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Deupirfenidone Program

Supplemental Slides

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Deupirfenidone (LYT-100): Potential New Standard-of-care (SOC) for IPF and other PPFs



**Lung Disease
with High
Patient Need**

Debilitating, fatal disease; current SOC agents **cannot be taken in high doses due to poor tolerability**, resulting in **suboptimal efficacy**



**Ideal Treatment
Goal in IPF**

Stabilization of lung function without compromising on safety and tolerability



**Robust
Deupirfenidone
Data**

Potential to set a new standard for IPF treatment: Phase 2b study **showed dose dependent lung function stabilization** with a **favorable tolerability profile**



**Significant
Commercial
Opportunity**

Blockbuster potential in a **multi-billion dollar market**



**Strong
Intellectual
Property (IP)**

Broad and layered IP protection with **exclusivities into at least 2043¹**

Initiation of pivotal Phase 3 trial expected by the end of 2025

Accelerating Program Advancement for Patients in Need



December 2024

Successful completion of Phase 2b trial

Open label extension (OLE) ongoing

- ✓ 140 patients continued in the OLE
- ✓ 85 patients received at least 52 weeks of treatment to date¹

March 2025

Additional data from Phase 2b to be presented at ATS

- ✓ Preliminary 52-week OLE data demonstrate durable treatment effect
- ✓ 101 patients received at least 52 weeks of treatment to date²

May 2025

September 2025

Additional OLE data (including “switch data”) at ERS International Congress

Before the end of Q3 2025

Expected meeting with FDA

H1 2026

Initiation of Phase 3

Unmet Needs in IPF

Idiopathic Pulmonary Fibrosis (IPF) Overview

IPF is a **progressive and fatal disease** with a **significantly unaddressed** patient population



>232,000

IPF patients in the US & EU¹

Involves scarring of the lungs, leading to shortness of breath and loss of lung function²



~2-5 years

Life expectancy of IPF ***without treatment³***



Two

FDA-approved agents to treat IPF⁴

For most patients, tolerability challenges outweigh suboptimal efficacy



~25%

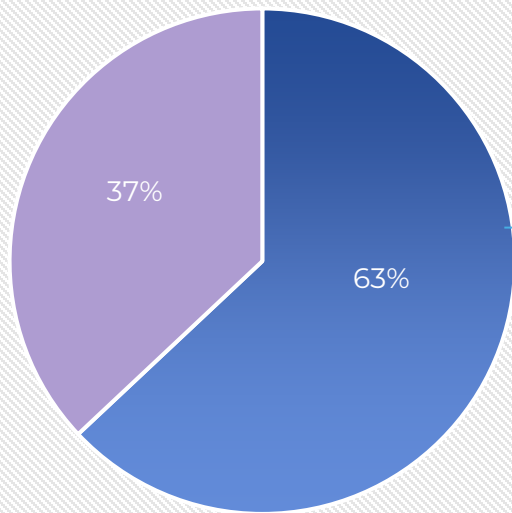
IPF patients ever start antifibrotic treatment

...of which >40% eventually discontinue⁵

Efficacy is the Key Prescribing Focus in IPF

The majority of respondents prioritize efficacy (over safety/tolerability) in trying to optimize therapy for IPF patients, regardless of practice setting (2025 analysis)

Recognizing the Tradeoffs Between Efficacy and Safety/Tolerability, If I Have to Choose One, I Most Prioritize...



IPF Center

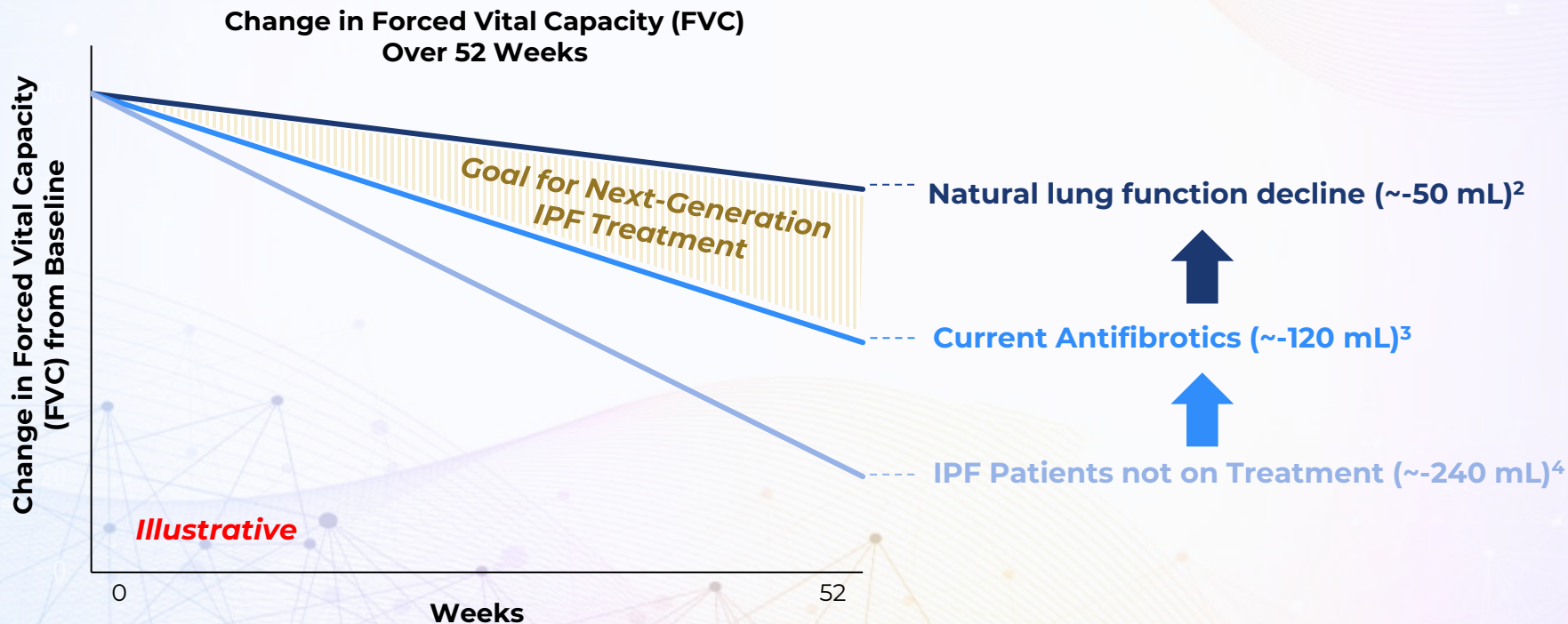
Yes 62%
No 65%

- Pushing for Incremental Efficacy Even if There is a Slight Safety/Tolerability Disadvantage
- Optimizing for a Safe/Tolerable Treatment Even if There is a Slight Efficacy Disadvantage

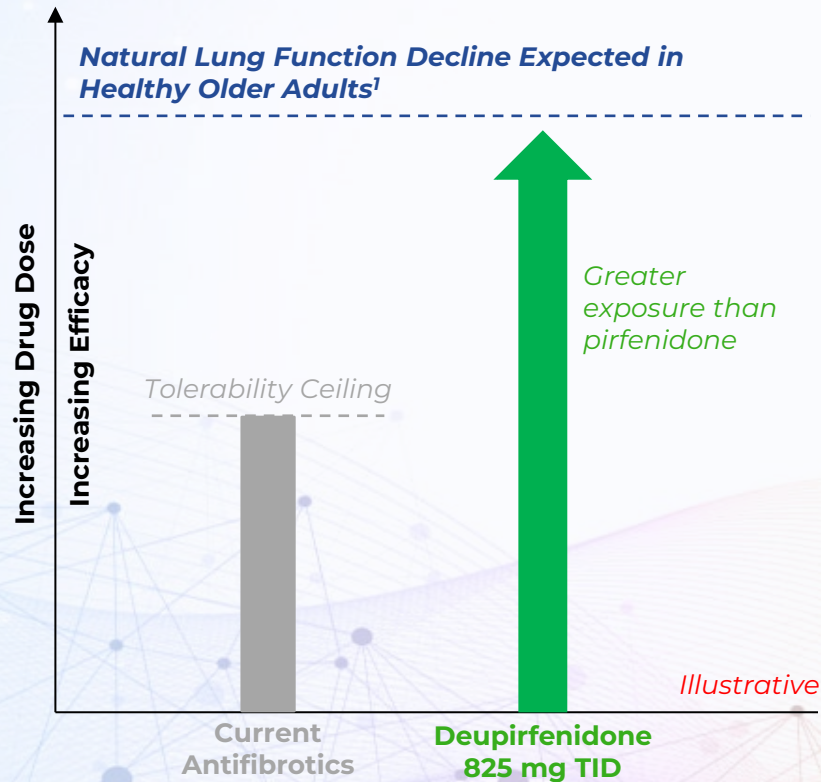
(n=30)

