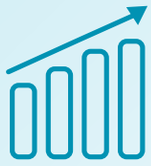
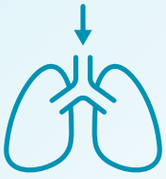
For the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to improve exercise ability[1]

# TAKE A LOOK AT WHAT TYVASO® CAN DO



**Demonstrated Efficacy[1-3]**



**Direct-to-Lung Delivery[1]**

**On-the-Go Dosing**

## 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

### 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

**Please see Important Safety Information throughout and on pages 22-23, and the accompanying Full Prescribing Information, Patient Product Information, and the TD-300 TYVASO Inhalation System Instructions for Use manual in pocket.**

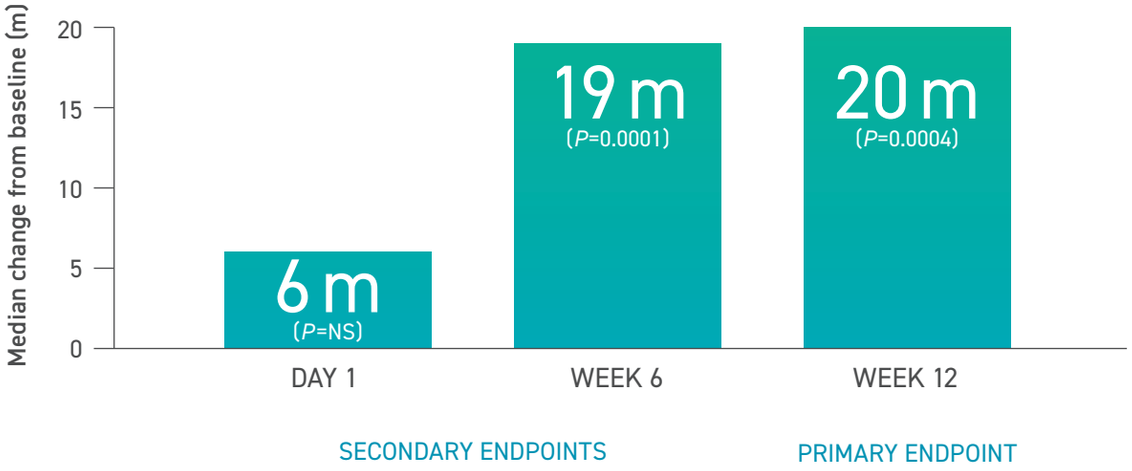
WHO=World Health Organization.

TYVASO® (treprostinil) INHALATION SOLUTION

# TYVASO provides significant improvements in 6MWD[1,2,4]

**TRIUMPH Study Design:** a 12-week, placebo-controlled, multicenter, randomized, double-blind trial of TYVASO or placebo added to an ERA (bosentan) or a PDE-5i (sildenafil) in 235 clinically stable patients who were NYHA FC III (98%) or IV (2%) at baseline.[1,2]

## Changes in 6MWD as early as Day 1[1,2]*




Hodges–Lehmann median difference between TYVASO treatment and placebo groups.[1,2]

## Even greater improvements in 6MWD were seen in nearly 1/3 of patients at week 12[2,4]

**>50 m**

**31% OF PATIENTS** INCREASED 6MWD BY **>50 m** WITH TYVASO COMPARED WITH 12% RECEIVING PLACEBO[2,4]

*6MWD was measured at peak exposure (10-60 minutes after dosing) and trough exposure (≥4 hours after dosing) at week 12 (trough data not shown).[1]

6MWD=6-minute walk distance; ERA=endothelin receptor antagonist; FC=functional class; NS=not significant; NYHA=New York Heart Association; PDE-5i=phosphodiesterase type 5 inhibitor; TRIUMPH=TReprostinil Sodium Inhalation Used in the Management of Pulmonary Arterial Hypertension.

## IMPORTANT SAFETY INFORMATION

### WARNINGS AND PRECAUTIONS (continued)

- TYVASO is a pulmonary and systemic vasodilator. In patients with low systemic arterial pressure, TYVASO may cause symptomatic hypotension

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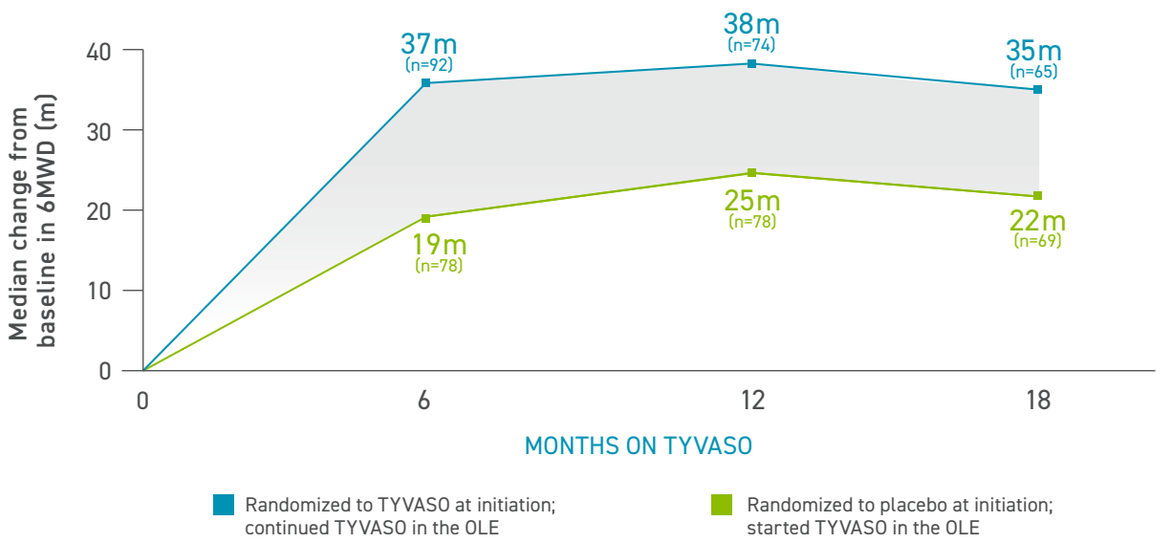
# TYVASO showed sustained improvements in 6MWD[3]

**TRIUMPH OLE Study Design:** an OLE of the TRIUMPH study to evaluate the safety and dosing of TYVASO over time. Patients (N=206) from the placebo-controlled 12-week TRIUMPH study initiated TYVASO and entered the long-term, uncontrolled OLE study. NYHA FC II (11%), III (86%), IV (3%) at baseline.[1,3]

## Improvements in 6MWD over 18 months[3]




**Without a control group, data must be interpreted cautiously.**

PATIENTS WHO STARTED TYVASO 12 WEEKS EARLIER HAD GREATER IMPROVEMENTS IN 6MWD[3]

OLE=open-label extension.

