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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

IPF STUDY 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



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



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



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 & EU51

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

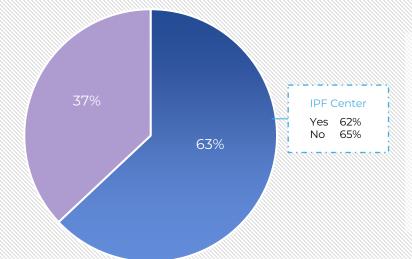


¹ GlobalData Epidemiology and Market Size Search, EUS=United Kingdom, France, Germany, Italy and Spain; ² Barratt SL, Creamer A, Hayton C, Chaudhuri N. Idiopathic Pulmonary Fibrosis (IPF): An Overview. J Clin Med. 2018 Aug 6;7(8):201; ³ Fisher, M., Nathan, S. D., Hill, C., Marshall, J., Dejonckheere, F., Thuresson, P., & Maher, T. M. (2017), Predicting Life Expectancy for Pirfenidone in Idiopathic Pulmonary Fibrosis. Journal of Managed Care & Specialty Pharmacy, 23(3-b Suppl), S17–S24. https://doi.org/10.18553/jmcp.2017.233-b.s17; *4 ESBRIET (pirfenidone) and OFEV (nintedanib) were approved in 2014; *5 Dempsey TM, Payne S, Sangaralingham L, Yao X, Shah ND, Limper AH. Adoption of the Antifibrotic Medications Pirfenidone and Nintedanib for Patients with Idiopathic Pulmonary Fibrosis. Ann Am Thorac Soc. 2021 Jul;18(7):1121-1128.

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)



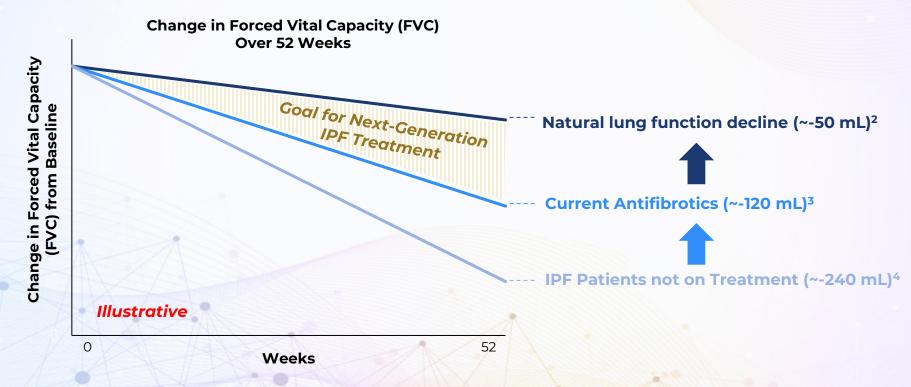


- Pushing for Incremental Efficacy Even if There is a Slight Safety/Tolerability Disadvantage
- Optimizing for a Safe/Tolerable
 Treatment Even if There is a Slight
 Efficacy Disadvantage

(n=30)

Stabilization of Lung Function is the Ideal Treatment Goal in IPF

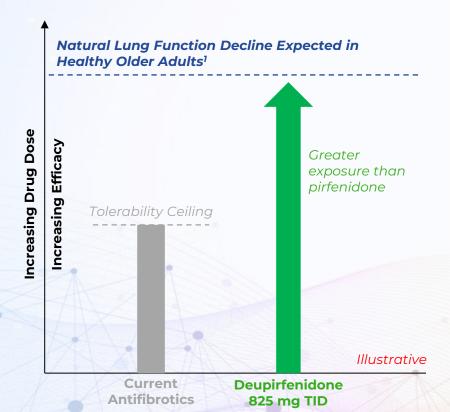
Pulmonologists and patients seek improved efficacy without sacrificing tolerability¹



VING LIFE TO SCIENCE

¹Per market research survey of 50 pulmonologists conducted by Day & Associates. No pricing information/assumptions was shared. Research completed in October 2024 based on hypothetical product profiles using the results of the Phase 1 healthy older adult crossover study. ²Per Valenzuela. Boehringer Ingelheim. ERS 2024 and Luoto. Eur Respir J. 2019. ³ Based on pirfenidone and nintedanib's pivotal studies. ⁴Raman, Lavanya et al. ⁴Nintedanib for non-IPF progressive pulmonary fibrosis: 12-month outcome data from a real-world multicentre observational study. ²ERJ open research vol. 9,2 00423-2022. 20 Mar. 2023, doi:10.1183/23120541.00423-2022.

