For Immediate Release

UNITED THERAPEUTICS HIGHLIGHTS POSTER PRESENTATIONS FROM THE RECENT CHEST 2020 MEETING

Clinical study data suggests Tyvaso® improved forced vital capacity, an important measure of lung function, in patients with pulmonary hypertension associated with interstitial lung disease

Seven poster presentations are available at ir.unither.com

SILVER SPRING, Md. and RESEARCH TRIANGLE PARK, N.C., Oct. 22, 2020 -- United Therapeutics Corporation (Nasdaq: UTHR) today announced new clinical data on Tyvaso® (treprostinil) Inhalation Solution in patients with pulmonary hypertension associated with interstitial lung disease (PH-ILD) at CHEST 2020, the annual meeting of the American College of Chest Physicians, held October 18-21. The presentation featured safety data from the phase 3 *INCREASE* study of Tyvaso, which showed that patients with PH-ILD receiving Tyvaso, compared to those receiving placebo, experienced fewer exacerbations of underlying lung disease and an improvement in forced vital capacity (FVC). The data were featured in one of seven abstracts sponsored by United Therapeutics at the conference.

Interstitial lung disease (ILD) is a group of lung diseases in which significant scarring occurs within the lungs. It is often complicated by pulmonary hypertension (PH; high blood pressure in the lungs). PH-ILD is estimated to affect 30,000 people in the United States. Currently, no drug therapy is approved by the U.S. Food and Drug Administration (FDA) to treat this serious and potentially life-threatening disease.

"Patients with both interstitial lung disease and pulmonary hypertension face severe difficulty breathing which often requires supplemental oxygen and substantially compromises patients' quality of life," said Gil Golden, M.D., Ph.D., Chief Medical Officer of United Therapeutics. "Yet, no therapies are currently approved to treat the condition."

"We are encouraged by the favorable impact on lung function in PH-ILD patients receiving Tyvaso versus placebo in the *INCREASE* study, as well as preclinical evidence demonstrating the antifibrotic activity of treprostinil," said Leigh Peterson, Ph.D., Vice President of Product Development at United Therapeutics. "These findings are the basis of additional studies we are planning to assess Tyvaso in treating various forms of interstitial lung disease. We look forward to launching our phase 3 *TETON* clinical program next year; the first study in this program will enroll subjects with idiopathic pulmonary fibrosis."

The research, *The Impact of Inhaled Treprostinil on Patient Lung Function: Results from the* INCREASE *Study,* was presented by 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, and provides further detail regarding Tyvaso's effects on FVC during the course of the study. The phase 3, multicenter, randomized, double-blind, placebo-controlled, 16-week, parallel group *INCREASE* study evaluated Tyvaso in adult patients suffering from World Health Organization (WHO) Group 3 PH-ILD. A total of 326 patients were enrolled at 93 centers and randomized to inhaled Tyvaso (n=163) four times daily or placebo (n=163). United Therapeutics previously announced top-line data from *INCREASE* showing it met all primary and secondary endpoints and the submission of a supplemental NDA which is currently under review by the FDA.

To evaluate lung function, pulmonary function testing (PFT) was conducted as a safety assessment at Study Weeks 8 and 16. Exacerbation of underlying lung disease, defined as an acute, clinically significant, respiratory deterioration accompanied by evidence of new widespread alveolar abnormality, was assessed over the course of the study and by each Principal Investigator.

Patients receiving Tyvaso, compared to those receiving placebo, experienced significantly fewer exacerbations of underlying lung disease (43 [26.4%] versus 63 [38.7%]; p=0.02 by Fisher's exact test). Other results include:

- Overall, FVC improved with Tyvaso by 28.47 mL and 44.40 mL at Weeks 8 and 16, respectively, when compared to placebo
- Percent predicted FVC also improved at Weeks 8 (1.79%; p=0.0139) and 16 (1.80%; p=0.0277)
- Subgroup analysis of patients with etiology of idiopathic interstitial pneumonia (IIP) demonstrated FVC improvements of 46.48 mL and 108.18 mL (N=146, p=0.0229) at Weeks 8 and 16, respectively, and improvements in % predicted FVC at Weeks 8 (1.95%, p=0.0373) and 16 (2.88%; p=0.0096) compared to placebo
- Further analysis for patients with etiology of idiopathic pulmonary fibrosis (IPF) demonstrated FVC improvements of 84.52 mL and 168.52 mL (N=92, p=0.0108) at Weeks 8 and 16, respectively, and improvements in % predicted FVC at Weeks 8 (2.54%; p=0.0380) and 16 (3.50%; p=0.0147) compared to placebo

Treatment with Tyvaso of up to 12 breaths per session, four times daily, was well tolerated. Most treatment-related adverse events were mild to moderate in intensity and included cough, headache, dyspnea, dizziness, nausea, fatigue, and diarrhea, many of which are consistent with the existing Tyvaso label. The safety profile was consistent with previous studies of Tyvaso in pulmonary arterial hypertension and known prostacyclin-related adverse events (see the Important Safety Information below under "About Tyvaso").