## IMPORTANT SAFETY INFORMATION

### WARNINGS AND PRECAUTIONS (continued)

- 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

TYVASO® (treprostinil) INHALATION SOLUTION

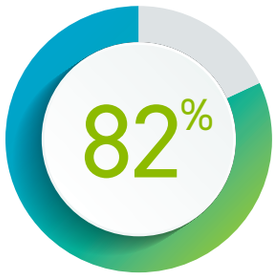
# Long-term benefits beyond 6MWD[3,4]

## Sustained improvements in NYHA functional class[3]


**maintained or improved NYHA FC from baseline at 2 years** (n=120)[3,4]

**36%** of patients had improvement in functional class from baseline at 6 months (n=174) and at 2 years (n=120)[3,4]

## Survival exceeded 80% at 3 years[1]




**survival rate at 3 years** (n=69)[1]

Based on a long-term follow-up of patients who were treated with TYVASO in the pivotal study and the OLE (Kaplan–Meier estimates of survival).[1]

**These data are from an OLE study. Without a control group, data must be interpreted cautiously.**

## IMPORTANT SAFETY INFORMATION

### WARNINGS AND PRECAUTIONS (continued)

- 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

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# The most common adverse events with TYVASO

## TRIUMPH study: adverse events in ≥4% of PAH patients receiving TYVASO and more frequent than placebo[1,2]

| Adverse Event | Treatment n (%) | |
|---|---|---|
| | TYVASO (n=115) | Placebo (n=120) |
| Cough | 62 (54%) | 35 (29%) |
| Headache | 47 (41%) | 27 (23%) |
| Throat irritation/pharyngolaryngeal pain | 29 (25%) | 17 (14%) |
| Nausea | 22 (19%) | 13 (11%) |
| Flushing | 17 (15%) | 1 (<1%) |
| Syncope | 7 (6%) | 1 (<1%) |

- Of the 23 total discontinuations, 7 patients from the TYVASO group discontinued due to adverse events, compared with 4 from the placebo group[2]
- In addition, AEs occurring in ≥10% of patients were dizziness and diarrhea[2]

## Safety from the OLE study[1]

- AEs observed during this chronic dosing study were qualitatively similar to those observed in the 12-week placebo-controlled trial[1]
- Serious AEs included pneumonia (n=15) and hemoptysis (n=3)[1]

AE=adverse event.

## IMPORTANT SAFETY INFORMATION

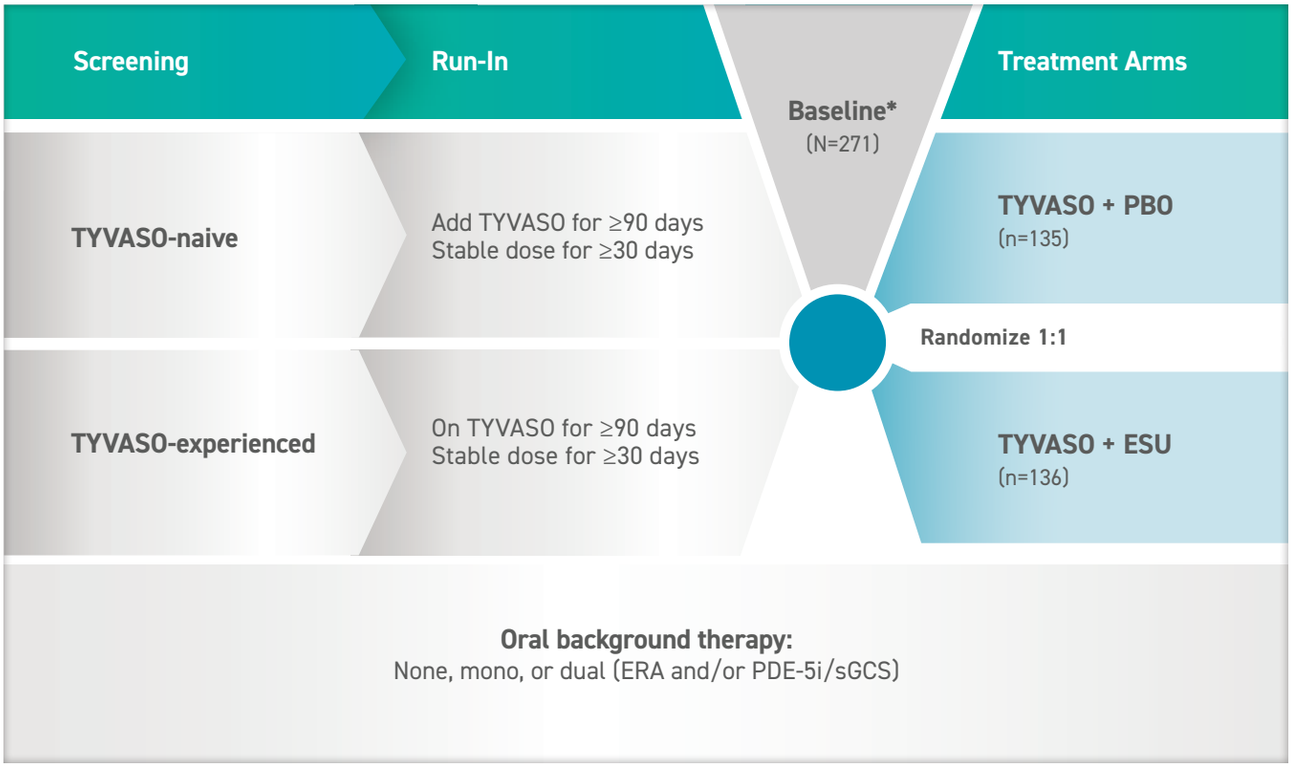
### DRUG INTERACTIONS/SPECIFIC POPULATIONS

- 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

TYVASO® (treprostinil) INHALATION SOLUTION

# BEAT: Study design

**A phase III, multicenter, double-blind, randomized, placebo-controlled, event-driven study of oral esuberaprost (ESU) vs placebo (PBO) when added to TYVASO in FC III/IV patients with PAH[4,5]**




Esuberaprost is not FDA approved and has not been evaluated for safety and tolerability.