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



Commonly Reported Side Effects with Use of Current Antifibrotics*Pirfenidone Label² (N=623)Nintedanib Label³ (N=723)Nausea36%24%Rash30%Not reportedURTI27%7%Diarrhea26%62%Fatigue26%<5%Abdominal Pain24%15%Liver enzyme elevation<5%14%			
Rash 30% Not reported URTI 27% 7% Diarrhea 26% 62% Fatigue 26% <5% Abdominal Pain 24% 15% Liver enzyme elevation <5% 14%	Effects with Use of	Label ²	Label ³
URTI 27% 7% Diarrhea 26% 62% Fatigue 26% <5%	Nausea	36%	24%
Diarrhea 26% 62% Fatigue 26% <5%	Rash	30%	Not reported
Fatigue 26% <5% Abdominal Pain 24% 15% Liver enzyme elevation <5% 14%	URTI	27%	7%
Abdominal Pain 24% 15% Liver enzyme elevation <5% 14%	Diarrhea	26%	62%
Liver enzyme elevation <5% 14%	Fatigue	26%	<5%
	Abdominal Pain	24%	15%
Versiting 260/ 120/	Liver enzyme elevation	<5%	14%
VOITILITY 20% 12%	Vomiting	26%	12%

^{*}Select, non-exhaustive list



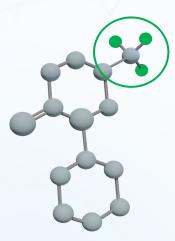
Introduction to Deupirfenidone



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

STRUCTURE

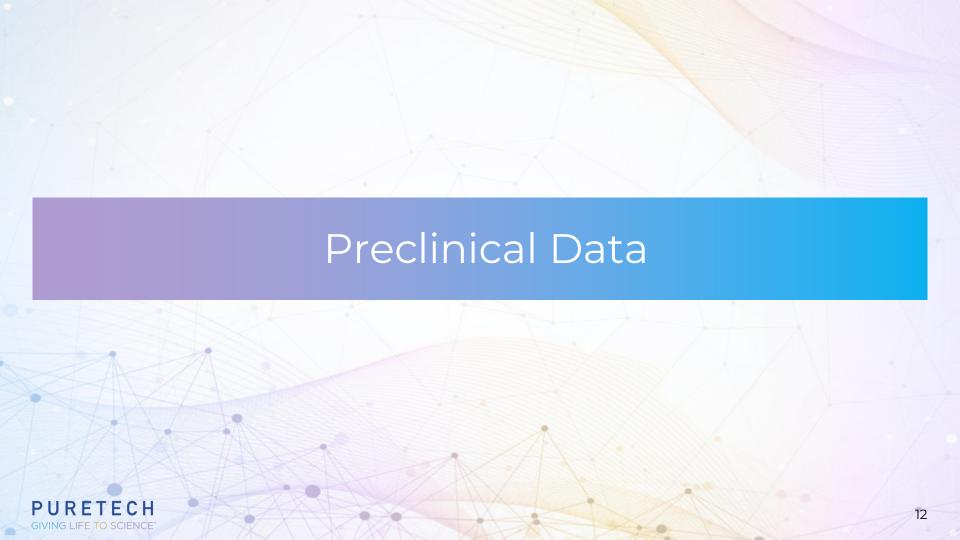
OVERVIEW



DEUTERIUM SUBSTITUTION

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

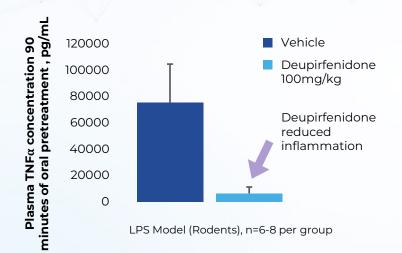
- Leverages clinically validated pirfenidone¹
 with potential for improved efficacy without sacrificing tolerability
- Composition of matter patent exclusivity up to 2033 with PTE; Additional broad and layered IP coverage to ~2043

