



## **United Therapeutics Corporation Announces *TETON-1* Pivotal Study of Tyvaso® Meets Primary Endpoint for Treatment of Idiopathic Pulmonary Fibrosis, Exceeding Impressive Treatment Effect Seen in *TETON-2***

*Nebulized Tyvaso® (treprostinil) Inhalation Solution demonstrated superiority over placebo for the change in absolute forced vital capacity by 130.1 mL and reduced the risk of clinical worsening in patients with idiopathic pulmonary fibrosis, with positive results observed across all subgroups*

*Integrated analyses of *TETON-1* and *TETON-2* showed statistically significant treatment effects across the primary and most secondary efficacy endpoints, reinforcing the robustness of the clinically meaningful results observed in each of the individual studies*

*Nebulized Tyvaso combines direct lung delivery with multimodal activity across fibrotic, vascular, and inflammatory pathways that are not currently addressed by existing IPF therapies*

*United Therapeutics plans to seek priority review of a supplemental New Drug Application to be submitted to the FDA by the end of this summer*

**SILVER SPRING, Md. and RESEARCH TRIANGLE PARK, N.C., March 30, 2026** – United Therapeutics Corporation (Nasdaq: **UTHR**), a public benefit corporation, today announced that its *TETON-1* study evaluating the use of nebulized Tyvaso for the treatment of idiopathic pulmonary fibrosis (**IPF**) met its primary efficacy endpoint, demonstrating superiority over placebo for the change in absolute forced vital capacity (**FVC**) by 130.1 mL (Hodges-Lehmann [**H-L**] estimate, 95% confidence interval [**CI**], 82.2 to 178.1 mL;  $p < 0.0001$ ) from baseline to week 52.

Nebulized Tyvaso achieved statistical significance for reducing the risk of clinical worsening and showed numerical improvement in other important secondary endpoints relative to placebo, including time to first acute exacerbation of IPF and changes in percent predicted FVC, King's Brief Interstitial Lung Disease quality of life questionnaire (**K-BILD**) score, and diffusion capacity of lungs for carbon monoxide (**DLCO**).

Benefits of nebulized Tyvaso were observed across all subgroups, such as use of background therapy (nintedanib, pirfenidone, or no background therapy), smoking status, and supplemental oxygen use. Treatment with nebulized Tyvaso was well-tolerated, and the safety profile was consistent with previous Tyvaso studies and known prostacyclin-related adverse events. No new safety signals were observed.

Integrated analyses of *TETON-1* and *TETON-2* showed statistically significant treatment effects compared to placebo from baseline to week 52 for the primary endpoint of change in absolute FVC by 111.8 mL (H-L estimate, 95% CI, 79.7 to 144.0;  $p < 0.0001$ ) and most secondary endpoints, including time to first clinical worsening and first acute exacerbation of IPF and changes in percent predicted FVC, K-BILD score, and DLCO. Overall survival at week 52 trended in favor of Tyvaso but did not meet statistical significance.

"The unprecedented results of *TETON-1*, which surpassed even the overwhelmingly positive results of *TETON-2*, represent a profound step forward for people living with IPF, a devastating disease with few treatment options. We remain sincerely grateful to the patients, caregivers, and investigators who made this trial possible," said **Martine Rothblatt, Ph.D.**, Chairperson and Chief Executive Officer of United Therapeutics. "In the past seven months, our three pivotal studies, *TETON-1*, *TETON-2*, and the *ADVANCE OUTCOMES* study of ralinepag, met their primary endpoints with  $p$ -values  $< 0.0001$ , an inflection point heralding a new era of even greater growth for United Therapeutics. These consecutive accomplishments were produced by our culture of innovation and our commitment to multiple shots on goal to advance treatments for rare cardiopulmonary and respiratory diseases."



"IPF is a progressive, life-limiting disease for which existing treatments provide only modest benefit and are often accompanied by significant side effects. *TETON-1* reinforces what was shown in *TETON-2*, with both studies demonstrating clinically meaningful treatment outcomes in IPF patients with or without background anti-fibrotic therapy. Together, both studies demonstrated not only better preservation of lung function, but also preservation of quality of life, as well as reduced disease worsening and reduced acute IPF exacerbations. These findings have the potential to fundamentally shift our approach to IPF management and could be a game changer," said **Steven D. Nathan, M.D.**, Schar Chair, Advanced Lung Disease and Lung Transplant Program at Inova Fairfax Hospital and Chair of the *TETON* Steering Committee.

"The *TETON* program has achieved statistical significance in endpoints that have never been attained in other IPF clinical trials. These results provide a compelling body of evidence for nebulized Tyvaso's differentiated direct lung delivery combined with multimodal activity across fibrotic, vascular, and inflammatory pathways that are not currently addressed by existing therapies," said **Peter Smith, Pharm.D.**, Senior Vice President, Product Development at United Therapeutics and the lead for the global *TETON* program.

United Therapeutics plans to seek priority review of a supplemental New Drug Application, to be submitted to the U.S. Food and Drug Administration (**FDA**) by the end of this summer, to add IPF to the labeled indications for nebulized Tyvaso based on data from the *TETON-1* and *TETON-2* studies. Both the FDA and the European Medicines Agency have granted orphan designation for treprostinil to treat IPF.

Additional *TETON-1* study results and data from the integrated analyses of *TETON-1* and *TETON-2* will be presented at the American Thoracic Society Annual Meeting in Orlando in May 2026. Full results of the *TETON-2* study were recently published in the *New England Journal of Medicine* and are available online at [NEJM.org](https://www.nejm.org).

### ***TETON* Clinical Program**

A post-hoc analysis of the *INCREASE* study in patients with pulmonary hypertension associated with interstitial lung disease 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**). *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. *TETON-PPF* is evaluating the use of nebulized Tyvaso in PPF in patients globally, and enrollment is ongoing.

### ***TETON-1* Study Design**

The *TETON-1* study ([NCT04708782](https://www.clinicaltrials.gov/ct2/show/study/NCT04708782)) was a 598-patient, multicenter, randomized, double-blind, placebo-controlled phase 3 registration study evaluating the safety and efficacy of nebulized Tyvaso in patients with IPF over a 52-week period at sites in the United States and Canada. The study reached full enrollment in January 2025.

The primary endpoint of the study was 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* study could enroll in the *TETON-OLE* study ([NCT04905693](https://www.clinicaltrials.gov/ct2/show/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.

## **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 0.33 and 4.51 people per 10,000 persons worldwide. Further, United Therapeutics estimates there are over 100,000 IPF patients 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  $C_{max}$  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.



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  $C_{max}$  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  $\geq 4\%$  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  $\geq 4\%$  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](http://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](http://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 timing and outcome of our planned regulatory submission to the FDA to seek approval to add IPF to the labeled indications for nebulized Tyvaso, including our plan to seek priority review; our expectations concerning the potential benefits of nebulized Tyvaso for IPF patients, including the possibility that the results of the *TETON-1* and *TETON-2* studies could fundamentally shift the approach to IPF management; our belief that the results of the *TETON-1*, *TETON-2*, and *ADVANCE OUTCOMES* studies will lead to a new era of growth for United Therapeutics; statements regarding our ongoing *TETON-PPF* study of nebulized Tyvaso in patients with PPF; 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 March 30, 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.

TYVASO is a registered trademark of United Therapeutics Corporation.

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