*273 patients were randomized; 271 received study drug. Study arms were stratified by TYVASO use (naive or experienced). The median TYVASO dose at baseline was 9 breaths QID. Patients taking ESU began at a dose of 14.2 µg QID and increased to a maximum dose of 28.4 µg QID as tolerated.[4-6]

BEAT=Beraprost-314d Added to TYVASO; QID=4 times daily; sGCS=soluble guanylate cyclase stimulator.

## IMPORTANT SAFETY INFORMATION

### DRUG INTERACTIONS/SPECIFIC POPULATIONS (continued)

- 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

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# BEAT: Study endpoints and summary[4,5]

## Patients were studied across a range of clinical endpoints[4,5]

| Primary Endpoint | Secondary Endpoints |
|---|---|
| Time to clinical worsening* | Change from baseline in:<br>• 6MWD<br>• Modified BDS<br>• WHO FC<br>• NT-proBNP |

### CONCLUSIONS:

- THERE WAS NOT A SIGNIFICANT TREATMENT EFFECT FAVORING ESUBERAPROST ACROSS ANY OF THE PRIMARY OR SECONDARY ENDPOINTS[5]

*Defined by death (all causes), hospitalization due to worsening PAH, use of parenteral prostacyclin, disease progression,† and unsatisfactory long-term clinical response.[4‡]

†Decrease in 6MWD of >15% and worsening PAH symptoms (increase in WHO FC or worsening symptoms of right heart failure).[4]

‡Must have received treatment for >24 weeks and experienced a >15% decrease in 6MWD or any suspected clinical worsening event.[4]

BDS=Borg dyspnea score; NT-proBNP=N-terminal pro–B-type natriuretic peptide.

## IMPORTANT SAFETY INFORMATION

### DRUG INTERACTIONS/SPECIFIC POPULATIONS (continued)

- 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

TYVASO® (treprostinil) INHALATION SOLUTION

# Evaluating the durability of TYVASO

**Although BEAT did not demonstrate a significant benefit for esuberaprost vs placebo, the design of this study allows an opportunity to examine the long-term use of TYVASO across multiple clinical endpoints[6]**

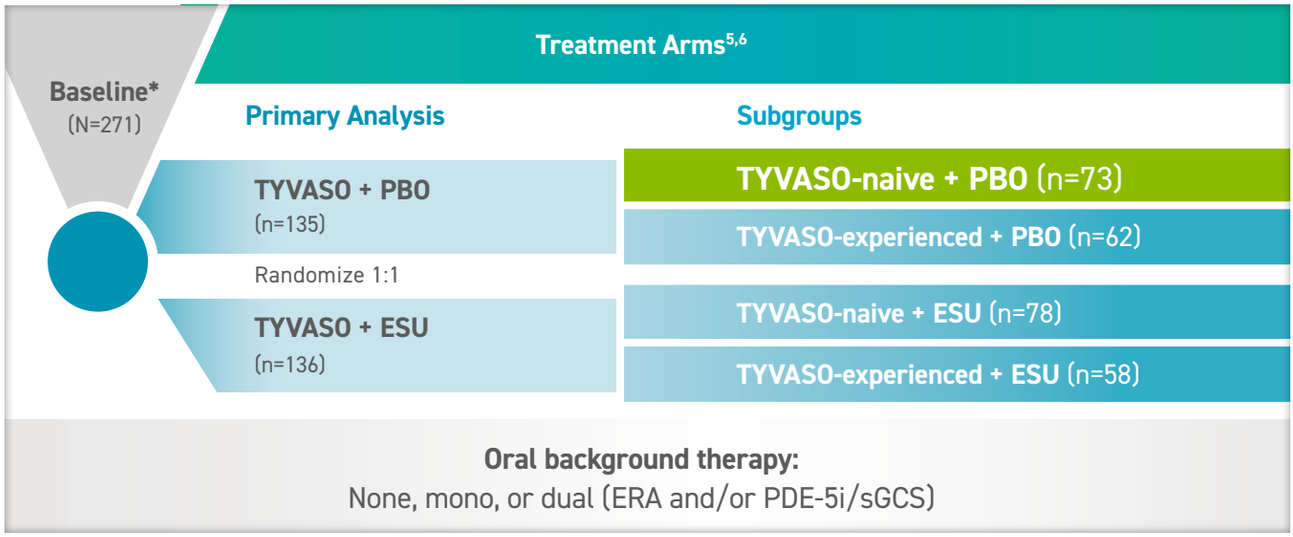
## Exploratory Analyses[6]

**Clinical responses**

- Time to clinical worsening
- 6MWD
- NT-proBNP
- WHO FC
- Treatment-emergent adverse events

**Risk profile**

- French noninvasive low-risk criteria
- REVEAL 2.0 score




**Only TYVASO-naive + PBO subgroup data are presented on the subsequent pages**

*The median TYVASO dose at baseline was 9 breaths QID.[6]

REVEAL=Registry to Evaluate Early and Long-Term PAH Disease Management.

## IMPORTANT SAFETY INFORMATION

### ADVERSE REACTIONS

- The most common adverse reactions seen with TYVASO in ≥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 ≥10% of patients were dizziness and diarrhea

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# Patient characteristics at screening for TYVASO-naive + PBO subgroup (n=73)[6]

## Studied in patients with more serious disease

**82%**

AT INTERMEDIATE OR HIGH RISK[6*]

Based on REVEAL 2.0, 34.2% of patients were intermediate risk and 47.9% were high risk

**>90%**

WITH NO OR ONE LOW-RISK CRITERIA[6†]

Based on French noninvasive criteria, 30.1% had 1 low-risk criteria and 60.3% had 0 low-risk criteria

**92%**

FC III[6]