Stabilization of Lung Function is the Ideal Treatment Goal in IPF

Pulmonologists and patients seek improved efficacy without sacrificing tolerability¹



Dose-limiting Tolerability Challenges Have Prevented Patients on SOC from Achieving Greater Efficacy



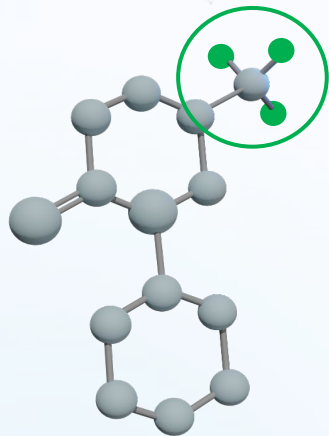
Commonly Reported Side Effects with Use of Current Antifibrotics*	Pirfenidone Label ² (N=623)	Nintedanib Label ³ (N=723)
Nausea	36%	24%
Rash	30%	Not reported
URTI	27%	7%
Diarrhea	26%	62%
Fatigue	26%	<5%
Abdominal Pain	24%	15%
Liver enzyme elevation	<5%	14%
Vomiting	26%	12%

*Select, non-exhaustive list

Introduction to Deupirfenidone

Deupirfenidone Is a Novel Compound with the Potential to Become the Next Standard-of-care Treatment in IPF

STRUCTURE



DEUTERIUM SUBSTITUTION

New chemical entity with strategically placed deuterium (heavy hydrogen) at site of metabolism

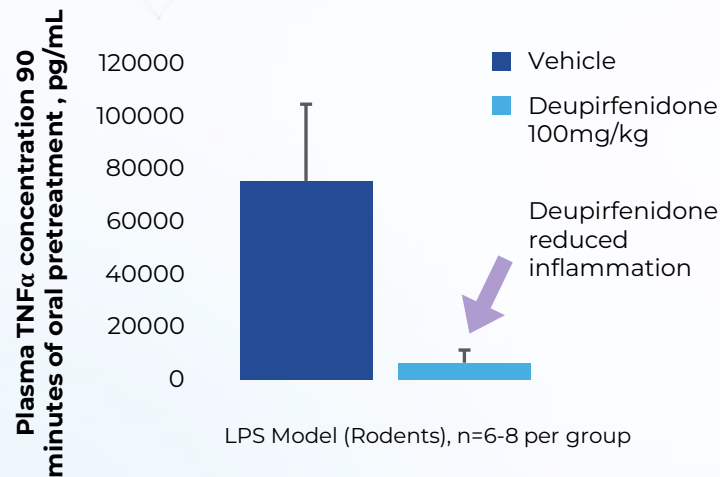
OVERVIEW

- ▶ Leverages clinically validated pirfenidone¹ with **potential for improved efficacy without sacrificing tolerability**
- ▶ Composition of matter patent exclusivity up to 2033 with PTE; Additional broad and layered IP coverage to ~2043

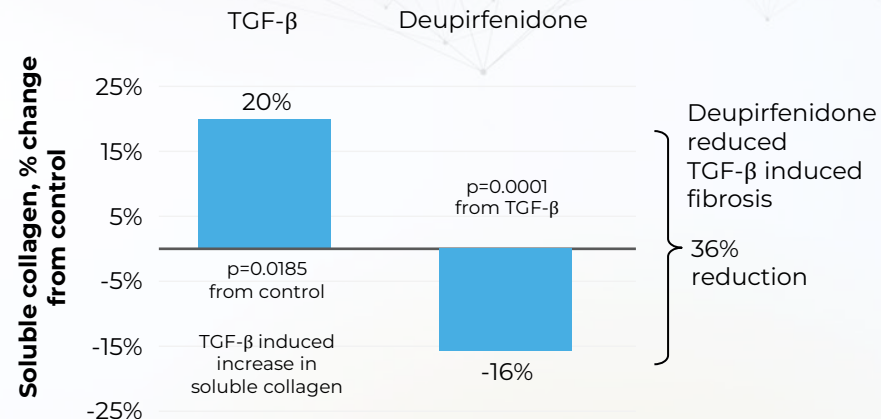
Preclinical Data

Deupirfenidone: Preclinical POC Demonstrates Anti-inflammatory & Anti-fibrotic Pharmacology

PRECLINICAL PLASMA CONCENTRATIONS OF TNF α WITH DEUPIRFENIDONE VERSUS CONTROL

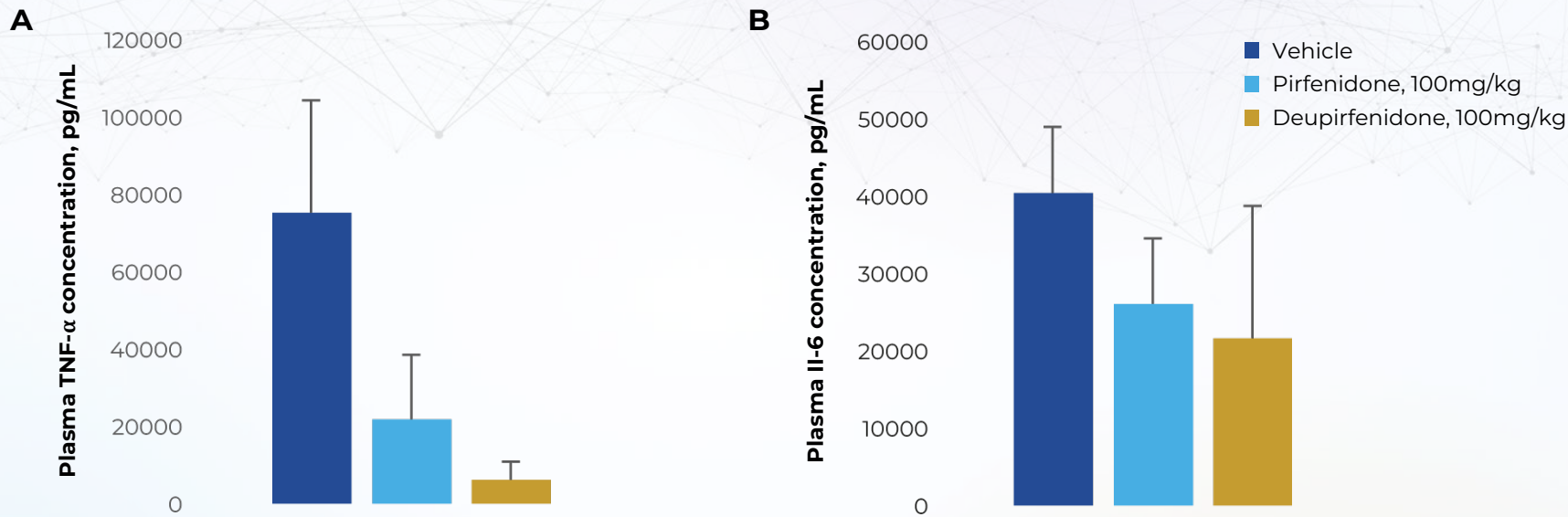


IN VITRO REDUCTION OF TGF- β INDUCED SOLUBLE COLLAGEN PRODUCTION (MOUSE FIBROBLASTS)



Deupirfenidone Preserves Pharmacologic Effect of Pirfenidone

Preclinical data shows improved anti-inflammatory and anti-fibrotic activity vs pirfenidone



Reduction in LPS-stimulated plasma concentrations of TNF- α and IL-6 by pirfenidone or deupirfenidone. Oral doses of vehicle, pirfenidone, or deupirfenidone (100mg/kg) administered 60 minutes prior to LPS (30 μ g/kg intravenous): TNF- α (A) and IL-6 (B) measured 90 min after LPS stimulation: N=6-8 animals per group. Data are presented as mean \pm standard deviation.