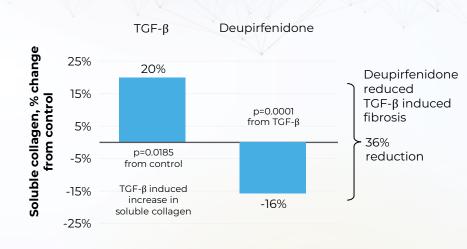


Deupirfenidone: Preclinical POC Demonstrates Antiinflammatory & Anti-fibrotic Pharmacology

PRECLINICAL PLASMA
CONCENTRATIONS OF TNFA WITH
DEUPIRFENIDONE VERSUS CONTROL

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



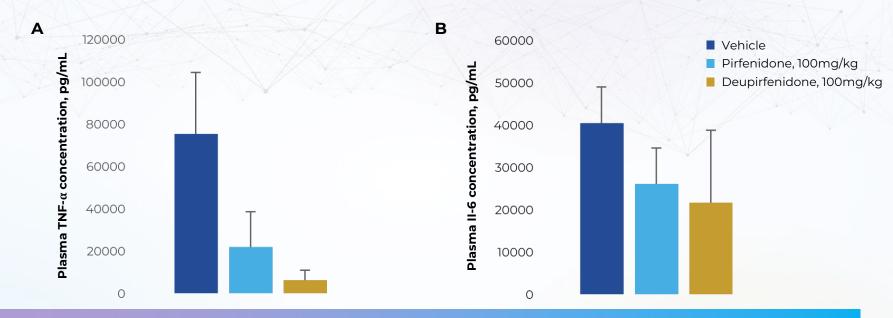




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Deupirfenidone Preserves Pharmacologic Effect of Pirfenidone

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 +/- standard deviation.



Phase 2b ELEVATE Data



ELEVATE Trial Demonstrated Unprecedented Efficacy for Deupirfenidone 825 mg TID



FUNCTION
STABILIZATION

Deupirfenidone 825 mg TID monotherapy approached the natural lung function decline expected in healthy older adults¹



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



SUPPORTING PHARMACOKINETIC (PK) DATA

Ongoing open-label extension highlights consistent effect of deupirfenidone at 52 weeks² Deupirfenidone 825 mg TID had **~50% greater exposure vs. pirfenidone**, which may have driven the greater efficacy observed

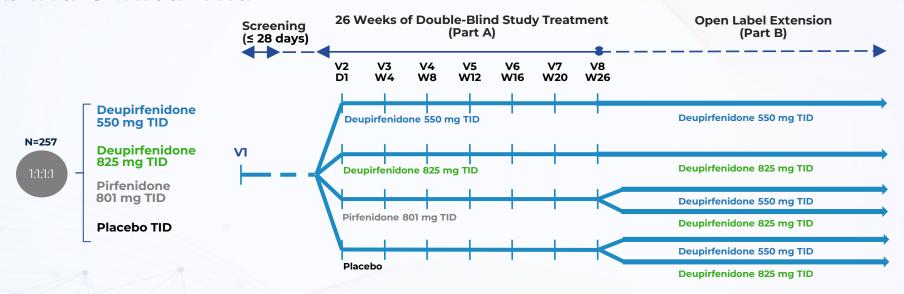
Data support potential for deupirfenidone to set a new standard for efficacy in IPF



¹ FVC decline at 6 months was estimated assuming linear decline over time. Valenzuela, C., Bonella, F., Moor, C., Weimann, G., Miede, C., Stowasser, S., Maher, T. (2024). Decline in forced vital capacity (FVC) in subjects with idiopathic pulmonary fibrosis (IPF) and progressive pulmonary fibrosis (IPF) compared with healthy references. Poster presented at the European Respiratory Society International Congress, Vienna, Austria; and Luoto, J., Pihlsgård, M., Wollmer, P., & Elmståhl, S. (2019). Relative and absolute lung function change in a general population aged 60-102 years. The European Respiratory Journal, 53(3), 170812. https://doi.org/10.1183/13993003.01812-2.017. Per integrated analysis of double-blind and preliminary open-label extension data from Phase 2b ELEVATE IPF trial as of May 9, 2025, using a random coefficient regression model with absolute FVC including baseline as response variable and week, treatment and interaction between week and treatment as fixed effect.