8% of patients were FC IV

### Patient demographics[6]

| Characteristic | TYVASO-Naive + PBO (n=73) |
|---|---|
| **Age, mean ± SD, y** | 57.9 ± 13.3 |
| **Gender, female/male (%)** | 69.9/30.1 |
| **Etiology, n (%)** | |
| IPAH/FPAH | 45 (61.6) |
| CVD-PAH | 21 (28.8) |
| **Time since diagnosis, mean ± SD, y** | 2.7 ± 4.3 |
| **Background therapy, n (%)** | |
| None | 13 (17.8) |
| Mono: PDE-5i or ERA | 24 (32.9) |
| Dual: PDE-5i/sGCS + ERA | 36 (49.3) |
| **6MWD, mean ± SD, m** | 320 ± 115.4 |
| **NT-proBNP, median (IQR), pg/mL** | 561 (211, 1210) |

*The REVEAL 2.0 calculation included 8 variables: PAH subgroup, demographics, eGFR (calculated from SCr), SBP, HR, 6MWD, WHO FC, and NT-proBNP. A score ≤6 was considered low risk, 7 or 8 was considered intermediate risk, and ≥9 was considered high risk.[6,7]

†Noninvasive low-risk criteria are defined as: 6MWD >440 m, WHO FC I/II, and NT-proBNP <300 pg/mL.[6,8]

CVD=collagen vascular disease; eGFR=estimated glomerular filtration rate; FPAH=familial pulmonary arterial hypertension; HR=heart rate; IPAH=idiopathic pulmonary arterial hypertension; IQR=interquartile range; SBP=systolic blood pressure; SCr=serum creatinine; SD=standard deviation.

## IMPORTANT SAFETY INFORMATION

### WARNINGS AND PRECAUTIONS

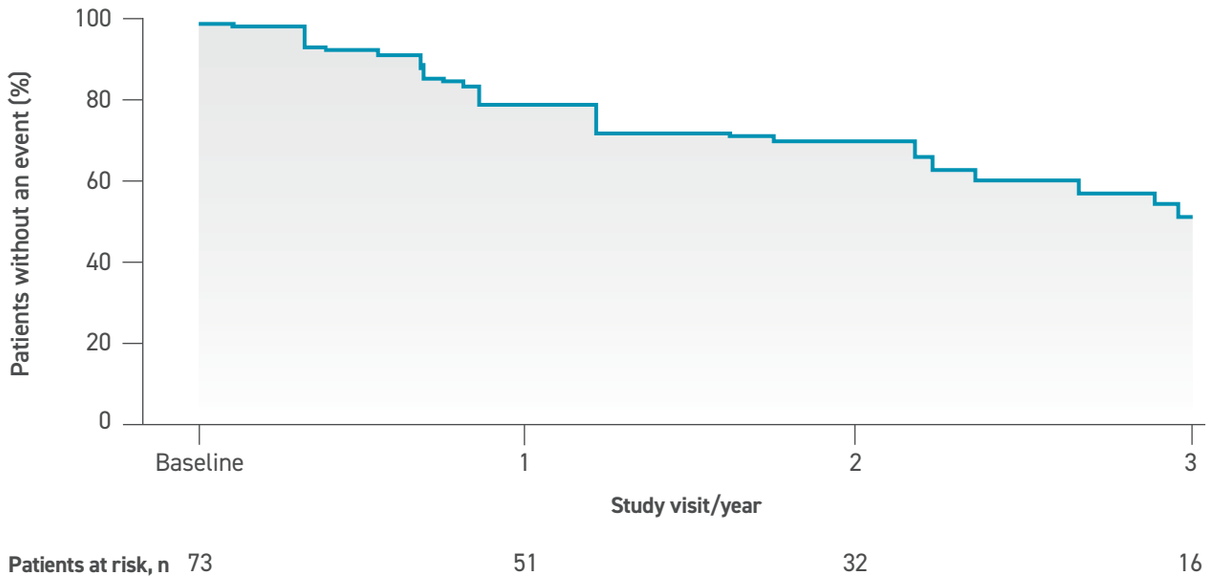
- The efficacy of TYVASO has not been established in patients with significant underlying lung disease (such as asthma or chronic obstructive pulmonary disease). Patients with acute pulmonary infections should be carefully monitored to detect any worsening of lung disease and loss of drug effect

TYVASO® (treprostinil) INHALATION SOLUTION

**Data are from a post hoc analysis and should be interpreted with appropriate caution.**

# Clinical worsening in an intermediate/high-risk population

**Time to first clinical worsening event[6]***




**CLINICAL WORSENING EVENTS, % (n)**[4,6]

- **17.8%** (13) AT 1 YEAR
- **26.0%** (19) AT 2 YEARS
- **34.2%** (25) AT 3 YEARS

*Estimates are provided from baseline, as clinical worsening events prior to baseline would have resulted in screen failure from the study. Estimates from screening would be greatly confounded by selection bias.

## IMPORTANT SAFETY INFORMATION

### WARNINGS AND PRECAUTIONS (continued)

- 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

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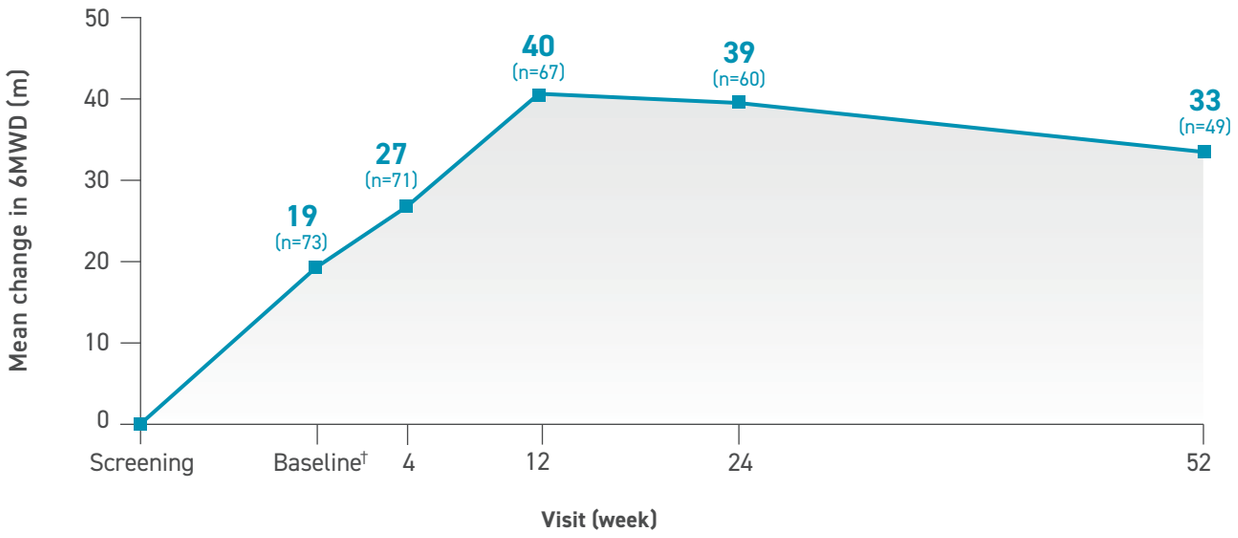
# Early and sustained increases in 6MWD[6]