Phase 2b ELEVATE Data

ELEVATE Trial Demonstrated Unprecedented Efficacy for Deupirfenidone 825 mg TID



POTENTIAL FOR LUNG FUNCTION STABILIZATION

Deupirfenidone 825 mg TID monotherapy **approached the natural lung function decline expected in healthy older adults**¹



ENHANCED EFFICACY VERSUS CURRENT STANDARD OF CARE

Deupirfenidone 825 mg TID demonstrated a **~50% greater treatment effect than pirfenidone** vs placebo



DURABLE EFFICACY RESPONSE OUT TO 52 WEEKS

Ongoing open-label extension highlights **consistent effect of deupirfenidone** at 52 weeks²

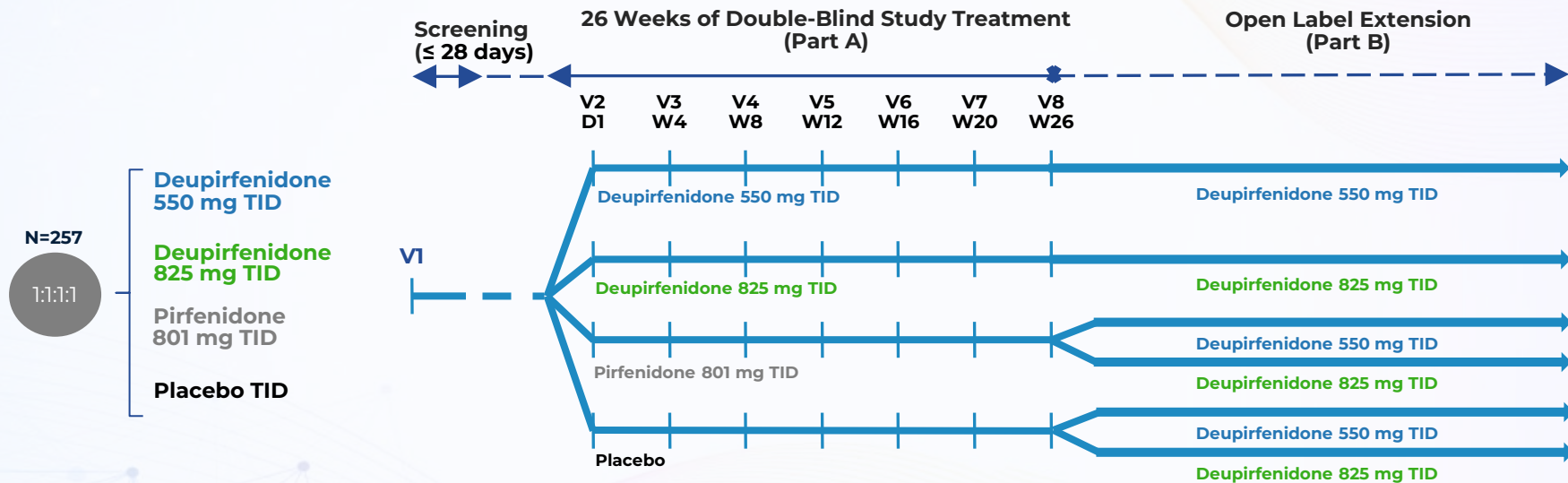


SUPPORTING PHARMACOKINETIC (PK) DATA

Deupirfenidone 825 mg TID had **~50% greater exposure vs. pirfenidone**, which may have driven the greater efficacy observed

Data support potential for deupirfenidone to set a new standard for efficacy in IPF

ELEVATE: Global, Phase 2b, Multicenter, Randomized, Double-blind Clinical Trial



Primary Endpoint
(pooled deupirfenidone arms)

Rate of decline in FVC over 26 weeks

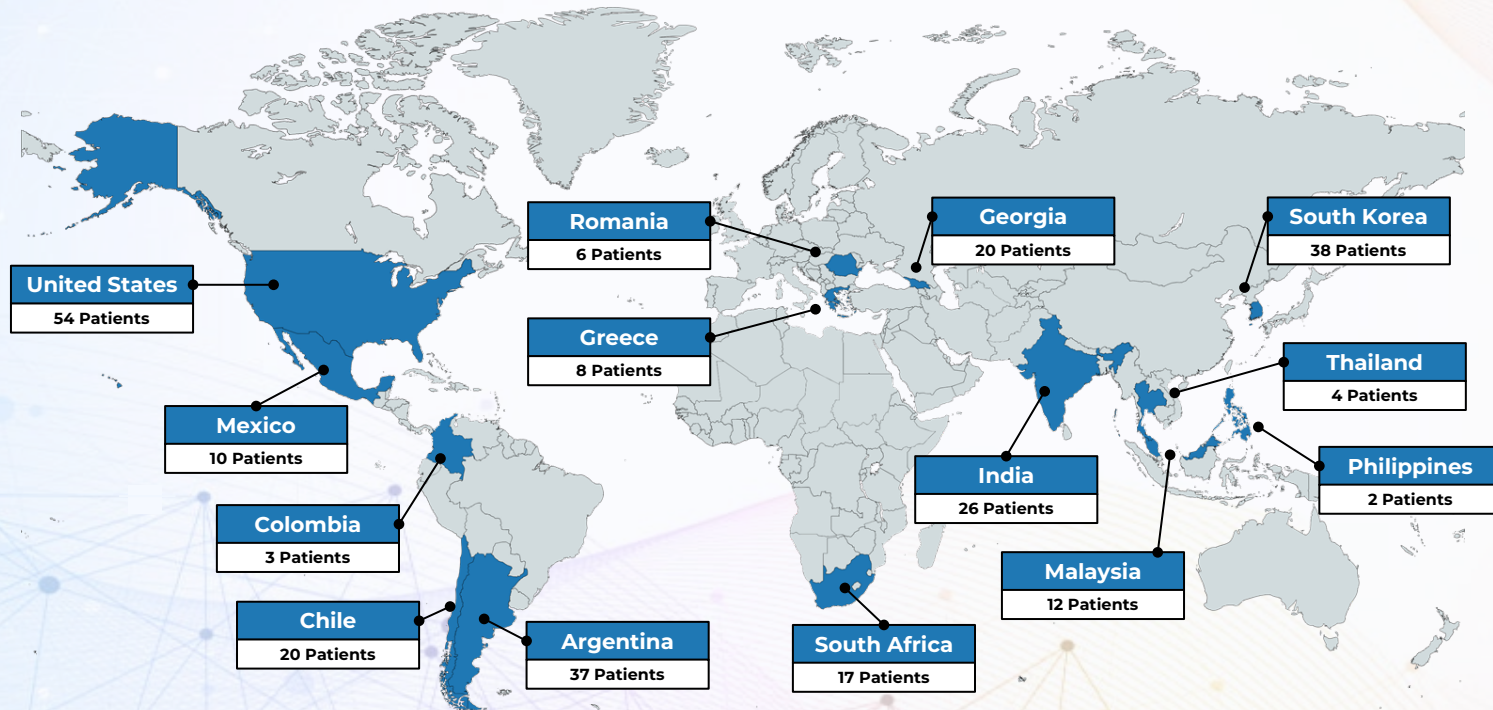
Key Secondary Endpoint

(pooled deupirfenidone arms)

Change in FVC percent predicted from baseline to Week 26

ELEVATE: Global, Phase 2b, Multicenter, Randomized, Double-blind Clinical Trial

257 patients were recruited from 87 sites across 14 countries



KEY DEMOGRAPHIC STATISTICS

- ▶ Median age: 72 years, 13.6% ≥ 80 years
- ▶ 71.2% Male, 28.8% Female
- ▶ 63% White or Caucasian, 33.5% Asian, 1.6% Black or African American, 1.9% Other
- ▶ 26.1% Hispanic or Latino