FVC: Forced Vital Capacity.

ELEVATE: Global, Phase 2b, Multicenter, Randomized, Doubleblind Clinical Trial



Primary Endpoint

(pooled deupirfenidone arms)

Rate of decline in FVC over 26 weeks

Key Secondary Endpoint

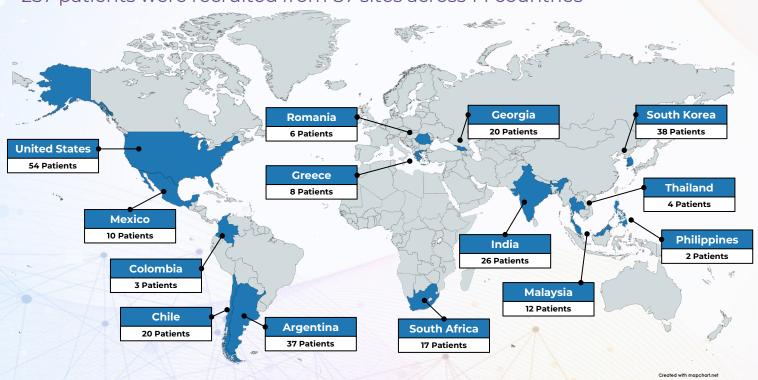
(pooled deupirfenidone arms)

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

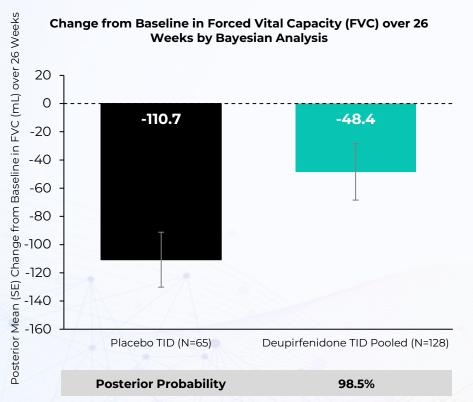
FREQUENTIST ANALYSIS

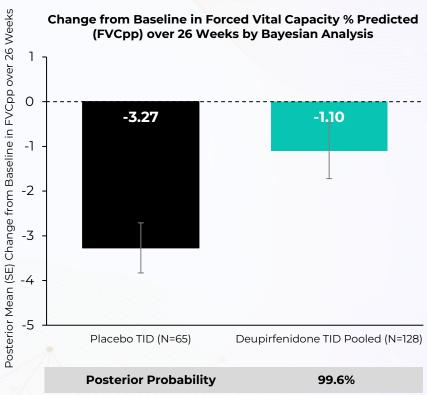
Used for Primary and Key Secondary Endpoints

- ► 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



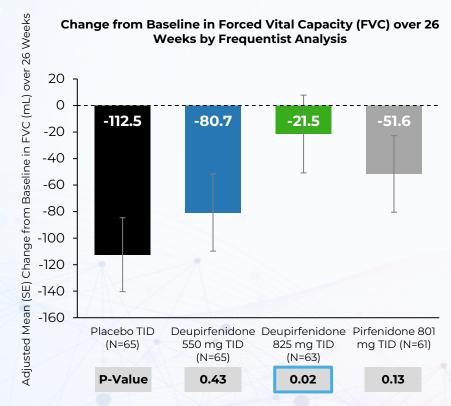
ELEVATE Achieved Primary and Key Secondary Endpoints

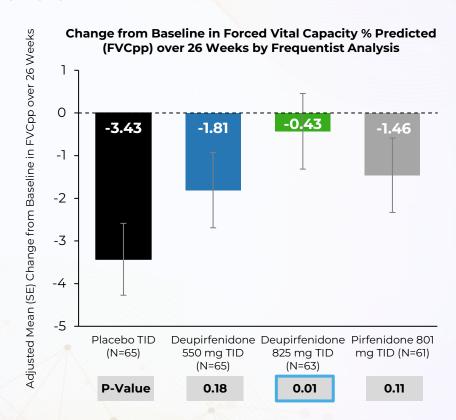






Deupirfenidone Demonstrated Potential to Serve as a New Standard-of-Care Treatment for IPF