## Improvements peaked at 40 m at week 12 and were sustained through week 52[4,6*]

**Change in 6MWD[4,6]**




## The mean 6MWD at screening was 320 ± 115 m[6]

6MWD IMPROVEMENTS WERE MAINTAINED, EVEN THOUGH MOST PATIENTS WERE AT INTERMEDIATE OR HIGH RISK AT SCREENING[4,6]

*Exploratory analysis based on MMRM data.[6]
†The median (IQR) time on TYVASO at baseline was 98 (94, 100) days for the TYVASO-naive + PBO subgroup.[6]
MMRM=mixed-effect model repeat measurement.

## IMPORTANT SAFETY INFORMATION

### WARNINGS AND PRECAUTIONS (continued)

- 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

TYVASO® (treprostinil) INHALATION SOLUTION

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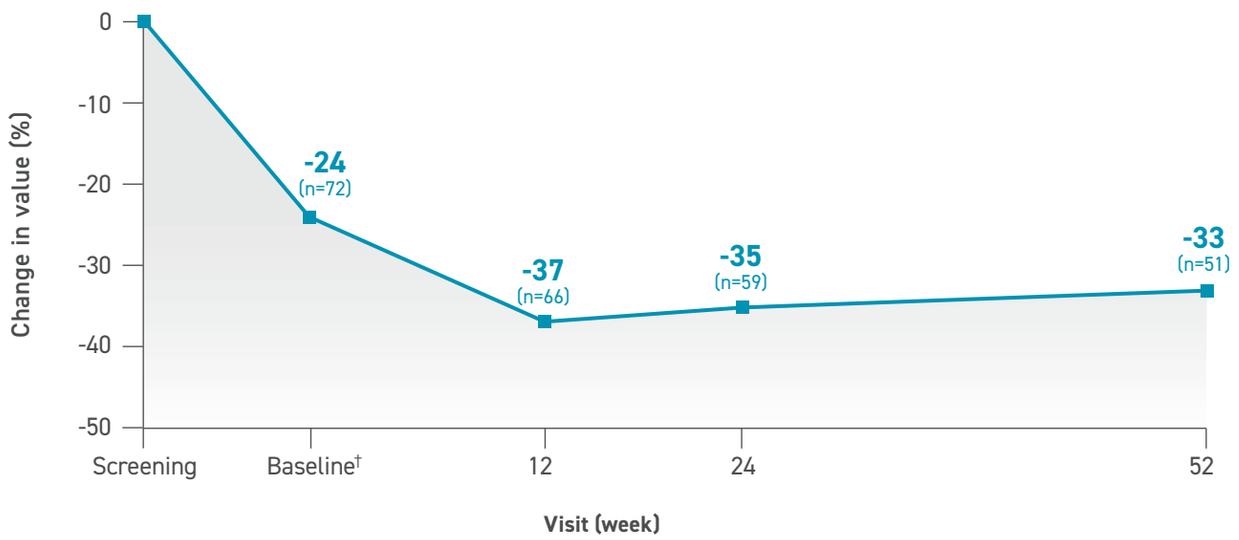
# Early and sustained reductions in NT-proBNP[4,6]

## 37% reduction observed at week 12 and reductions sustained through week 52[4,6*]

**NT-proBNP reductions from screening[4,6]**




## Median (IQR) NT-proBNP at screening: 561 (211, 1210) pg/mL[6]

EVEN IN INTERMEDIATE/HIGH-RISK PATIENTS, NT-proBNP IMPROVEMENTS WERE MAINTAINED THROUGH WEEK 52[4,6]

*Exploratory analysis based on MMRM data.[6]
†The median (IQR) time on TYVASO at baseline was 98 (94, 100) days for the TYVASO-naive + PBO subgroup.[6]

## IMPORTANT SAFETY INFORMATION

### 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

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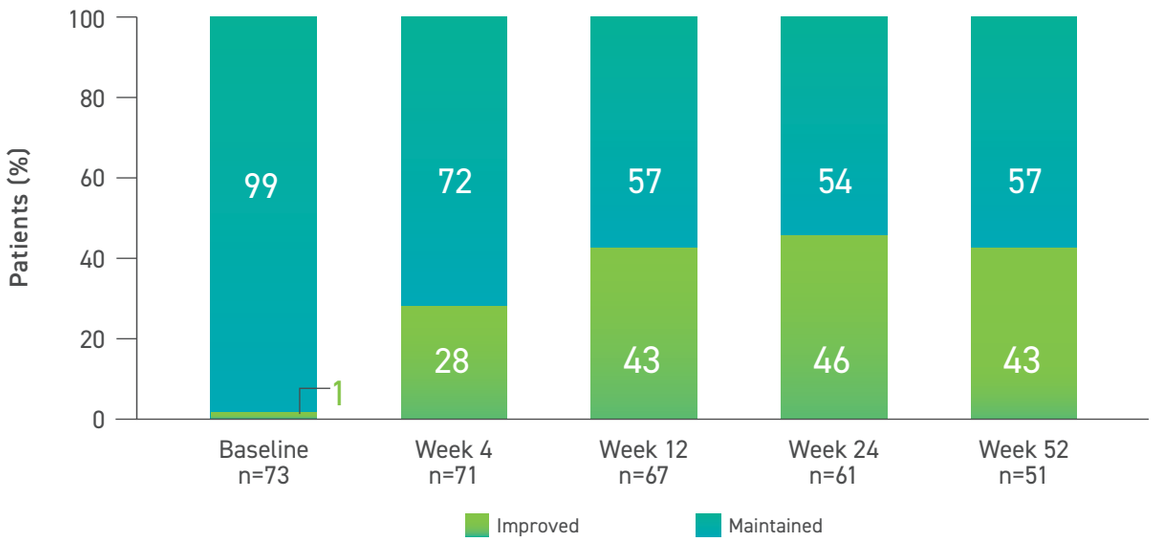
# Early and sustained improvements in WHO functional class[4,6]

