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This document and the Presentation contain statements that are or may be fonward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. We intend such forward-looking statements to be covered by the safe harbor provisions for forward looking statements contained in Section 27A of the U.S. Securities Act of 1933, as amended and Section 21E of the Exchange Act of 1934, as amended. These statements are based on our management's current beliefs, expectations and assumptions about future events, conditions and results, and on information currently available to us. This document and the Presentation also contain estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

All statements other than statements of historical facts included in this document and the Presentation should be considered forward-looking statements, including without limitation, statements that relate to our expectations around our and our Founded Entities' therapeutic candidates and approach towards addressing major diseases, operational plans, future prospects, objectives, developments, strategies and expectations, the progress and timing of clinical trials and data readouts, the timing of regulatory approvals or clearances from the FDA, our future results of operations and financial outlook, including our anticipated cash runway and our forecasted cash, cash equivalents and short-term investments, and our ability to realize value for our shareholders.

Words such as "expect," "anticipate," "intend," "plan," "believe," "seek," "estimate," 'think," "may," "could," "will," "would," "continue," "potential," "likely," "opportunity" and similar expressions or variations of such words are intended to identify forward-looking statements, but are not the exclusive means of identifying forward-looking statements. Additionally, statements concerning future matters such as our expectations of business and market conditions, development and commercialization of new products, enhancements of existing products or technologies, and other statements regarding matters that are not historical are forward-looking statements.

The forward-looking statements are based on current expectations and currently available operating, financial and competitive information and are subject to known and unknown risks, uncertainties and other important factors that could cause actual results, performance and achievements to differ materially from current expectations, including, but not limited to, the following: our history of incurring significant operating losses since our inception; our ability to realize value from our Founded Entities; our need for additional funding to achieve our business goals, which may not be available and which may force us to delay, limit or terminate certain of our therapeutic development efforts; our limited information about and limited control or influence over our Non-Controlled Founded Entities; the lengthy and expensive process of preclinical and clinical drug development, which has an uncertain outcome and potential for substantial delays; potential difficulties with enrolling patients in clinical trials, which could delay our clinical development activities; side effects, adverse events or other safety risks which could be associated with our therapeutic candidates and delay or halt their clinical development; our ability to obtain regulatory approval for and commercialize our therapeutic candidates; our ability to compete with companies currently marketing or engaged in the development of treatments for indications within our programs are designed to target; our ability to realize the benefits of our collaborations, licenses and other arrangements; the impact of government laws and regulations; our ability to maintain and protect our intellectual property rights; our reliance on third parties, including clinical research organizations, clinical investigators and manufacturers; our vulnerability to natural disasters, global economic factors, geopolitical actions and unexpected events; and the risks, uncertainties and other important factors described under the caption "Risk Factors" in our Annual Report on Form 20-F for the year ended December 31, 2024 filed with the SEC and in our other regulatory filings. These forward-looking statements are based on assumptions regarding the present and future business strategies of the Company and the environment in which it will operate in the future.

Given these risks, uncertainties and other factors, many of which are beyond the Company's control, you should not place undue reliance on these forward-looking statements.

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Our Founded Entities are comprised of Founded Entities we control and Founded Entities we do not control, all of which are incorporated in the United States. We formed each of our Founded Entities and have been involved in development efforts in varying degrees. In the case of Founded Entities we control, we continue to maintain majority voting control. With respect to Founded Entities we do not control, we may benefit from appreciation in our minority equity investment as a shareholder of such companies.



## Our Proven and Seasoned Team



**Bharatt Chowrira, PhD, JD** 

Chief Executive Officer

30+ years of leadership roles as CEO, President, COO, and GC held in multiple biotechs; including former COO at Auspex (acq. by Teva \$3.5B), COO at Nektar, GC at SIRNA (acq. by Merck \$1.1B), VP at Merck & Co.; Board Member



Eric Elenko, PhD
Co-founder & President

Co-founder and acting C-level executive of multiple PureTech founded entities (e.g., Karuna Therapeutics.) Leading innovation and development of internal PureTech programs in PureTech's "hub." Former consultant at McKinsey & Company.



Michael Inbar, CPA, MBA
Chief Accounting Officer

Former CFO at Acronis Inc.; Previously interim CFO at Wallarm, Inc.; Held several leadership roles at Solid Biosciences, Inc., Syros Pharmaceuticals, Inc., and GlassHouse Technologies, Inc.



Robert Lyne, JD

Chief Portfolio Officer

Former CEO at Arix Bioscience (acq. by RTW Biotech \$250M); Previously at Touchstone Innovations, Bird & Bird; worked on >80 VC financings as well as multiple trade exits & IPOs.



Charles Sherwood, JD

General Counsel

Former VP, Corporate Legal Counsel at Anika Therapeutics with extensive expertise in strategic transactions, IP, product & brand marketing, financing securities compliance.



Spencer Ball Executive VP, HR

Former Director, Talent Acquisition/Executive Search at PAREXEL International; Previously at Ball & Company, J. Robert Scott/Fidelity Investments, PAR Associates, and The Onstott Group.



Frank Salisbury Senior VP, Commercial & Product Strategy

Held leadership roles at Acceleron, Sage Therapeutics, Genentech, and Actelion, among others; Oversaw the launch of ESBRIET (pirfenidone) for IPF in the US.