Overview of ELEVATE Statistical Approach

Commonly used Bayesian¹ and frequentist analyses were applied

BAYESIAN STATISTICS

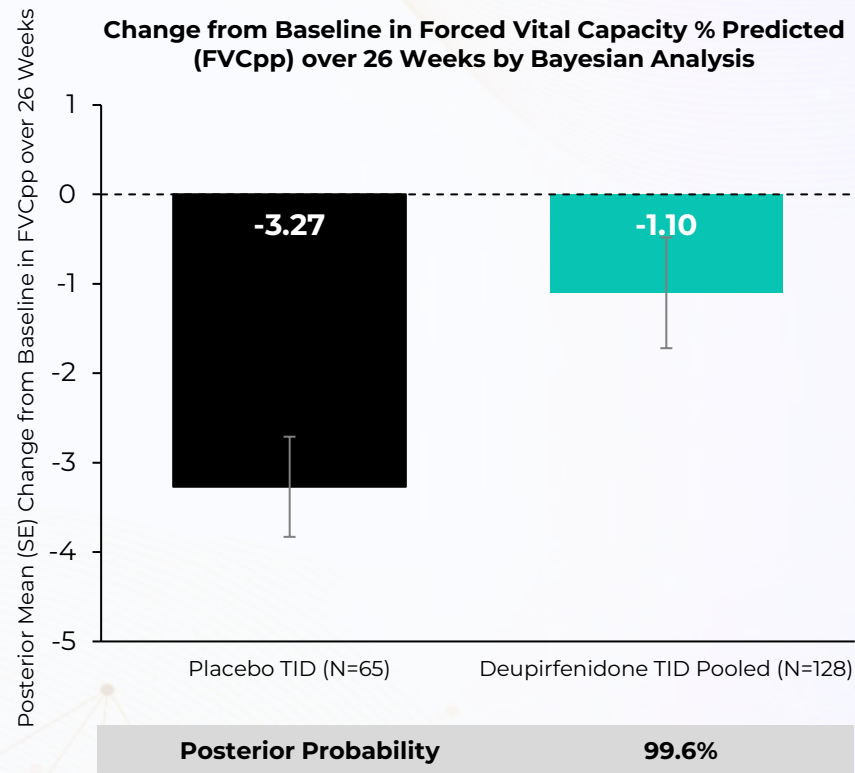
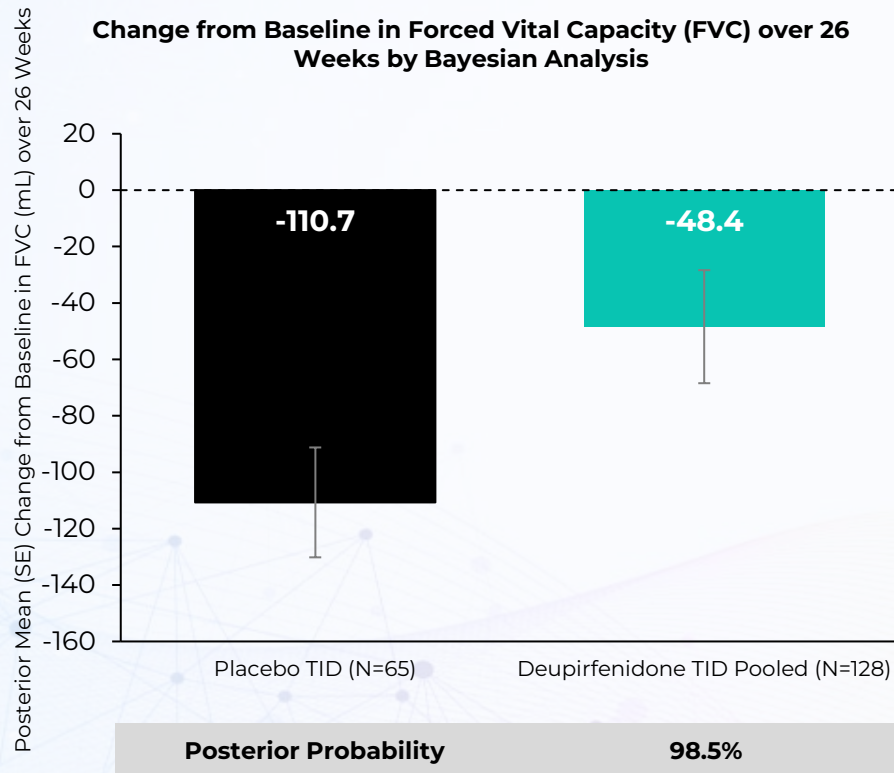
Used for Primary and Key Secondary Endpoints

FREQUENTIST ANALYSIS

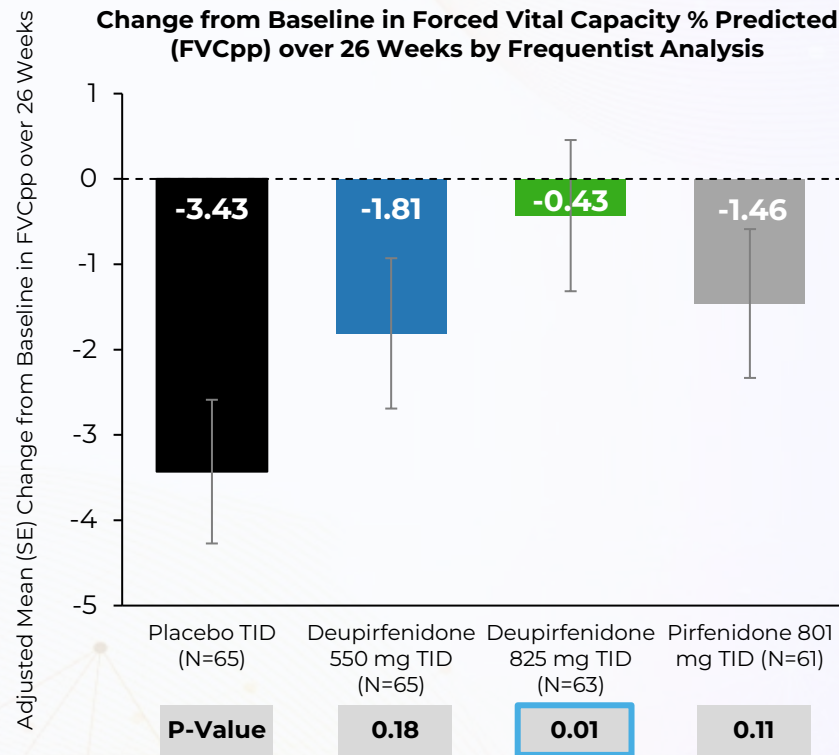
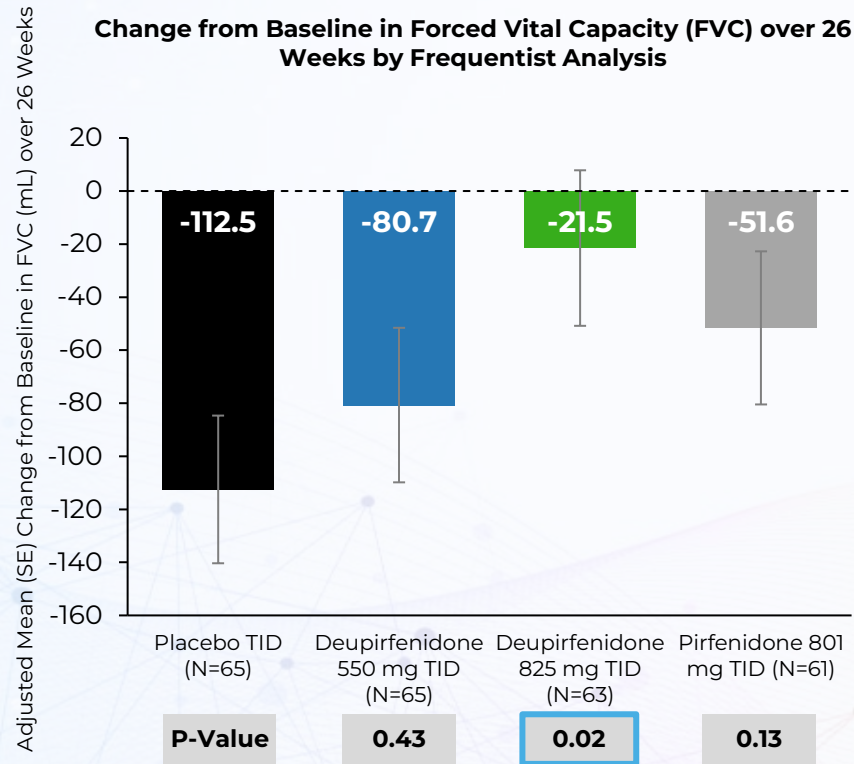
Used for Primary and Key Secondary Endpoints

- ▶ We obtained FVC data per patient over time, commonly referred to as observed data
- ▶ Observed data doesn't account for missing data due to variety of reasons (e.g., drop-outs, missed visits, etc.)
- ▶ The gold standard is to use population-level models, such as mixed models for repeated measures (MMRM), that account for missing data
- ▶ The FDA mandates accounting for missing data in efficacy analyses

