United Therapeutics Corporation Announces FDA Acceptance of Supplemental New Drug Application for Nebulized Tyvaso® to Treat Idiopathic Pulmonary Fibrosis

*Nebulized Tyvaso® (treprostinil) Inhalation Solution will be the first and only inhaled anti-fibrotic treatment for idiopathic pulmonary fibrosis (**IPF**) if approved by the U.S. Food and Drug Administration* (**FDA**)

SILVER SPRING, Md. & RESEARCH TRIANGLE PARK, N.C – September 2, 2026 – United Therapeutics Corporation (Nasdaq: **UTHR**), a public benefit corporation, today announced that the FDA has accepted the supplemental New Drug Application (**sNDA**) for nebulized Tyvaso® (treprostinil) Inhalation Solution to treat IPF. United Therapeutics anticipates the agency's review to be complete in late April 2027. Nebulized Tyvaso has not been approved by the FDA for IPF and remains investigational for this indication.

"Nebulized Tyvaso combines direct lung delivery with multimodal activity across fibrotic, vascular, and inflammatory pathways that are central to IPF, with the potential to help address a significant unmet need for this life-threatening disease," said **Martine Rothblatt, Ph.D.**, Chairperson and Chief Executive Officer of United Therapeutics. "We're galvanized by the FDA's acceptance of the nebulized Tyvaso sNDA for review and believe the strength and rigor of our *TETON* clinical program support an approvable application for this differentiated multi-pathway treatment for patients managing this life-threatening disease."

The filing was based on positive results from the phase 3 *TETON-1* and *TETON-2* studies. Combined analyses of *TETON-1* and *TETON-2* met the primary efficacy endpoint, with nebulized Tyvaso demonstrating statistically significant superiority over placebo for the change in absolute forced vital capacity (**FVC**) by 111.8 mL (Hodges-Lehmann estimate, 95% confidence interval, 79.7 to 144.0 mL; $p<0.0001$) from baseline to week 52 in an IPF population broadly treated with background therapy.

The combined analyses also showed that nebulized Tyvaso achieved statistical significance for most key secondary endpoints, including reduced risk of a clinical worsening event, reduced risk of acute IPF exacerbation, and changes in percent of predicted FVC, King's Brief Interstitial Lung Disease quality of life questionnaire (**K-BILD**), and diffusion capacity of lungs for carbon monoxide (**DLCO**).

TETON-1 data were presented as part of the Breaking News: 2026 Clinical Trial Results in Pulmonary Medicine session at the 2026 annual meeting of the American Thoracic Society (**ATS**). *TETON-2* data were published in *The New England Journal of Medicine*. Combined results from *TETON-1* and *TETON-2* were presented during an oral session at ATS and simultaneously published in *The New England Journal of Medicine*.

Both the FDA and the European Medicines Agency have granted orphan designation for treprostinil to treat IPF.

TETON Clinical Program

A post-hoc analysis of the *INCREASE* study in patients with pulmonary hypertension associated with interstitial lung disease (**PH-ILD**) suggested that nebulized Tyvaso was associated with a significant improvement in FVC, laying the foundation for the *TETON* clinical program to evaluate the use of nebulized Tyvaso in IPF and progressive pulmonary fibrosis (**PPF**).

The *TETON-1* (NCT04708782) and *TETON-2* (NCT05255991) studies were multicenter, randomized, double-blind, placebo-controlled phase 3 registration studies evaluating the safety and efficacy of nebulized Tyvaso in patients with IPF over a 52-week period. *TETON-1* enrolled patients with IPF in the United States and Canada, and *TETON-2* enrolled patients with IPF outside the United States and Canada. The primary endpoints of the studies were the change in absolute FVC from baseline to week 52. Secondary endpoints included: (1) time to clinical worsening; (2) time to first

acute exacerbation of IPF; (3) overall survival at week 52; (4) change in percent predicted FVC from baseline to week 52; (5) change in the K-BILD questionnaire from baseline to week 52; and (6) change in DLCO from baseline to week 52. Safety assessments included the development of adverse events, serious adverse events, vital signs, clinical laboratory parameters, and electrocardiogram parameters.

Eligible patients completing the *TETON-1* and *TETON-2* studies could enroll in the *TETON-OLE* study (NCT04905693), an ongoing open-label extension study to evaluate the long-term safety and tolerability of nebulized Tyvaso in patients with fibrotic lung disease.

TETON-PPF is evaluating the use of nebulized Tyvaso in PPF in patients globally, and enrollment is complete. Nebulized Tyvaso has not been approved by the FDA for IPF or PPF and remains investigational for these indications.

About IPF

Idiopathic pulmonary fibrosis, or IPF, is a scarring disease of the lungs of an unknown (idiopathic) cause and is the most common of the idiopathic interstitial pneumonias. IPF is characterized by the progressive loss of the ability of the lungs to transfer oxygen into the blood, ultimately resulting in respiratory failure and death. While the precise causes of IPF remain unknown, IPF rarely presents before age 50 and can be associated with cigarette smoking and certain genetic dispositions. In addition, some evidence suggests that gastroesophageal reflux (acid reflux, or heartburn), certain viral infections, air pollution, and workplace exposures may be risk factors for IPF. IPF is estimated to affect between 2.4 and 2.98 people per 10,000 persons in North America. Further, United Therapeutics estimates there are at least 100,000 people living with IPF in the United States.

About Tyvaso® (treprostinil) Inhalation Solution

INDICATION

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

- Pulmonary arterial hypertension (PAH; WHO Group 1) to improve exercise ability. Studies with TYVASO 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 clinical experience with inhaled treprostinil has been on a background of an endothelin receptor antagonist (ERA) and/or a phosphodiesterase type 5 (PDE-5) inhibitor. The controlled clinical experience with TYVASO 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 with TYVASO 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 Cmax 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.

Like other inhaled prostaglandins, TYVASO may cause acute bronchospasm. Patients with asthma or chronic obstructive pulmonary disease (COPD), or other bronchial hyperreactivity, are at increased risk for bronchospasm. Ensure that such patients are treated optimally for reactive airway disease prior to and during treatment with TYVASO.

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 Cmax 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 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 with TYVASO were similar to the experience in studies of PAH.
Please see Full Prescribing Information for TYVASO, the TD-300 TYVASO® Inhalation System Instructions for Use manual, and additional information at www.TYVASOHCP.com or call 1 844 UNITHER (1-844-864-8437).

About United Therapeutics

Founded by CEO Martine Rothblatt to discover a cure for her daughter's life-threatening rare disease, pulmonary arterial hypertension, United Therapeutics transforms the treatment of rare diseases and pioneers alternatives to expand the supply of transplantable organs. From our innovative therapies to our groundbreaking manufactured organs, we are bold and unconventional. We move quickly from scientific theory to practical technologies that can save lives. As a public benefit corporation, even our legal structure reflects our commitments. We serve patients, act with integrity, create long-term shareholder value, and operate with sustainable practices that protect the future we are working to build. Visit us at www.unither.com and follow us on LinkedIn, Facebook, and Instagram.

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 potential timing and outcome the FDA's review of our sNDA to add IPF to the labeled indications for nebulized Tyvaso; the potential for nebulized Tyvaso to become a treatment option for IPF patients; our *TETON-PPF* study of nebulized Tyvaso in PPF patients; and our goals of expanding the supply of transplantable organs, developing practical technologies that can save lives, creating long-term shareholder value, and operating with sustainable practices. 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 September 2, 2026, 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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