The poster, entitled "The Impact of Inhaled Treprostinil on Patient Lung Function: Results from the *INCREASE* Study," is available here.

Other posters presented at CHEST 2020 included:

Title: Low Utilization of Prostacyclin Therapy Prior to Death Among Medicare Patients with Pulmonary Arterial Hypertension
Lead Author: Stephen Mathai
Available: here

Title: Interim Data from the *ADAPT* Registry: Patient-Reported Real-World Tolerability and Management of Adverse Events with Oral Treprostinil
Lead Author: John Kingrey
Available: here

Title: Reasons for Refusing Parenteral Therapy: A Qualitative Study of Patients with Pulmonary Arterial Hypertension
Lead Author: Kellie Morland
Available: here

Title: Contemporary Dosing Characteristics of Oral Treprostinil in Real-world Clinical Practice in Patients with Pulmonary Arterial Hypertension
Lead Author: Karim El-Kersh
Available: here

Title: Development of the Pulmonary Hypertension Functional Classification Self-Report (PH-FC-SR)
Lead Author: Kristin Highland
Available: here

Title: Understanding the Psychological Mindset of People with Pulmonary Arterial Hypertension
Lead Author: Lillian Hansen

Available: here

About PH-ILD

Interstitial lung disease (ILD) is a group of lung diseases that are characterized by significant 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. 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.

An estimated 30,000 patients in the United States may suffer from PH-ILD, which is included within Group 3 of the World Health Organization (WHO) classification of PH. However, no treatments are approved by the FDA for patients with this disease.

About TYVASO® (treprostinil) Inhalation Solution

INDICATION

TYVASO (treprostinil) is a prostacyclin vasodilator indicated for the treatment of pulmonary arterial hypertension (PAH; WHO Group 1) to improve exercise ability. Studies establishing effectiveness included predominately 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.

IMPORTANT SAFETY INFORMATION FOR TYVASO

WARNINGS AND PRECAUTIONS

- The efficacy of TYVASO has not been established in patients with significant underlying lung disease (such as asthma or chronic obstructive pulmonary disease). Patients with acute pulmonary infections should be carefully monitored to detect any worsening of lung disease and loss of drug effect
- TYVASO is a pulmonary and systemic vasodilator. In patients with low systemic arterial pressure, TYVASO may cause symptomatic hypotension
- Titrate slowly in patients with hepatic or renal insufficiency, as exposure to treprostinil may be increased in these patients
- TYVASO inhibits platelet aggregation and increases the risk of bleeding
- Co-administration of the cytochrome P450 (CYP) 2C8 enzyme inhibitor gemfibrozil may increase exposure to treprostinil. Co-administration of the CYP2C8 enzyme inducer rifampin may decrease exposure to treprostinil. Increased exposure is likely to increase adverse events, 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
- Co-administration of the CYP2C8 enzyme inhibitor gemfibrozil increases exposure to oral treprostinil. Co-administration of the CYP2C8 enzyme inducer rifampin decreases exposure to oral 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
- It is unknown if geriatric patients respond differently than younger patients. Caution should be used when selecting a dose for geriatric patients

ADVERSE REACTIONS
- The most common adverse reactions seen with TYVASO in ≥4% of PAH patients and more than 3% greater than placebo in the placebo-controlled clinical 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 ≥10% of patients were dizziness and diarrhea

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

For Consumer Important Safety Information, please see https://www.tyvaso.com/dtc/isi

About Orenitram® (treprostinil) Extended-Release Tablets

INDICATION

Orenitram is a prostacyclin mimetic indicated for treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to delay disease progression and to improve exercise capacity. The studies that established effectiveness included predominately patients with WHO functional class II-III symptoms and etiologies of idiopathic or heritable PAH (66%) or PAH associated with connective tissue disease (26%).

IMPORTANT SAFETY INFORMATION FOR ORENITRAM

CONTRAINDICATIONS

- Avoid use of Orenitram in patients with severe hepatic impairment (Child Pugh Class C) due to increases in systemic exposure.

WARNINGS AND PRECAUTIONS

- Abrupt discontinuation or sudden large reductions in dosage of Orenitram may result in worsening of PAH symptoms.
- The Orenitram tablet shell does not dissolve. In patients with diverticulosis, Orenitram tablets can lodge in a diverticulum.