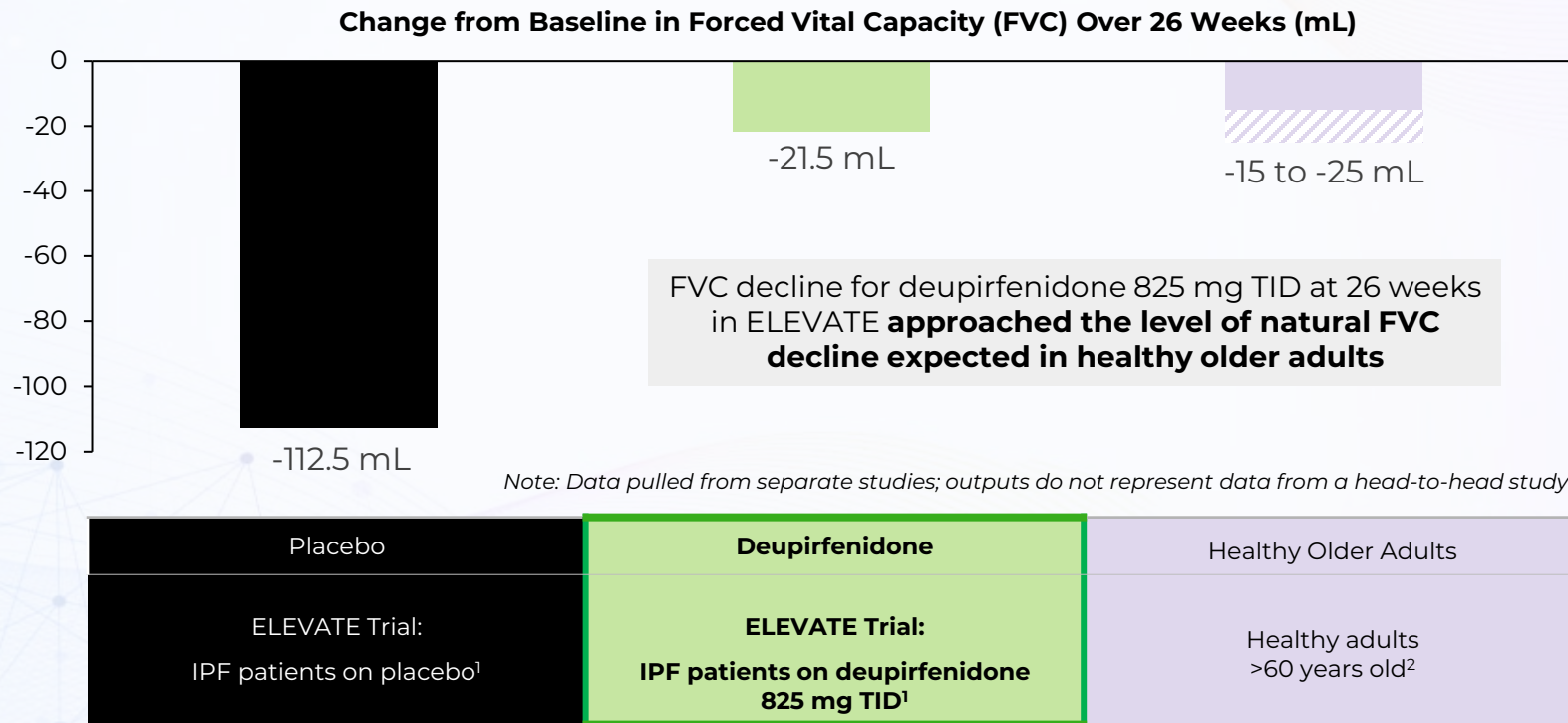
ELEVATE Achieved Primary and Key Secondary Endpoints



Deupirfenidone Demonstrated Potential to Serve as a New Standard-of-Care Treatment for IPF

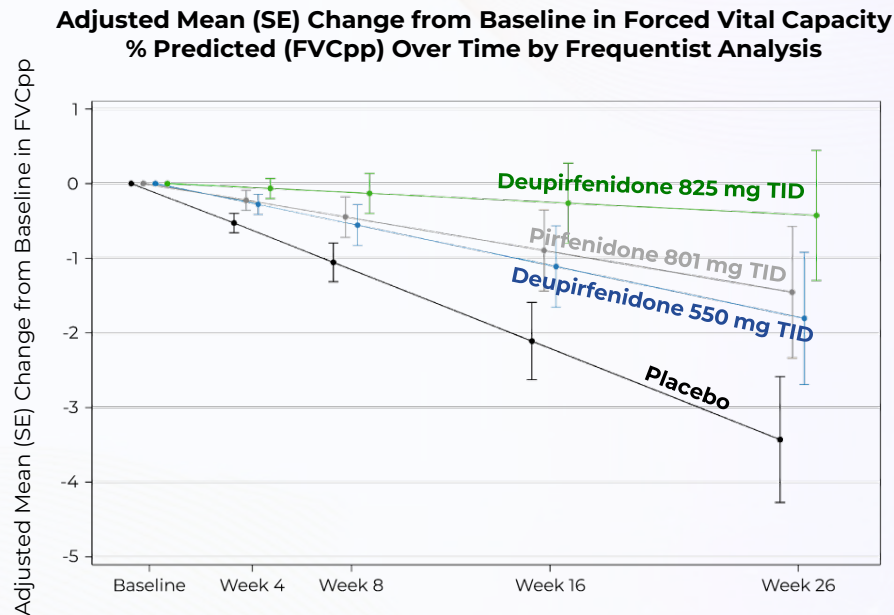
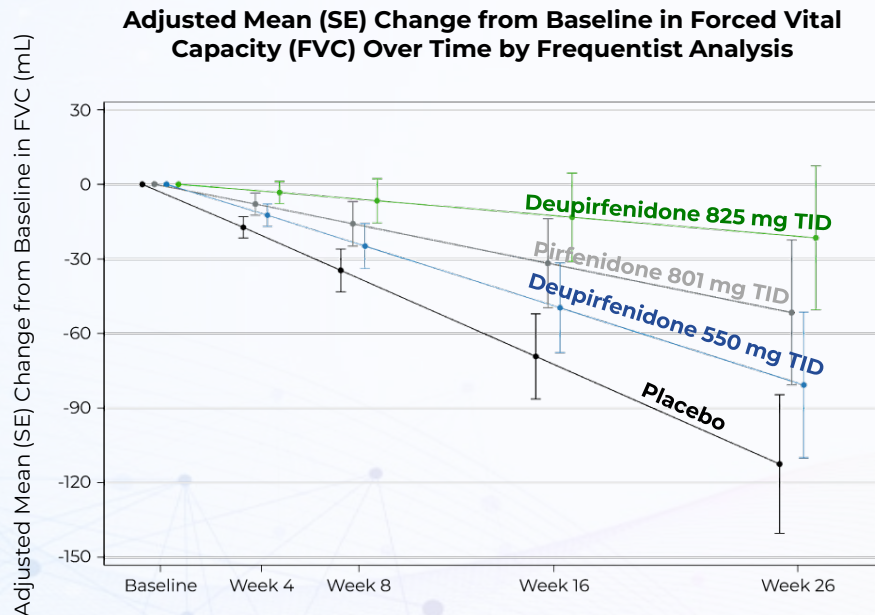


Deupirfenidone 825 mg TID Preserved Lung Function; Rate of Decline Similar to Healthy Older Adults



