TD-300 TYVASO® Inhalation System Instructions for Use manuals at www.tyvaso.com or call 1-877-UNITHER (1-877-864-8437).

About United Therapeutics

United Therapeutics Corporation focuses on the strength of a balanced, value-creating biotechnology model. We are confident in our future thanks to our fundamental attributes, namely our obsession with quality and innovation, the power of our brands, our entrepreneurial culture and our bioinformatics leadership. We also believe that our determination to be responsible citizens – having a positive impact on patients, the environment and society – will sustain our success in the long term.

Through our wholly owned subsidiary, Lung Biotechnology PBC, we are focused on addressing the acute national shortage of transplantable lungs and other organs with a variety of technologies that either delay the need for such organs or expand the supply. Lung Biotechnology is the first public benefit corporation subsidiary of a public biotechnology or pharmaceutical company.

Forward-looking Statements

Statements included in this press release that are not historical in nature are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements include, among others, statements regarding the timing and outcome of our supplement to the Tyvaso NDA to reflect the *INCREASE* study results, the potential benefits to patients, and the anticipated expansion of the market opportunity for Tyvaso. These forward-looking statements are subject to certain risks and uncertainties, such as those described in our periodic and other reports filed with the Securities and Exchange Commission that could cause actual results to differ materially from anticipated results. In particular, we note that analysis of the full *INCREASE* study results is ongoing. These further analyses could have a

material impact on how useful the full results will be to healthcare providers and payers, and how they will be viewed by the FDA and other regulators. All of these factors could have a material impact on how useful the final results will be to healthcare providers, and how they will be viewed by the FDA and other regulators. In addition, the forward-looking statements in this press release are qualified by the cautionary statements, cautionary language and risk factors set forth in our periodic reports and documents filed with the Securities and Exchange Commission, including our most recent Annual Report on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K. We claim the protection of the safe harbor contained in the Private Securities Litigation Reform Act of 1995 for forward-looking statements. We are providing this information as of February 24, 2020, and assume no obligation to update or revise the information contained in this press release whether as a result of new information, future events or any other reason.