ADVERSE REACTIONS

- In the 12-week, placebo-controlled, monotherapy study, and an event-driven, placebo-controlled, combination therapy study, adverse reactions that occurred at rates at least 5% higher on Orenitram

than on placebo included headache, diarrhea, nausea, vomiting, flushing, pain in jaw, pain in extremity, hypokalemia, abdominal discomfort, and upper abdominal pain.

DRUG INTERACTIONS

- Co-administration of Orenitram and the CYP2C8 enzyme inhibitor gemfibrozil increases exposure to treprostinil; therefore, Orenitram dosage reduction may be necessary in these patients.

SPECIFIC POPULATIONS

- Animal reproductive studies with Orenitram have shown an adverse effect on the fetus. There are no adequate and well-controlled studies with Orenitram in pregnant women.
- It is not known whether treprostinil is excreted in human milk or if it affects the breastfed infant or milk production.
- Safety and effectiveness of Orenitram in pediatric patients have not been established.
- Use of Orenitram in patients aged 65 years and over demonstrated slightly higher absolute and relative adverse event rates compared to younger patients. Caution should be used when selecting a dose for geriatric patients.
- There is a marked increase in the systemic exposure to treprostinil in hepatically impaired patients.

Please see Full Prescribing Information and Patient Information at www.orenitram.com or call 1-877-UNITHER (1-877-864-8437).

For Consumer Important Safety Information, please see https://www.orenitram.com/#isi

About Remodulin® (treprostinil) Injection

INDICATION

Remodulin is a prostacyclin vasodilator indicated for the treatment of pulmonary arterial hypertension (PAH; WHO Group 1) to diminish symptoms associated with exercise. Studies establishing effectiveness included patients with NYHA Functional Class II-IV symptoms and etiologies of idiopathic or heritable PAH (58%), PAH associated with congenital systemic-to-pulmonary shunts (23%), or PAH associated with connective tissue diseases (19%).

In patients with PAH requiring transition from epoprostenol, Remodulin is indicated to diminish the rate of clinical deterioration. Consider the risks and benefits of each drug prior to transition.

IMPORTANT SAFETY INFORMATION FOR REMODULIN

WARNINGS AND PRECAUTIONS

- Chronic intravenous (IV) infusions of Remodulin delivered using an external infusion pump with an indwelling central venous catheter are associated with the risk of blood stream infections (BSIs) and sepsis, which may be fatal. Therefore, continuous subcutaneous (SC) infusion is the preferred mode of administration.
- Avoid abrupt withdrawal or sudden large reductions in dosage of Remodulin, which may result in worsening of PAH symptoms.
- Titrate slowly in patients with hepatic or renal insufficiency, because such patients will likely be exposed to greater systemic concentrations relative to patients with normal hepatic or renal function.

- Remodulin is a pulmonary and systemic vasodilator. In patients with low systemic arterial pressure, treatment with Remodulin may produce symptomatic hypotension.
- Remodulin inhibits platelet aggregation and increases the risk of bleeding.

ADVERSE REACTIONS

- In clinical studies of SC Remodulin infusion, the most common adverse events reported were infusion site pain and infusion site reaction (redness, swelling, and rash). These symptoms were sometimes severe and sometimes required treatment with narcotics or discontinuation of Remodulin. The IV infusion of Remodulin with an external infusion pump has been associated with a risk of blood stream infections, arm swelling, paresthesias, hematoma, and pain. Other common adverse events (≥3% more than placebo) seen with either SC or IV Remodulin were headache (27% vs. 23%), diarrhea (25% vs. 16%), nausea (22% vs. 18%), rash (14% vs. 11%), jaw pain (13% vs. 5%), vasodilatation (11% vs. 5%), edema (9% vs. 3%), and hypotension (4% vs. 2%).

DRUG INTERACTIONS

- Remodulin dosage adjustment may be necessary if inhibitors or inducers of CYP2C8 are added or withdrawn.

SPECIFIC POPULATIONS

- In patients with mild or moderate hepatic insufficiency, decrease the initial dose of Remodulin to 0.625 ng/kg/min of ideal body weight, and monitor closely. Remodulin has not been studied in patients with severe hepatic insufficiency.
- Safety and effectiveness of Remodulin in pediatric patients have not been established.
- It is unknown if geriatric patients respond differently than younger patients. Caution should be used when selecting a dose for geriatric patients.
- There are no adequate and well-controlled studies with Remodulin in pregnant women. It is not known whether treprostinil is excreted in human milk or if it affects the breastfed infant or milk production.

Please see accompanying Full Prescribing Information for Remodulin.
For additional information, visit www.remodulin.com or call Customer Service at 1-877-UNITHER (1-877-864-8437).

For Consumer Important Safety Information, please see https://www.remodulin.com/#isi

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 relating to our upcoming TETON research program, 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 October 22, 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.

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