For Immediate Release

UNITED THERAPEUTICS ANNOUNCES FDA APPROVAL AND LAUNCH OF TYVASO® FOR THE TREATMENT OF PULMONARY HYPERTENSION ASSOCIATED WITH INTERSTITIAL LUNG DISEASE

First and only approved therapy in the United States for patients with PH-ILD, a serious, life-threatening disease with potentially more than 30,000 patients in need

FDA approval based on data from the INCREASE clinical trial

PH-ILD is the second FDA-approved indication for Tyvaso, which was initially approved for the treatment of pulmonary arterial hypertension

SILVER SPRING, Md., and RESEARCH TRIANGLE PARK, N.C., April 1, 2021 – United Therapeutics Corporation (Nasdaq: UTHR) today announced that the U.S. Food and Drug Administration (FDA) has approved Tyvaso® (treprostinil) Inhalation Solution for the treatment of patients with pulmonary hypertension associated with interstitial lung disease (PH-ILD; WHO Group 3) to improve exercise ability. This is the second FDA-approved indication for Tyvaso, which was first approved in July 2009 for the treatment of pulmonary arterial hypertension (PAH; WHO Group 1) to improve exercise ability.

"Adults living with both interstitial lung disease and pulmonary hypertension typically have a poor quality of life because of increased shortness of breath, poor exercise tolerance, and increased mortality. Until now, clinicians treating these patients did not have any approved treatment options," 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. "The regulatory approval of Tyvaso, an inhaled treatment, is exciting news both for patients with PH-ILD and the physicians who treat adults living with this serious, life-threatening disease. This will change the way we manage these patients."

Interstitial lung disease (ILD) is a group of lung diseases in which marked scarring occurs within the lungs. It is often complicated by pulmonary hypertension (PH; high blood pressure in the lungs), which further symptoms and decreases survival. PH is estimated to affect at least 15% of patients with early-stage ILD (approximately 30,000 PH-ILD patients in the United States) and may affect up to 86% of patients with more severe ILD.

"The FDA approval of Tyvaso for patients with PH-ILD is a landmark treatment advancement for this vulnerable patient population," said Martine Rothblatt, Ph.D., Chairperson and Chief Executive Officer of United Therapeutics. "It also underscores our commitment to driving innovation in the field of pulmonary hypertension and expanding the number of patients who can achieve a clinical benefit from Tyvaso. We plan to tap into our experience and expanded infrastructure to bring this safe and effective inhaled therapy to the many patients living with PH-ILD in the United States."

"With this approval representing such a breakthrough for PH-ILD patients, we're treating this indication launch with a sense of urgency," said Michael Benkowitz, President and Chief Operating Officer of United Therapeutics. "We've already expanded our field-based teams by 40% to educate the ILD community on the benefits of Tyvaso and how to properly diagnose PH-ILD. We expect rapid uptake of Tyvaso in this indication and expect to double the number of patients on Tyvaso therapy by the end of 2022, barring any COVID-related delays."

The FDA approval of the supplemental New Drug Application (sNDA) for Tyvaso for PH-ILD is supported by data from *INCREASE*, the largest and most comprehensive completed study of adult patients with PH-ILD. The multicenter, randomized, double-blind, placebo-controlled, 16-week, parallel-group study of 326 patients met its primary endpoint, demonstrating a significant improvement in six-minute walk distance (6MWD). Results,

published in the *New England Journal of Medicine*, and discussed at a recent United Therapeutics investor meeting, also showed benefits 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 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. Additional observations included placebo-corrected improvements in forced vital capacity (FVC) and significantly fewer exacerbations of underlying lung disease in patients receiving Tyvaso. 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 and known prostacyclin-related adverse events (see the Important Safety Information below under "About TYVASO® (treprostinil) Inhalation Solution").

About PH-ILD

Interstitial lung disease (ILD) is a group of lung diseases that are characterized by marked scarring or fibrosis of the bronchioles and alveolar sacs within the lungs. Increased fibrotic tissue in ILD prevents oxygenation and free gas exchange between the pulmonary capillaries and alveolar sacs, and the condition can present with a wide range of symptoms, including shortness of breath with activity, labored breathing, and fatigue.

WHO Group 3 Pulmonary hypertension (PH) frequently complicates the course of patients with interstitial lung disease and is associated with worse functional status measured by exercise capacity, greater supplemental oxygen needs, decreased quality of life, and worse outcomes. PH is estimated to affect at least 15% of patients with early-stage ILD (approximately 30,000 PH-ILD patients in the United States) and may affect up to 86% of patients with more severe ILD.

About TYVASO® (treprostinil) Inhalation Solution

INDICATION

TYVASO (treprostinil) is a prostacyclin mimetic indicated for the treatment of:

- Pulmonary arterial hypertension (PAH; WHO Group 1) to improve exercise ability. Studies establishing effectiveness predominately included patients with NYHA Functional Class III symptoms and etiologies of idiopathic or heritable PAH (56%) or PAH associated with connective tissue diseases (33%).

