



## **UNITED THERAPEUTICS RECEIVES FDA ORPHAN DRUG DESIGNATION FOR TREPROSTINIL FOR THE TREATMENT OF IDIOPATHIC PULMONARY FIBROSIS**

*Phase 3 TETON study planned in 2021 for Tyvaso® in patients with idiopathic pulmonary fibrosis*

SILVER SPRING, Md. and RESEARCH TRIANGLE PARK, N.C., Wednesday, December 9, 2020: United Therapeutics Corporation (Nasdaq: UTHR) announced today that the United States Food and Drug Administration (FDA) has granted orphan drug designation to treprostinil for the treatment of patients with idiopathic pulmonary fibrosis (IPF). United Therapeutics intends to initiate a phase 3 study, called *TETON*, to evaluate the use of Tyvaso® (treprostinil) Inhalation Solution in patients with IPF. FDA recently cleared United Therapeutics' investigational new drug application (IND) for the *TETON* study, and the company expects to commence enrollment in 2021. Orphan drug designation is the first step in receiving orphan drug exclusivity following approval, which confers seven years of market exclusivity for the relevant indication. This exclusivity would also benefit Treprostinil Technosphere®, United Therapeutics' next-generation dry powder inhalation form of treprostinil, upon FDA approval of that product for the IPF indication.

"We're excited that treprostinil has received orphan drug designation, as it validates our drive to address orphan diseases, like IPF, with a significant unmet need," said Martine Rothblatt, Ph.D., Chairman and Chief Executive Officer of United Therapeutics. "*TETON* represents a significant move outside the pulmonary hypertension space, but based on data collected during the recent *INCREASE* study we're confident that inhaled treprostinil can help address clinical gaps presented by existing therapies in IPF."

Orphan drug designation is granted by the FDA Office of Orphan Products Development (OOPD) to advance the evaluation and development of safe and effective therapies for the treatment of rare diseases or conditions affecting fewer than 200,000 people in the U.S. Under the Orphan Drug Act, FDA may provide grant funding toward clinical trial costs, tax advantages, FDA user-fee benefits, and seven years of market exclusivity in the United States following marketing approval by FDA. The granting of an orphan drug designation request does not alter the standard regulatory requirements and process for obtaining marketing approval. For more information about orphan drug designation, please visit the OOPD [website](#).

### **About IPF**

Idiopathic pulmonary fibrosis, or IPF, is a serious, chronic, progressive, fibrosing interstitial pneumonia with no known cause; typically occurring in patients above 50 years of age. It is characterized by progressive fibrosis, lung scarring, and a radiological pattern known as usual interstitial pneumonia, or UIP. IPF is associated with increasing cough and dyspnea, greatly impacting patient quality of life and eventually leading to death from respiratory failure or complicating comorbidities. Diagnosis is based on the exclusion of other interstitial lung diseases and similar conditions, and the identification of the UIP pattern on a high-resolution computed tomography scan and/or surgical lung biopsy.

Currently, there is no cure for IPF and only two drugs are approved in the United States to treat the condition. According to the U.S. National Library of Medicine at the National Institutes of Health, about 100,000 people are affected in the United States, and 30,000 to 40,000 new cases are diagnosed each year.

### **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  $\geq 4\%$  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  $\geq 10\%$  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](http://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 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 TETON clinical development efforts, our Treprostinil Technosphere development program, our ability to obtain FDA approval to market treprostinil for IPF, and our expectations concerning regulatory exclusivities, 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 December 9, 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.

TYVASO is a registered trademark of United Therapeutics Corporation.  
TECHNOSPHERE is a registered trademark of MannKind Corporation.

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