Deupirfenidone Demonstrated a Clear Dose-dependent Effect

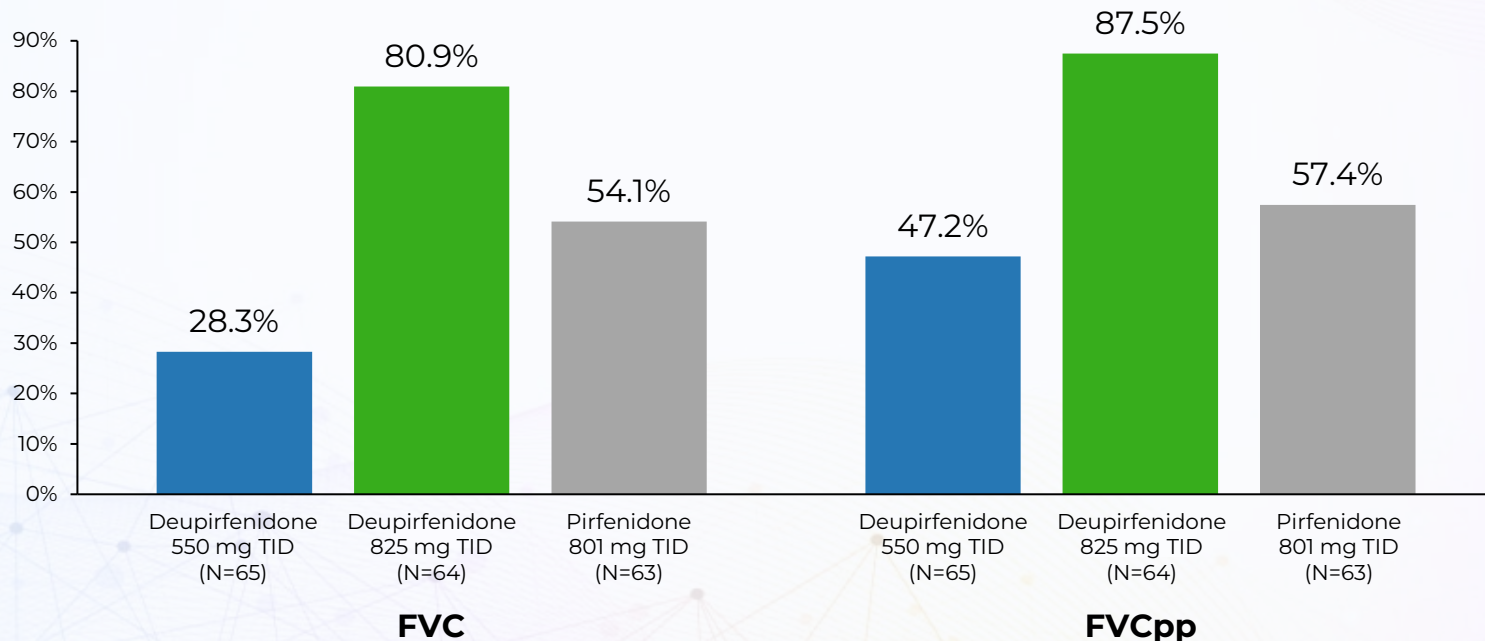
Change from baseline in FVC and FVCpp (Mixed Model Repeated Measure with Random Slope Regression)



● Placebo TID ● Pirfenidone 801 mg TID ● Deupirfenidone 550 mg TID ● Deupirfenidone 825 mg TID

Versus Placebo, Deupirfenidone 825 mg TID Had ~50% Greater Effect Size than Pirfenidone in ELEVATE Trial

Treatment Effect from Change in Forced Vital Capacity (FVC) and Percent Predicted Forced Vital Capacity (FVCpp) Across Arms



PK Analysis From ELEVATE Showed That Deupirfenidone 825 mg TID Has ~50% Greater Exposure than Pirfenidone

Analysis of Estimated AUC for Deupirfenidone and Pirfenidone

	Deupirfenidone 550 mg TID vs. Pirfenidone 801 mg TID		Deupirfenidone 825 mg TID vs. Pirfenidone 801 mg TID	
	AUC Ratio	p-value	AUC Ratio	p-value
PK Population¹ (446 Samples)	~14% Lower	0.1493	~46% Greater	0.0002
Subjects with >95% Adherence² (221 Samples)	~19% Lower	0.0939	~50% Greater	0.0012

ELEVATE PK Summary

- ▶ Deupirfenidone 825 mg TID had **greater exposure** than pirfenidone 801 mg TID, which may have **driven the greater efficacy observed**
- ▶ Increased exposure of 825 mg TID **did not result in increased tolerability challenges**, suggesting the deuterated structure of deupirfenidone may **overcome the dose-limiting adverse events associated with pirfenidone**

Deupirfenidone Had Favorable Tolerability in ELEVATE Trial

Summary of Most Common ($\geq 5\%$ in Any Treatment Group) TEAEs by SOC, PT, and Treatment Group (Safety Set)

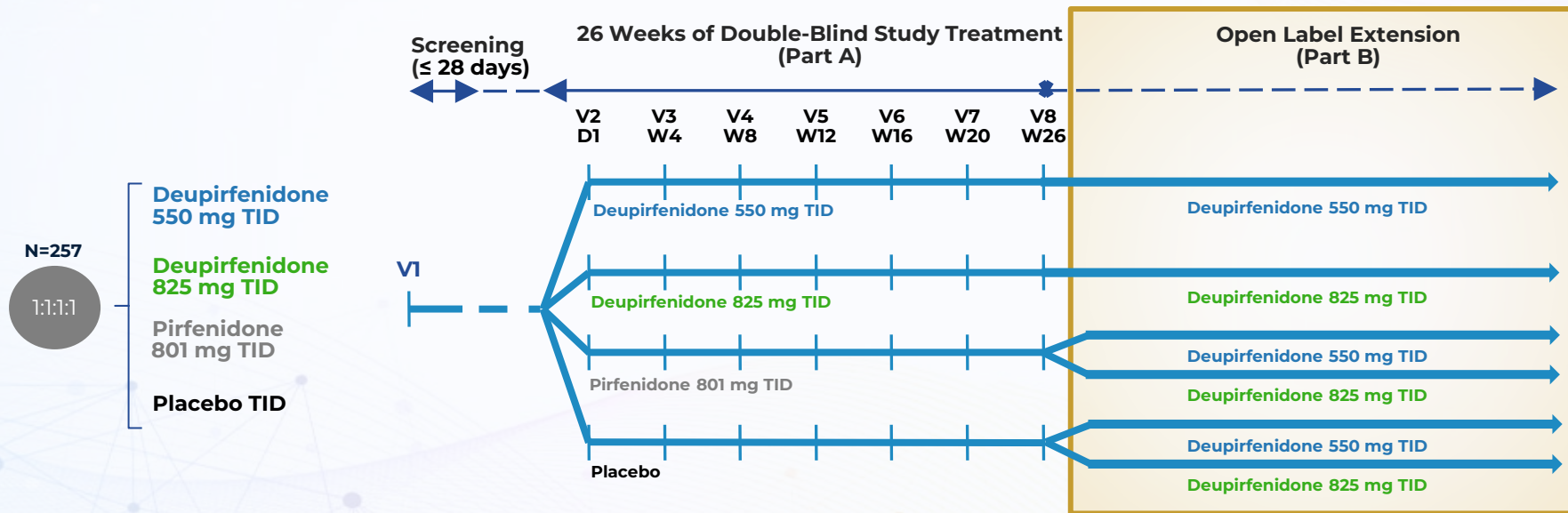
SOC/PT	Placebo TID (N=65) n (%)	Pirfenidone 801 mg TID (N=63) n (%)	Deupirfenidone 550 mg TID (N=65) n (%)	Deupirfenidone 825 mg TID (N=64) n (%)
Nausea	5 (7.7)	17 (27.0)	11 (16.9)	13 (20.3)
Dyspepsia	2 (3.1)	14 (22.2)	8 (12.3)	9 (14.1)
Diarrhea	6 (9.2)	7 (11.1)	7 (10.8)	5 (7.8)
Abdominal pain	3 (4.6)	5 (7.9)	4 (6.2)	9 (14.1)
Upper Respiratory Infections	6 (9.2)	9 (14.3)	8 (12.3)	6 (9.4)
Urinary tract infection	2 (3.1)	5 (7.9)	4 (6.2)	3 (4.7)
Cough	7 (10.8)	3 (4.8)	1 (1.5)	8 (12.5)
IPF (acute exacerbation)	10 (15.4)	2 (3.2)	3 (4.6)	4 (6.3)
Dyspnoea	4 (6.2)	3 (4.8)	2 (3.1)	1 (1.6)
Rash	1 (1.5)	6 (9.5)	3 (4.6)	6 (9.4)
Photosensitivity reaction	0	5 (7.9)	4 (6.2)	5 (7.8)
Pruritus	0	3 (4.8)	5 (7.7)	5 (7.8)
Decreased appetite	5 (7.7)	9 (14.3)	12 (18.5)	13 (20.3)
Dizziness	2 (3.1)	5 (7.9)	6 (9.2)	8 (12.5)
Headache	3 (4.6)	8 (12.7)	5 (7.7)	2 (3.1)
Fatigue	1 (1.5)	7 (11.1)	5 (7.7)	6 (9.4)

Orange = Higher reported incidence than pirfenidone arm
Green = Lower reported incidence than pirfenidone arm

