United Therapeutics Corporation Announces Full Results of *TETON-2* Phase 3 Clinical Trial Published in *The New England Journal of Medicine*

*The pivotal study of Tyvaso® (treprostinil) Inhalation Solution demonstrated a statistically significant preservation of lung function across all subgroups, as measured by absolute forced vital capacity (**FVC**), and fewer clinical worsening events, compared with placebo over 52 weeks in patients with idiopathic pulmonary fibrosis (**IPF**)*

Study authors noted TETON-2 is the first study to show that an inhaled therapy slowed progression of fibrosis as assessed by FVC change in patients with IPF

The trial population reflected the characteristics of a general population of IPF patients, with 75% on background antifibrotic therapy, demonstrating nebulized Tyvaso's differentiated anti-fibrotic properties

If approved, nebulized Tyvaso will be the first and only inhaled anti-fibrotic treatment for IPF

SILVER SPRING, Md. and RESEARCH TRIANGLE PARK, N.C., March 11, 2026 – United Therapeutics Corporation (Nasdaq: **UTHR**), a public benefit corporation, today announced that the *New England Journal of Medicine* has published full results of its phase 3 *TETON-2* study evaluating the use of nebulized Tyvaso for the treatment of IPF. The publication is available online at NEJM.org.

The study met its primary efficacy endpoint, with nebulized Tyvaso demonstrating statistically significant improvement in absolute FVC relative to placebo from baseline to week 52 in an IPF population broadly treated with background therapy. The median change in FVC at week 52 was −49.9 mL (95% confidence interval [**CI**], −79.2 to −19.5) in the nebulized Tyvaso group and −136.4 mL (95% CI, −172.5 to −104.0) in the placebo group, and the between group difference was 95.6 mL (95% CI, 52.2 to 139.0; P<0.001).

Nebulized Tyvaso reduced risk of a clinical worsening event by 29% (hazard ratio, 0.71; 95% CI, 0.53 to 0.95; P=0.02) relative to placebo, a statistically significant improvement in this key secondary endpoint. Nebulized Tyvaso showed improvement in other important secondary endpoints, including improved change in percent of predicted FVC, King's Brief Interstitial Lung Disease quality of life questionnaire (**K-BILD**), and change in percent of predicted diffusion capacity of lungs for carbon monoxide (**DLCO**).

Benefits of Tyvaso were observed across all subgroups, such as use of background therapy (nintedanib, pirfenidone, or no background therapy), smoking status, and supplemental oxygen use.

"*TETON-2* not only met its primary endpoint of change in FVC but also attained statistical significance for time to clinical worsening. We also saw improved change in the diffusing capacity and, importantly, in patients' quality of life. This achievement in patients with mild to moderate IPF over 52 weeks speaks to both the efficacy of the medication and the advantage of direct deposition through the inhaled route," said lead study author **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 publication of *TETON-2* in *The New England Journal of Medicine* marks a pivotal moment for the IPF community. For too long, patients have had limited options to treat this devastating disease. At United Therapeutics, our mission has always been to develop innovative therapies for patients with life-threatening pulmonary conditions. Nebulized Tyvaso has the potential to be the first and only inhaled anti-fibrotic treatment for IPF – a true advancement for patients and physicians alike," said **Martine Rothblatt, Ph.D.**, Chairperson and Chief Executive Officer of United Therapeutics.

"Tyvaso's unique antifibrotic mechanism, combined with notable clinical trial observations of improved lung function, led us to hypothesize that it could potentially serve as an effective treatment for patients with fibrotic lung disease. The full results of this study support our theory and show that nebulized

Tyvaso has the potential to transform IPF treatment and could serve as a first-line, inhaled therapy," said **Peter Smith, Pharm. D.,** Senior Vice President, Product Development at United Therapeutics and the lead for the global *TETON* program.

The *TETON-2* study population reflected the characteristics of a general population of patients with IPF. The mean age of the patients was 71.7 years, 80.1% were male, the baseline percent predicted FVC was 76.8%, and 75.4% of the patients were on background antifibrotic therapy. Eligible patients were randomly assigned to nebulized Tyvaso (n=298) or placebo (n=295).

Treatment with nebulized Tyvaso was well-tolerated, and the safety profile was consistent with previous Tyvaso studies and known prostacyclin-related adverse events. The most frequent adverse events were cough, headache, and diarrhea. Most of these events were of mild to moderate intensity. No new safety signals were observed.

United Therapeutics plans to submit a supplemental New Drug Application (**sNDA**) to the FDA by the second half of 2026 to add IPF to the labeled indications for nebulized Tyvaso following results from the ongoing *TETON-1* study, which are expected soon. 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 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**). *TETON-1* is evaluating the use of nebulized Tyvaso in IPF in patients in the United States and Canada. *TETON-2* evaluated the use of nebulized Tyvaso in IPF in patients 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-2 **Study Design**

The *TETON-2* study (NCT05255991) was a 597-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 Argentina, Australia, Belgium, Chile, Denmark, France, Germany, Israel, Italy, Mexico, the Netherlands, New Zealand, Peru, South Korea, Spain, and Taiwan. The study achieved full enrollment in July 2024.

Patients were randomly assigned 1:1 to receive nebulized Tyvaso or placebo, stratified by IPF background therapy use. All patients initiated nebulized Tyvaso or placebo at a dose of three breaths administered four times daily (**QID**) and titrated to a target dosing regimen of 12 breaths QID. Study drug doses were titrated up as tolerated, until the target dose or maximum clinically tolerated dose was achieved.

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-2* study 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.

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 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, our mission to develop innovative therapies for patients with life-threatening pulmonary conditions; our expectation that nebulized Tyvaso would, if approved, by the first and only inhaled anti-fibrotic treatment for IPF; our expectation that nebulized Tyvaso has the potential to transform IPF treatment and serve as a first-line, inhaled therapy; the timing and anticipated outcome of our regulatory strategy to add IPF to the labeled indications for nebulized Tyvaso; the timing and outcome of our ongoing *TETON-1* clinical study; 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 11, 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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