## 100% of patients improved or maintained FC through week 52[4,6]*

**Change in FC from screening[4,6]**




## 92% of patients were FC III and 8% were FC IV at screening[4,6]

AN IMPORTANT GOAL OF PAH TREATMENT IS TO IMPROVE WHO FUNCTIONAL CLASS[9]

*"Improved" indicates a shift from a higher to lower FC; "maintained" indicates the same FC.[6]

## IMPORTANT SAFETY INFORMATION

### DRUG INTERACTIONS/SPECIFIC POPULATIONS (continued)

- 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

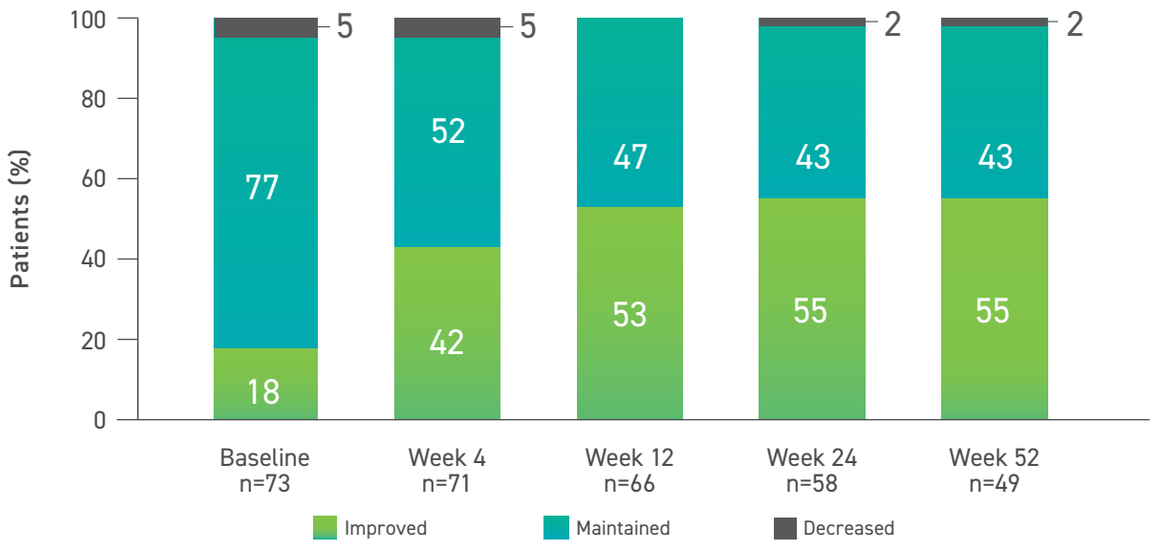
TYVASO® (treprostinil) INHALATION SOLUTION

**Data are from a post hoc analysis and should be interpreted with appropriate caution.**

# Early and sustained improvements in French noninvasive risk status[4,6]

## 98% of patients improved or maintained their risk status at week 52[4,6]

**Shift in number of low-risk criteria from screening[4,6]***




## Number of low-risk criteria at screening[4,6†]


**90% OF PATIENTS** HAD NO OR 1 LOW-RISK CRITERIA AT SCREENING

*"Improved" indicates any increase in the number of low-risk criteria met; "maintained" indicates no shift; "decreased" indicates any decrease in the number of low-risk criteria met.[6]

†Low-risk criteria include: WHO FC I/II, 6MWD >440 m, and NT-proBNP <300 pg/mL.[8]

## IMPORTANT SAFETY INFORMATION

### ADVERSE REACTIONS

- The most common adverse reactions seen with TYVASO in ≥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 ≥10% of patients were dizziness and diarrhea

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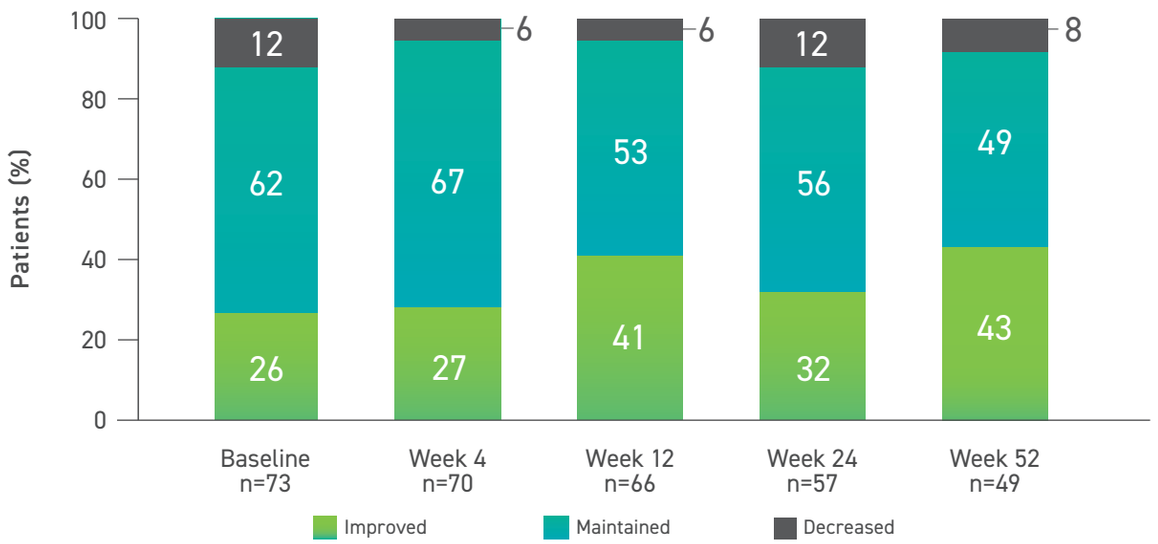
# Early and sustained improvements in REVEAL 2.0 risk category[4,6]