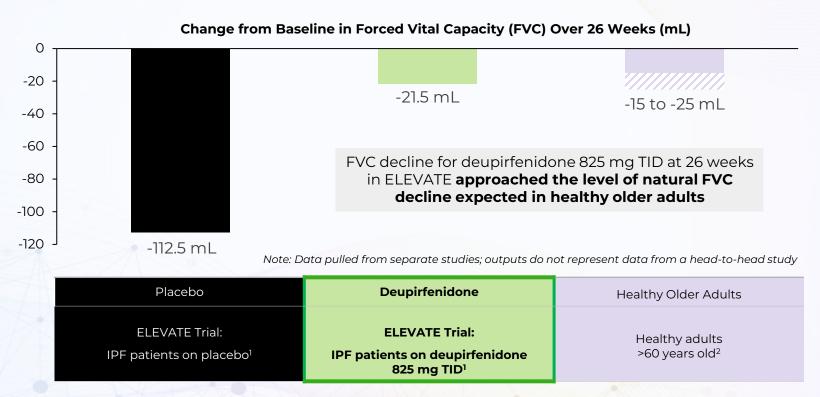




Efficacy analyses used a random coefficient regression model with absolute FVC or FVCpp including baseline as response variable and week, treatment and interaction between week and treatment as fixed effect. The analyses were performed based on the predefined Full Analysis Set. p values are two-sided and have not been corrected for multiplicity. Note: Change from baseline FVC is not adjusted for patient characteristics such as height, age, race, or sex.

TID = 3 times per day

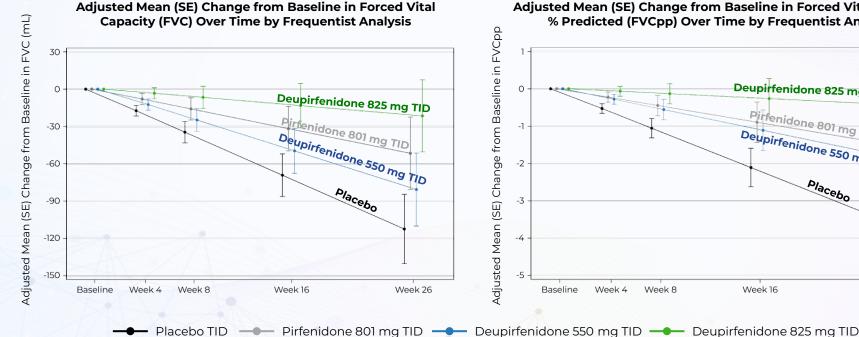
Deupirfenidone 825 mg TID Preserved Lung Function; Rate of Decline Similar to Healthy Older Adults



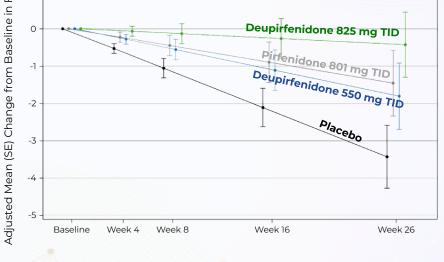


Deupirfenidone Demonstrated a Clear Dose-dependent Effect

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



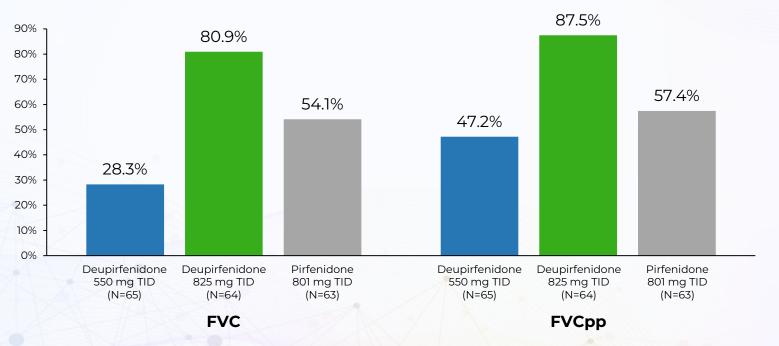






Versus Placebo, Deupirfenidone 825 mg TID Had ~50% Greater Effect Size than Pirfenidone in ELEVATE Trial