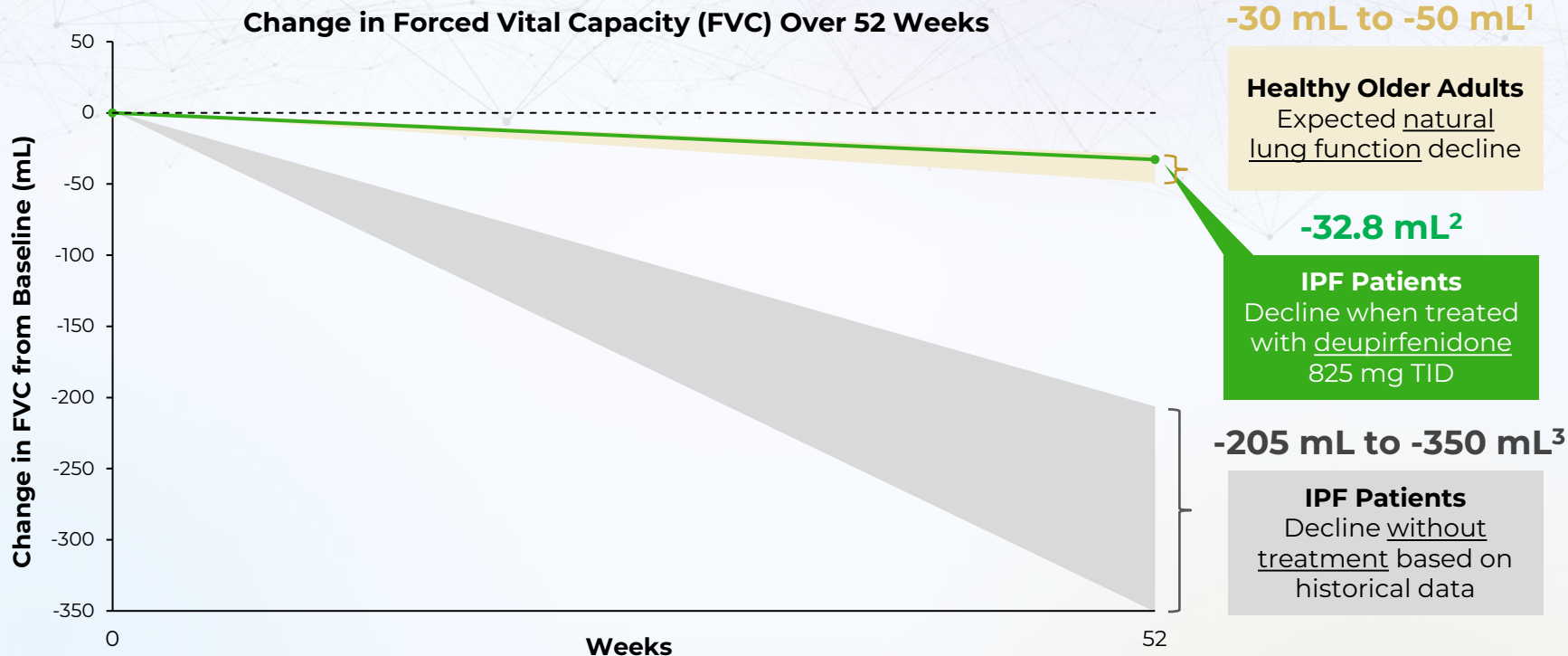
Deupirfenidone's Favorable Tolerability Profile Allows for Higher Drug Exposure and Greater Efficacy



>90% of Patients Opted to Enroll in the Ongoing Open-label Extension



Preliminary Open Label Extension Data Demonstrate Strong and Durable Efficacy with Deupirfenidone 825 mg TID over at Least 52 Weeks



Preliminary 52-week Data (Part A + Part B) Reaffirm Potential for Deupirfenidone to Become a New Standard of Care for IPF

FVC Change from Baseline Over 52 Weeks

Indirect comparison; not based on head-to-head data¹

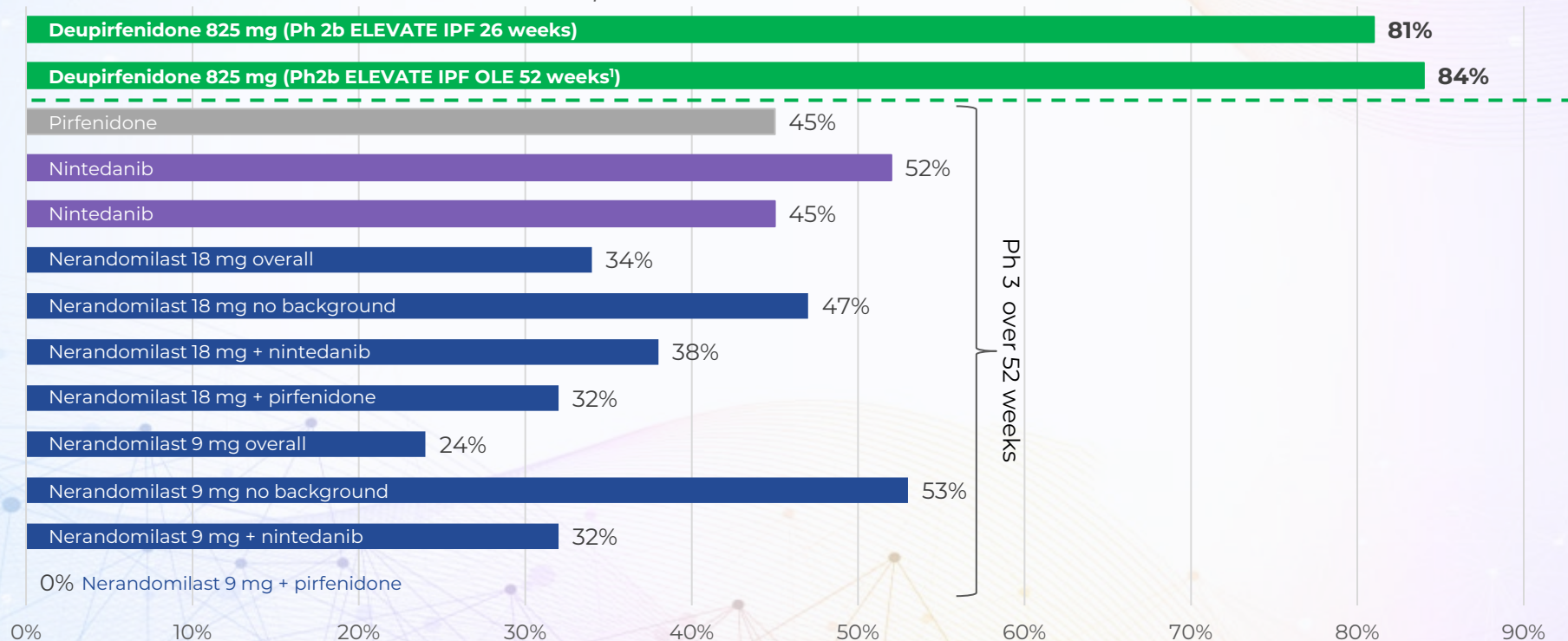
HEALTHY OLDER ADULTS	INVESTIGATIONAL IPF AGENTS	
Expected natural lung function decline	Deupirfenidone 825 mg TID	Nerandomilast Monotherapy (9 mg; 18 mg BID)
-30 to -50 mL ²	-32.8 mL³	-70.4 mL; -79.2 mL ^{4,5}

Additional details from the ongoing open-label extension study are expected to be shared in a future scientific forum

Deupirfenidone Has Demonstrated Potential for Best-in-class Efficacy

FVC Relative Benefit Over Placebo

Indirect comparison. Not based on head-to-head data



Historical IPF Trial Failures & PureTech Differentiation

Deupirfenidone Differentiates from Other IPF Programs

Idiopathic Nature of Disease

Short Phase 2 Trial Duration

Small Study Size

Study Quality

Lack of Active Control

Deviation from Phase 2 Design

Observations From IPF Trial Failures

Evaluating a **new mechanism of action** for an idiopathic disease is inherently risky

Many Phase 2 IPF studies are **12-week trials** that may not be predictive of a 52-week trial (treatment duration required for pivotal)

Smaller Phase 2 trials may not be representative of Phase 3 population

Variability (e.g., outliers, decentralized FVC) in Phase 2 lead to false assumptions for Phase 3

IPF studies have not historically used an active control arm

Phase 3 studies that deviate from their Phase 2 design (e.g., change in dosing or background SOC use) increase technical risk

Deupirfenidone Differentiation

Deupirfenidone builds on >10 years of **established human efficacy** and safety data for pirfenidone

Robust **26-week ELEVATE trial** with deupirfenidone, with additional durable **52-week OLE** data

257 patients in 4 arms. High Dose achieved **statistical significance** vs placebo

No outliers observed in ELEVATE study. Phase 3 trial will include rigorous QC systems employed in ELEVATE

First trial to compare an investigational drug to an approved antifibrotic; pirfenidone and placebo performed as expected, increasing data confidence

Phase 3 design will recapitulate key aspects of ELEVATE (e.g., dose)

Examples:



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Example Phase 2 IPF Trial Failures: Biogen, Galecto, Horizon, Pliant; Example Phase 3 IPF Trial Failures: FibroGen, Galapagos, Roche/Promedior
OLE = open-label extension; TID = three times a day; FVC = forced vital capacity; QC = quality control; SOC = standard of care

Commercial Opportunity

Deupirfenidone Has the Potential to be Best-in-class in IPF

- ✓ **Strong data package as a monotherapy**; first therapy to show potential lung function normalization in IPF
- ✓ **Best-in-class efficacy**: first and only IPF treatment to show improved efficacy over SOC treatment (pirfenidone)
- ✓ **Favorable tolerability**; increased efficacy without compromising tolerability
- ✓ **Promising Phase 3 translatability**; supported by the rigorous/well-run Phase 2b trial

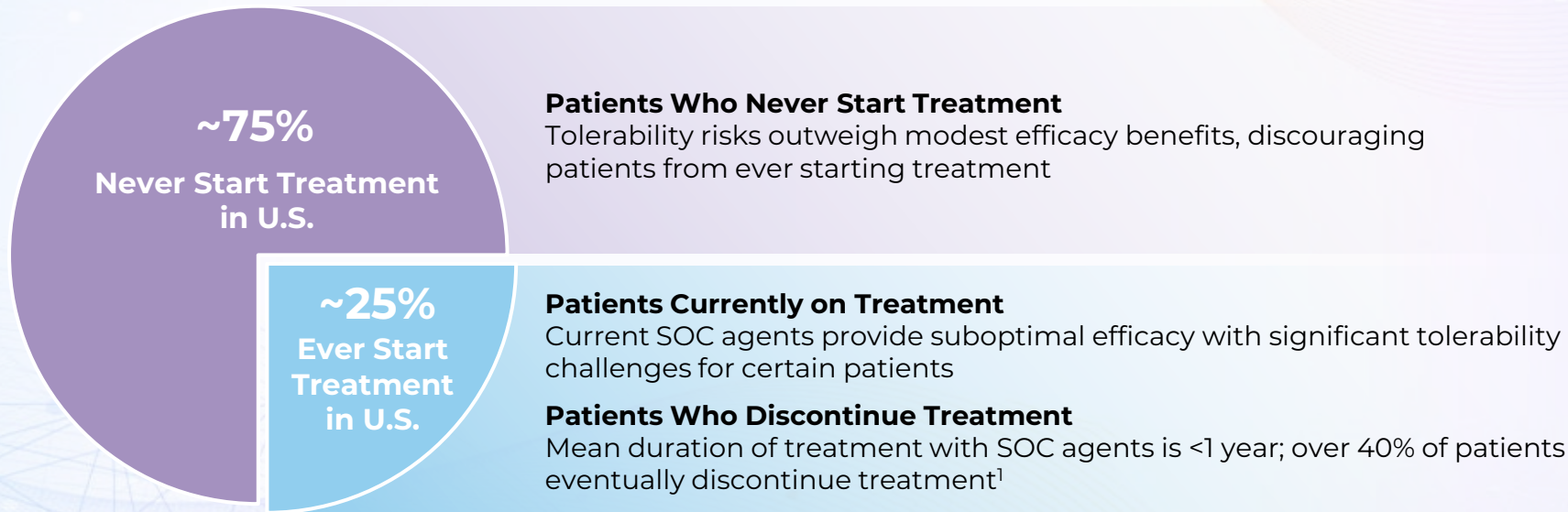
Why Deupirfenidone?



- ✓ **Broad potential to be the new SOC** for IPF patients
- ✓ Estimated total addressable market of **>\$10B** by 2033¹
- ✓ Potential to **capture additional markets** with expansion into non-IPF PF-ILDs
- ✓ **Broad and layered IP** protection

Deupirfenidone Has the Potential to Be Used Across Multiple Patient Segments

Potential to capture patients currently on SOC (~25%) AND expand to those who never start (~75%)



✓ **Deupirfenidone has the potential for significantly improved efficacy without sacrificing tolerability, making it a treatment option for a wide range of IPF patients**

ELEVATE Data Suggests Multi-billion Dollar Revenue Potential

The ELEVATE data for 825 mg TID are a “home run” scenario for deupirfenidone as defined by stakeholder market research

Potential for Best-in-Class Efficacy

- ▶ Versus placebo, 825 mg TID dose **showed 50% better efficacy than pirfenidone**
- ▶ Stabilization of lung function will **set a new standard for IPF treatment**

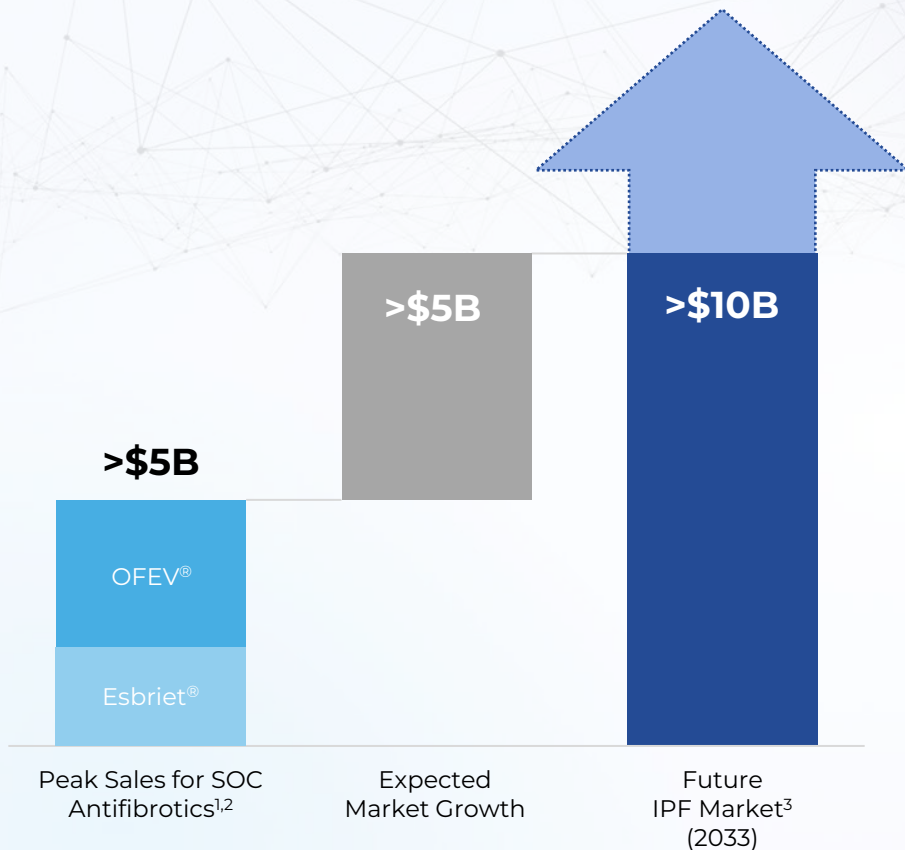
Addresses Stakeholder Needs

- ▶ Pulmonologist market research conducted pre-ELEVATE readout suggested **~50% FVC improvement relative to pirfenidone would be highly attractive**

Potential for Significant Revenue

- ▶ 825 mg TID data suggests **blockbuster potential in IPF**, with **additional upside in other ILDs**

IPF Market Has the Potential for Substantial Market Growth



Global IPF Market:

- Despite **only ~25%** of IPF patients ever starting therapy⁴, SOC agents have achieved blockbuster status
- Expected market growth in coming years is driven by:
 - 1) **Increased patient uptake & adherence** via the development of more efficacious and better tolerated therapies
 - 2) **Increased disease awareness / diagnosis**
- Beyond IPF, deupirfenidone has the potential to capture **additional markets** with expansion into non-IPF PF-ILDs

Potential to Expand into Other Progressive, Fibrotic Diseases with High Unmet Need

Progressive pulmonary fibrosis (PPF), also termed progressive fibrotic ILD (PF-ILD), is estimated to affect ~675,000 patients in the US and EU5

CURRENT ADDRESSABLE MARKET:

US AND EU5 >232,000 patients¹



FUTURE ADDRESSABLE MARKETS:

+ ~675,000 additional patients²

PF-
Connective
Tissue
Disease -
ILD

PF -
Sarcoidosis

Unclassifiable
PF-ILD

PF - Chronic
Fibrotic
Hypersensitivity
Pneumonitis

PF -
Idiopathic
Non-Specific
Interstitial
Pneumonia

Other PPFs

TOTAL FUTURE ADDRESSABLE MARKET: >900K IPF and other PPF Patients