  The effects diminish over the minimum recommended dosing interval of 4 hours; treatment timing can be adjusted for planned activities.

  While there are long-term data on use of treprostinil by other routes of administration, nearly all controlled clinical experience with inhaled treprostinil has been on a background of bosentan (an endothelin receptor antagonist) or sildenafil (a phosphodiesterase type 5 inhibitor). The controlled clinical experience was limited to 12 weeks in duration.

- Pulmonary hypertension associated with interstitial lung disease (PH-ILD; WHO Group 3) to improve exercise ability. The study establishing effectiveness predominately included patients with etiologies of idiopathic interstitial pneumonia (IIP) (45%) inclusive of idiopathic pulmonary fibrosis (IPF), combined pulmonary fibrosis and emphysema (CPFE) (25%), and WHO Group 3 connective tissue disease (22%).

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

- TYVASO is a pulmonary and systemic vasodilator. In patients with low systemic arterial pressure, TYVASO may produce symptomatic hypotension.
- TYVASO inhibits platelet aggregation and increases the risk of bleeding.
- Co-administration of a cytochrome P450 (CYP) 2C8 enzyme inhibitor (e.g., gemfibrozil) may increase exposure (both C_{max} and AUC) to treprostinil. Co-administration of a CYP2C8 enzyme inducer (e.g., rifampin) may decrease exposure to treprostinil. Increased exposure is likely to increase adverse events associated with treprostinil administration, whereas decreased exposure is likely to reduce clinical effectiveness.

DRUG INTERACTIONS/SPECIFIC POPULATIONS

- The concomitant use of TYVASO with diuretics, antihypertensives, or other vasodilators may increase the risk of symptomatic hypotension.
- Human pharmacokinetic studies with an oral formulation of treprostinil (treprostinil diolamine) indicated that co-administration of the cytochrome P450 (CYP) 2C8 enzyme inhibitor, gemfibrozil, increases exposure (both C_{max} and AUC) to treprostinil. Co-administration of the CYP2C8 enzyme inducer, rifampin, decreases exposure to treprostinil. It is unclear if the safety and efficacy of treprostinil by the inhalation route are altered by inhibitors or inducers of CYP2C8.
- Limited case reports of treprostinil use in pregnant women are insufficient to inform a drug-associated risk of adverse developmental outcomes. However, pulmonary arterial hypertension is associated with an increased risk of maternal and fetal mortality. There are no data on the presence of treprostinil in human milk, the effects on the breastfed infant, or the effects on milk production.
- Safety and effectiveness in pediatric patients have not been established.
- Across clinical studies used to establish the effectiveness of TYVASO in patients with PAH and PH-ILD, 268 (47.8%) patients aged 65 years and over were enrolled. The treatment effects and safety profile observed in geriatric patients were similar to younger patients. In general, dose selection for an elderly patient should be cautious, reflecting the greater frequency of hepatic, renal, or cardiac dysfunction, and of concomitant diseases or other drug therapy.

ADVERSE REACTIONS

- Pulmonary Arterial Hypertension (WHO Group 1)
  In a 12-week, placebo-controlled study (TRIUMPH I) of 235 patients with PAH (WHO Group 1 and nearly all NYHA Functional Class III), the most common adverse reactions seen with TYVASO in ≥4% of PAH patients and more than 3% greater than placebo in the placebo-controlled study were cough (54% vs 29%), headache (41% vs 23%), throat irritation/pharyngolaryngeal pain (25% vs 14%), nausea (19% vs 11%), flushing (15% vs <1%), and syncope (6% vs <1%). In addition, adverse reactions occurring in ≥4% of patients were dizziness and diarrhea.

- Pulmonary Hypertension Associated with ILD (WHO Group 3)
  In a 16-week, placebo-controlled study (INCREASE) of 326 patients with PH-ILD (WHO Group 3), adverse reactions were similar to the experience in studies of PAH.

Please see Full Prescribing Information, the TD-100 and TD-300 TYVASO® Inhalation System Instructions for Use manuals, and other additional information at www.tyvaso.com or call 1-877-UNITHER (1-877-864-8437).

United Therapeutics: Enabling Inspiration
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.

Please visit unither.com to learn more.

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 relating to the potential for the approval of Tyvaso in PH-ILD to change the way PH-ILD patients are treated, our expectation of a rapid uptake of Tyvaso in PH-ILD patients, and our expectation that we will double the number of patients on Tyvaso therapy by the end of 2022, our ability to create value and sustain our success in the long-term, as well as our efforts to develop technologies that either delay the need for transplantable organs or expand the supply of transplantable organs. These forward-looking statements are subject to certain risks and uncertainties, such as those described in our periodic reports filed with the Securities and Exchange Commission, that could cause actual results to differ materially from anticipated results. Consequently, such forward-looking statements 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 April 1, 2021, 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.

TYVASO is a registered trademark of United Therapeutics Corporation.

For Further Information Contact:
Dewey Steadman at (202) 919-4097
Email: ir@unither.com

# # #