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 Population ¹ (446 Samples)	<mark>~14%</mark> Lower	0.1493	<mark>~46%</mark> Greater	0.0002
Subjects with >95% Adherence ² (221 Samples)	<mark>~19%</mark> Lower	0.0939	<mark>~50%</mark> 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 (≥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

Deuteration PK
Differentiation

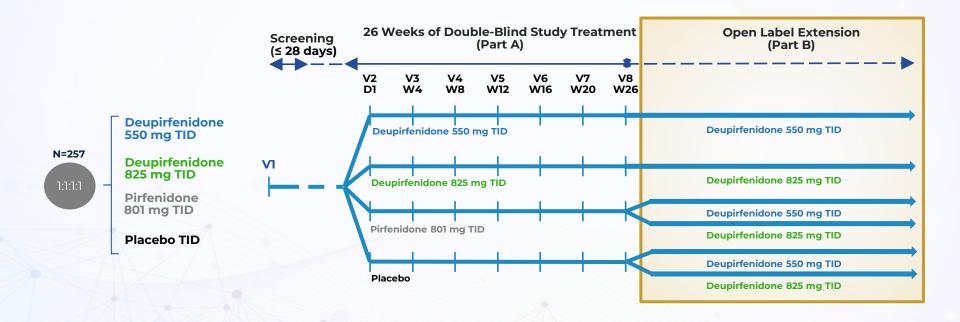
Favorable
Tolerability
Profile

Higher
Dose & Higher
Exposure

Greater
Efficacy

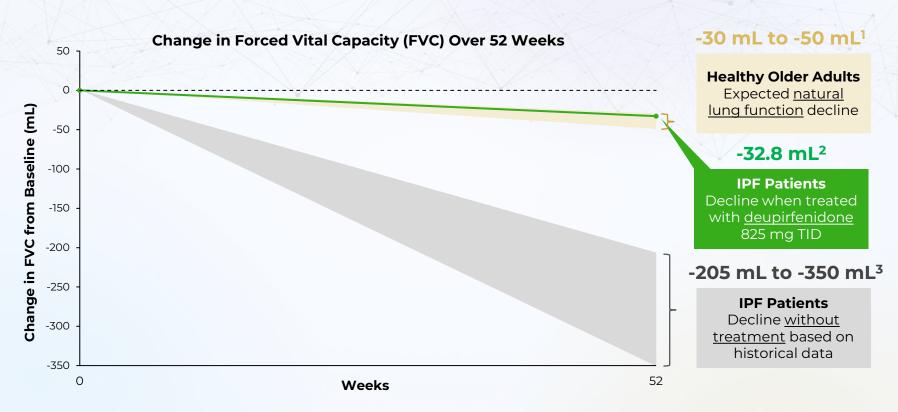


>90% of Patients Opted to Enroll in the Ongoing Open-label Extension





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



PURETECH

GIVING LIFE TO SCIENCE*

¹ Per Valenzuela. Boehringer Ingelheim. ERS 2024 and Luoto. Eur Respir J. 2019.

² Integrated analysis of double-blind and preliminary open-label extension data from Phase 2b ELEVATE IPF trial as of May 9, 2025, using a random coefficient regression model with absolute FVC including baseline as response variable and week, treatment and interaction between week and treatment as fixed effect.

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 mL ³	-70.4 mL; -79.2 mL ^{4,5}	

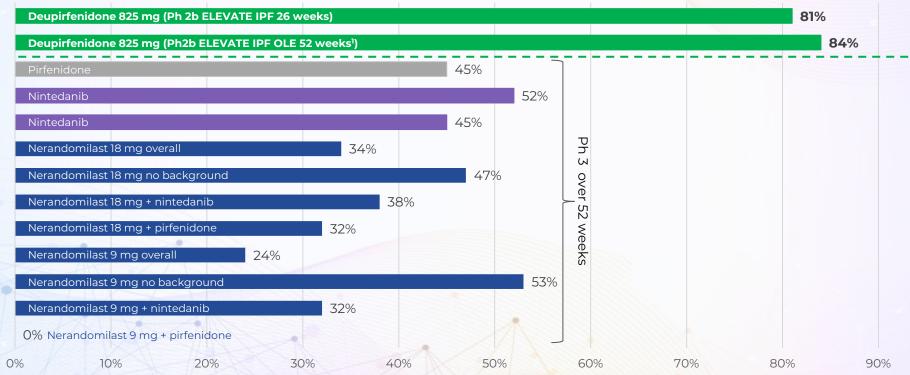
Additional details from the ongoing open-label extension study are expected to be shared in a future scientific forum