## 92% of patients improved or maintained their risk category at week 52[4,6]

**Shift in risk category from screening[4,6]***




## REVEAL 2.0 risk category at screening[4,6†]


**~HALF OF PATIENTS** WERE HIGH RISK AT SCREENING

*"Improved" indicates any increase in the number of low-risk criteria met; "maintained" indicates no shift; "decreased" indicates any decrease in the number of low-risk criteria met.[6]

†The REVEAL 2.0 calculation included 8 variables: PAH subgroup, demographics, eGFR (calculated from SCr), SBP, HR, 6MWD, WHO FC, and NT-proBNP. A score ≤6 was considered low risk, 7 or 8 was considered intermediate risk, and ≥9 was considered high risk.[6,7]

## IMPORTANT SAFETY INFORMATION

### WARNINGS AND PRECAUTIONS

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# Most frequent treatment-emergent adverse events (TEAEs)[4,6]

## Adverse events occurring in ≥10% of TYVASO-naive + PBO patients[4,6]

| Treatment-Emergent AE* | TYVASO-Naive + PBO, n=73, n (%) |
|---|---|
| Upper respiratory infection | 17 (23.3) |
| Nausea | 16 (21.9) |
| Diarrhea | 13 (17.8) |
| Cough | 12 (16.4) |
| Fatigue | 12 (16.4) |
| Headache | 11 (15.1) |
| Pneumonia | 10 (13.7) |
| Vomiting | 10 (13.7) |
| Urinary tract infection | 9 (12.3) |

- Most frequent TEAEs were similar across all subgroups[6]

*TEAEs are those that occurred after randomization.

## IMPORTANT SAFETY INFORMATION

### WARNINGS AND PRECAUTIONS (continued)

- TYVASO is a pulmonary and systemic vasodilator. In patients with low systemic arterial pressure, TYVASO may cause symptomatic hypotension
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# Early and sustained improvements across multiple endpoints with TYVASO[6]

## 6MWD and NT-proBNP

## Functional class

## Risk status

French noninvasive and REVEAL 2.0 measures



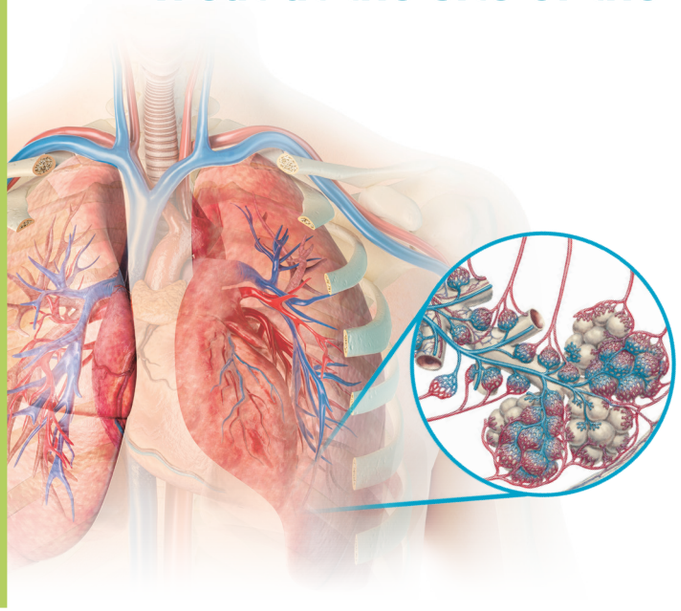
## IMPORTANT SAFETY INFORMATION

**WARNINGS AND PRECAUTIONS (continued)**

- 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

TYVASO® (treprostinil) INHALATION SOLUTION

# Treat at the site of the disease



- TYVASO is delivered directly to the lungs, which are highly vascularized, providing an enormous surface area for drug absorption and an attractive target for drug delivery[1,10,11]
- TYVASO is inhaled directly to distal airspaces that are in close proximity to pulmonary arterioles affected by PAH[12]

**Direct-to-lung delivery results in higher concentrations in the pulmonary arterial vasculature, which may selectively enhance blood flow for better ventilation and perfusion matching with less off-target exposure[10]**

## Allows for fast titration


Patients can titrate with an additional 3 breaths per treatment session at 1- to 2-week intervals (as tolerated)[1]

### TRIUMPH

**72%** of patients taking TYVASO achieved the target dose of 9 breaths, 4x daily[2]

### TRIUMPH OLE

**89%** achieved 9 breaths, 4x daily[1]*

AVERAGE TIME TO TARGET DOSE WAS **~3 WEEKS[2]**

*42% achieved 12 breaths, 4x daily. The label dosage recommendation is 9 breaths, 4x daily.[1]

## IMPORTANT SAFETY INFORMATION

### DRUG INTERACTIONS/SPECIFIC POPULATIONS

- The concomitant use of TYVASO with diuretics, antihypertensives, or other vasodilators may increase the risk of symptomatic hypotension

**Please see Important Safety Information throughout and on pages 22-23, and the accompanying Full Prescribing Information, Patient Product Information, and the TD-300 TYVASO Inhalation System Instructions for Use manual in pocket.**

# TYVASO fits into your patient's routine[1]

## Dosing at home or on-the-go

**Convenient once-daily setup**

**Each treatment session only takes approximately 2 to 3 minutes[1]**

**Cordless flexibility**

Compared with other nebulizer systems

**Treatment sessions can be scheduled around daily activities,** approximately every 4 waking hours[1]:

Waking | Lunch | Dinner | Bedtime

CORDLESS FLEXIBILITY FOR DOSING AT HOME OR ON-THE-GO

Shown: TD-300

## IMPORTANT SAFETY INFORMATION

### DRUG INTERACTIONS/SPECIFIC POPULATIONS (continued)

- 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

TYVASO® (treprostinil) INHALATION SOLUTION

# Setting your patients up for success

## Proactively manage adverse events

- **Set** realistic expectations.
- **Prepare** for common AEs.
- **Ensure** patients understand the dosing plan.

## Selected AE management approaches[13]*

### Cough

- Before treatment, drink very cold water or very warm water
- Review proper technique; be sure to keep the device level
- Temporary dose reductions and/or slower titration (eg, 1 breath, 4x daily)
- Inhaled anticholinergics
- Inhaled steroids
- OTC or prescription cough medicines

### Headache

- OTC pain relievers
- Temporary dose reductions

### Throat irritation

- Oral analgesic spray

**Approaches to AE management are based on anecdotal evidence cited in Poms et al[13] and should not be construed as medical advice. United Therapeutics does not recommend or endorse using healthcare products other than as directed or prescribed.**

*AE management strategies should be dealt with in accordance with the TYVASO Full Prescribing Information and your clinical judgment.
OTC=over-the-counter.

