For Immediate Release

UNITED THERAPEUTICS PROVIDES AN UPDATE ON THE PROGRESS OF THE TYVASO DPI™ NEW DRUG APPLICATION

Draft label contains both PAH and PH-ILD indications; no contraindications and no boxed warning

Complete response cites an open inspection issue at a third-party analytical testing facility; no other deficiencies cited

Approval and launch expected in summer 2022 or earlier

SILVER SPRING, Md., and RESEARCH TRIANGLE PARK, N.C., October 18, 2021 – United Therapeutics Corporation (Nasdaq: UTHR) today announced an update on the U.S. Food and Drug Administration (**FDA**) review of the new drug application (**NDA**) for Tyvaso DPI™, for the treatment of pulmonary arterial hypertension (**PAH**) and pulmonary hypertension associated with interstitial lung disease (**PH-ILD**), to improve exercise capacity. On Friday, October 15, 2021, the FDA issued a complete response declining to approve the NDA at this time. The FDA's letter noted only a single deficiency preventing approval of Tyvaso DPI, related to an open inspection issue at a third-party facility that performs analytical testing of treprostinil drug substance.

In addition, the FDA did not cite any deficiencies or issues related to operations performed at the MannKind Corporation facility for manufacture, testing, and packaging of finished Tyvaso DPI, including its associated device. All other requests from the agency have been addressed.

The draft labeling for Tyvaso DPI, as revised by FDA, includes the same indications as Tyvaso® (treprostinil) Inhalation Solution for PAH and PH-ILD, to improve exercise ability, and does not contain any contraindications or a boxed warning.

"We are very pleased with the FDA's feedback on the label, which will ultimately enable us to bring Tyvaso DPI to thousands of patients in need," said Martine Rothblatt, Ph.D., Chairperson and Chief Executive Officer of United Therapeutics. "We are confident that the single deficiency identified in the complete response will be resolved quickly and that Tyvaso DPI can receive approval by the summer of 2022, if not earlier."

"Tyvaso DPI will be a groundbreaking advancement for PAH and PH-ILD patients, and we look forward to launching this product no later than the summer of 2022," said Michael Benkowitz, President and Chief Operating Officer of United Therapeutics. "We reaffirm the achievability of our near-term goal of doubling the number of patients on Tyvaso by the end of 2022, and our longer-term goal of having 25,000 patients on our products by the end of 2025."

The complete response also notes, but does not cite as a deficiency, that the FDA has not yet completed its review of a Citizen's Petition submitted to FDA in July 2021 concerning the safety of an excipient in Tyvaso DPI.

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.

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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

We build on the strength of our research and development expertise and a distinctive, entrepreneurial culture that encourages diversity, innovation, creativity, sustainability, and, simply, fun. Since inception, our mission has been to find a cure for pulmonary arterial hypertension and other life-threatening diseases. Toward this goal we have successfully gained FDA approval for five medicines, we are always conducting new clinical trials, and we are working to create an unlimited supply of manufactured organs for transplantation.

We are the first publicly-traded biotech or pharmaceutical company to take the form of a public benefit corporation (PBC). Our public benefit purpose is *to provide a brighter future for patients through (a) the development of novel pharmaceutical therapies; and (b) technologies that expand the availability of transplantable organs*. At the same time, we seek to provide our shareholders with superior financial performance and our communities with earth-sensitive energy utilization.

You can learn more about what it means to be a PBC here: unither.com/PBC.

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 plans to resolve the issues raised by FDA in the Tyvaso DPI complete response, the timing of our planned resubmission of the Tyvaso DPI NDA and FDA approval thereof, the anticipated benefits of Tyvaso DPI, our expectation that we will double the number of patients on Tyvaso therapy by the end of 2022, and our goals of furthering our public benefit purpose, providing superior financial performance for shareholders, and providing our communities with earth-sensitive energy utilization. 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 18, 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.

TYVASO DPI is a trademark of United Therapeutics Corporation.

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

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