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

Observations From IPF Trial Failures

Idiopathic Nature of Disease

Short Phase 2 Trial Duration

Small Study Size

Study Quality

Lack of Active Control

Deviation from Phase 2 Design

Examples:

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)





Commercial Opportunity PURETECH

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%)

~**75**%

Never Start Treatment in U.S.

Patients Who Never Start Treatment

Tolerability risks outweigh modest efficacy benefits, discouraging patients from ever starting treatment

~25%
Ever Start
Treatment
in U.S.

Patients Currently on Treatment

Current SOC agents provide suboptimal efficacy with significant tolerability challenges for certain patients

Patients Who Discontinue Treatment

Mean duration of treatment with SOC agents is <1 year; over 40% of patients eventually discontinue treatment¹

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

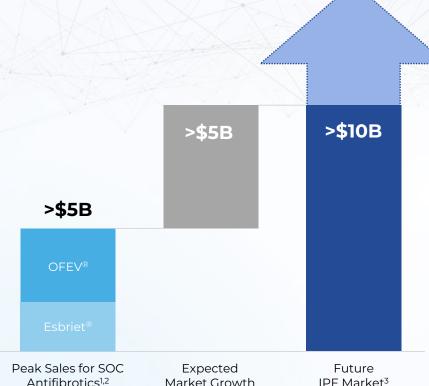
Pulmonologist market research conducted pre-ELEVATE readout suggested
 *50% FVC improvement relative to pirfenidone would be highly attractive

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

Market Growth

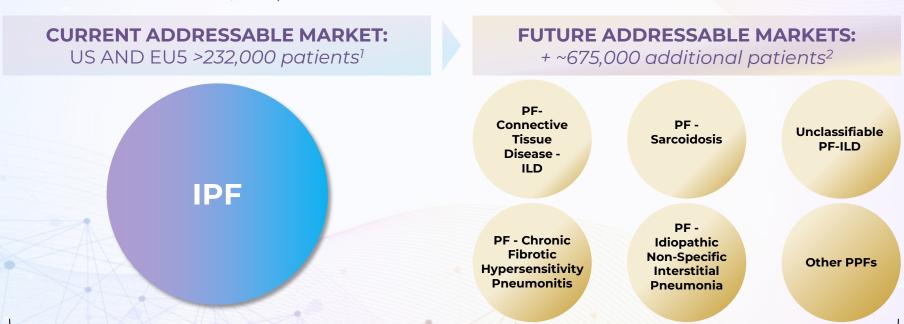
IPF Market³ (2033)



Note: Certain third-party trademarks are included here; PureTech does not claim any rights to any third-party trademarks... IPF = Idiopathic pulmonary fibrosis; SOC = Standard of care; PF-ILD = Progressive Fibrosing Interstitial Lung Disease, 1 Boehringer Ingelheim 2024 Financial Results, Ofev peak sales (2024) include those for all approved indications – IPF, PF-ILD, and systemic sclerosis-associated interstitial lung disease (SSc-ILD), 2 Roche 2021 Financial Results. Esbriet peak sales (2020), 3 Straits Research Report, Idiopathic Pulmonary Fibrosis Market Size, Share & Trends Analysis Report By Drug Type (Nintedanib, Pirfenidone, Other Drug Types), By Mode of Action (Antifibrotic Agents, Tyrosine Kinase Inhibitors, Other Modes of Action), By End-User (Hospitals and Clinics, Pharmacies, Other end-users) and By Region (North America, Europe, APAC, Middle East and Africa, LATAM) Forecasts, 2025-2033; 4 Dempsey TM, Payne S, Sangaralingham L, Yao X, Shah ND, Limper AH. Adoption of the Antifibrotic Medications Pirfenidone and Nintedanib for Patients with Idiopathic Pulmonary Fibrosis. Ann Am Thorac Soc. 2021 Jul;18(7):1121-1128.

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



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