## IMPORTANT SAFETY INFORMATION

### DRUG INTERACTIONS/SPECIFIC POPULATIONS (continued)

- 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

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# Support for your patients taking TYVASO

## Specialty Pharmacy providers

- Specialty Pharmacies work to get your patients started on therapy in a timely manner

accredo®

CVS specialty™

## Access and financial assistance

assist
Access Solutions and Support Team

- Helping patients determine if they qualify for United Therapeutics' patient assistance programs
- Web portal available for healthcare professionals at www.utassist.com

## Co-Pay Assistance Card*

$5
CO-PAY

- With the Co-Pay Assistance Card, most eligible patients who enroll may pay as little as a $5 co-pay per prescription, up to $8000 savings per year

*To enroll in this Program, your patients must understand and agree to comply with the eligibility requirements and terms of use.

Eligibility requirements for this Program are:

- Patients must be 18 years or older to use this Program.
- Patients using Medicare, Medicaid, or any other state or federal government program to pay for their medications are not eligible. Patients who start utilizing government coverage during the term of the Program will no longer be eligible.
- The Program is valid only for patients with commercial (also known as private) insurance who are taking the medication for an FDA-approved indication. The Program is only valid for the cost of the treprostinil product and not applicable to any related supplies or other medical expenses associated with administering the product.
- Eligible patients must be residents of the US or Puerto Rico. The Program is subject to additional state law restrictions. Patients residing in select states may not be eligible for the Program.

**For full program details and Terms and Conditions, visit www.UTcopay.com.**

## IMPORTANT SAFETY INFORMATION

### DRUG INTERACTIONS/SPECIFIC POPULATIONS (continued)

- 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

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

### 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

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## DRUG INTERACTIONS/SPECIFIC POPULATIONS (continued)

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- 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 ≥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 ≥10% of patients were dizziness and diarrhea

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**Please see the Full Prescribing Information, Patient Product Information, and the TD-300 TYVASO Inhalation System Instructions for Use manual in pocket.**

**For additional information about TYVASO, visit www.tyvaso.com or call 1-877-UNITHER (1-877-864-8437).**

**References: 1.** TYVASO [package insert]. Research Triangle Park, NC: United Therapeutics Corporation; 2017. **2.** McLaughlin VV, Benza RL, Rubin LJ, et al. Addition of inhaled treprostinil to oral therapy for pulmonary arterial hypertension: a randomized controlled clinical trial. *J Am Coll Cardiol.* 2010;55(18):1915-1922. **3.** Benza RL, Seeger W, McLaughlin VV, et al. Long-term effects of inhaled treprostinil in patients with pulmonary arterial hypertension: the Treprostinil Sodium Inhalation Used in the Management of Pulmonary Arterial Hypertension (TRIUMPH) study open-label extension. *J Heart Lung Transplant.* 2011;30(12):1327-1333. **4.** Data on file. United Therapeutics Corporation. Research Triangle Park, NC. **5.** Ford HJ, Kremer MR, Bartolome S, et al. Primary results from the randomized double-blind, placebo-controlled phase 3 trial–Beraprost-314*d* Added to Tyvaso (BEAT) in World Health Organization (WHO) functional class III and IV patients with pulmonary arterial hypertension. Poster presented at: PVRI Annual World Congress on Pulmonary Vascular Disease; January 30-February 2, 2020; Lima, Peru. **6.** Bartolome S, Bourge RC, Ford HJ, et al. The effect of inhaled treprostinil in the randomized, double-blind, placebo-controlled, phase-III BEAT study. Poster presented at: PVRI Annual World Congress on Pulmonary Vascular Disease; January 30-February 2, 2020; Lima, Peru. **7.** Benza RL, Gomberg-Maitland M, Elliott CG, et al. Predicting survival in patients with pulmonary arterial hypertension: the REVEAL risk score calculator 2.0 and comparison with ESC/ERS-based risk assessment strategies. *Chest.* 2019;156(2):323-337. **8.** Boucly A, Weatherald J, Savale L, et al. Risk assessment, prognosis and guideline implementation in pulmonary arterial hypertension. *Eur Respir J.* 2017;50(2). doi:10.1183/13993003.00889-2017 **9.** Galiè N, Humbert M, Vachiery JL, et al. 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension: the Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS). *Eur Respir J.* 2015;46(4):903-975. **10.** Hill NS, Preston IR, Roberts KE. Inhaled therapies for pulmonary hypertension. *Respir Care.* 2015;60(6):794-805. **11.** Patton JS, Brain JD, Davies LA, et al. The particle has landed—characterizing the fate of inhaled pharmaceuticals. *J Aerosol Med Pulm Drug Deliv.* 2010;23(suppl 2):S71-S87. **12.** Channick RN, Voswinckel R, Rubin LJ. Inhaled treprostinil: a therapeutic review. *Drug Des Devel Ther.* 2012;6:19-28. **13.** Poms A, Kingman M. Inhaled treprostinil for the treatment of pulmonary arterial hypertension. *Crit Care Nurse.* 2011;31(6):e1-e10.

TYVASO® (treprostinil) INHALATION SOLUTION

**For the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to improve exercise ability[1]**

# TAKE A LOOK AT WHAT TYVASO CAN DO

## Demonstrated early and sustained efficacy

- Significant improvements in 6MWD[1,2,4*]
- Long-term improvements in NYHA functional class[3†]
- Robust survival rates at 3 years[1†]

*$P$=0.0001 at week 6; $P$=0.0004 at week 12.[2]
†These data are from an OLE study. Without a control group, data must be interpreted cautiously.

## Direct-to-lung delivery

- Delivers to the site of disease with less off-target exposure[10]
- Allows for fast titration to reach target dose[1,2]
- Convenience and flexibility that fits into patients' daily routine[1]

INCORPORATE TYVASO INTO YOUR PRACTICE TODAY

## IMPORTANT SAFETY INFORMATION

### ADVERSE REACTIONS

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United Therapeutics CORPORATION



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