Allison Mead Talbot

Senior VP, Communications

Former leader at award-winning PR agencies, TogoRun (FleishmanHillard) & Feinstein Kean Healthcare (Ogilvy); Extensive experience in healthcare, tech, policy, and patient advocacy.



Anita Terpstra, PhD, JD

Senior VP, IP

Former Sr. Patent Counsel, and later as Associate General Counsel at Synlogic; Previously at Sigma-Aldrich, McDonnell, Boehnen, and Hulbert & Berghoff.



Luba Greenwood, JD

Entrepreneur-in-Residence

Currently serves as the Founder & Managing Partner of the Dana Farber Cancer Institute Venture Fund, Binney Street Capital (BSC) & Board of several biopharmaceutical companies; Former CEO & Chair of the Board at Kojin Therapeutics.



Sven Dethlefs, PhD

Entrepreneur-in-Residence

Former Executive Vice President & CEO at Teva North America; A pharmaceutical leader with 25+ years of experience in P&L leadership, R&D strategy, manufacturing, M&A, business transformation, capital markets, and board management.

## Our World Class Board of Directors

Our board has contributed to **regulatory approvals of over 20 drugs** and has led multi-billion-dollar strategic transactions



Raju Kucherlapati, PhD
Board Chair
Harvard, Co-Founder of Millennium (acq. by
Takeda \$8.8B) & Abgenix (acq. by Amgen \$2.2B)



Sharon Barber-Lui
Board
CFO & Senior VP of Teva Pharma, Former CFO of
Merck & Co. Inc. U.S. Oncology & Senior VP of
EQRx



Robert Langer, ScD
Board
MIT, Award winning materials science pioneer,
Former member of the US FDA's SCIENCE
Board, Co-founder of multiple biotech
companies incl. Moderna & PureTech



Michele Holcomb, PhD
Board
Former EVP, Chief Strategy and Business
Development Officer at Cardinal Health, SVP of
Strategy, Portfolio, Search & Partnership of Teva,
McKinsey & Company



John LaMattina, PhD

Board

Former President of Pfizer Global R&D, Forbes
Contributor



Robert Horvitz, PhD

Board Observer & Chair of R&D Committee
Nobel Prize in Medicine, MIT, HHMI,
neurobiologist at MGH, Former Novartis
Scientific Advisory Board Member



Kiran Mazumdar-Shaw
Board
Founder & Chairperson of Biocon, Board of
Trustees Member at MIT, Member of National
Academy of Engineering



Senior Advisor & Board Observer
Founder & CEO of Seaport Therapeutics, BIO
Board Member, Founding CEO of PureTech,
Named to STAT's 2025 STATUS list, amongst
other top industry recognitions

## 2024 & Early 2025 Highlights

Successful clinical trial readouts

\$339.1M

PureTech Level Cash, Cash Equivalents and Short-term Investments as of March 31, 2025<sup>1</sup>



FDA approval COBENFY (1) \$397.5M

Amount of funding secured for Founded Entities<sup>2</sup> (>88% came from 3<sup>rd</sup> parties)







\$327.4M

Proceeds generated from Founded Entity monetization events<sup>3</sup>





## Our Innovative R&D Approach with Track Record of Success



>80%

Clinical trial success rate1

3

FDA Approvals
Including the most recent
landmark approval of
COBENFY.



## Our Portfolio of First & Best-in-Class Medicines

Robust portfolio of new medicines balances risk with potential for tremendous growth

**PROGRAMS** INDICATION **PRECLINICAL** PHASE 1 PHASE 2 PHASE 3 Deupirfenidone Idiopathic Pulmonary Fibrosis (LYT-100) (IPF) 100% Equity1 Acute myeloid leukemia (AML) **Gallop Oncology** High-risk myelodysplastic LYT-200 100% Equity1 syndrome (MDS)

#### **PURETECH-FOUNDED PROGRAMS<sup>2</sup>**



**COBENFY.** □ FDA approved for schizophrenia in adults

Seaport Therapeutics 35.6% Equity

Neuropsychiatric conditions



C. Difficile
Ulcerative colitis



Peptide therapeutics (e.g., GLP-1 agonists)



Completed ////// In progress

Voice-based Al platform

PURETECH

Wholly-Owned Programs are comprised of the Company's current and future therapeutic candidates and technologies that are developed by the Company's wholly-owned gubsidiaries, whether they were announced as a Founded Entity or not, and will be advanced through with either the Company's current and Callop Oncology, inc. and included per primarily the programs were developed by the wholly-owned repetition of the Company's wholly-owned repetition of Callop Oncology, inc. and included primarily the programs were developed by the Tech in which Pure Tech maintains ownership of an equity interest and, in certain cases, is eligible to receive sublicense income and royalities on product sales. Relevant ownership interests were calculated on a partially diluted basis (as opposed to vioring basis) as of December 37, 2024, including outstanding shares, options and warrants, glue reculting unallocated shares. Pure Tech controls, inc.? 3 And March, inc.? 3 And Mar

## Karuna Therapeutics Case Study

A wholly owned subsidiary of Bristol Myers Squibb as of March 18, 2024

- ► **COBENFY** (formerly Karuna's KarXT) now FDA approved for the treatment of schizophrenia in adults
- ▶ 1<sup>st</sup> new mechanism for treating schizophrenia in over 50 years

## **PURETECH'S ROLE**

- ▶ PureTech invented & filed patents to cover KarXT
- ► PureTech funded and executed the early derisking human studies
- PureTech is entitled to milestone payments/ royalties

~\$400M<sup>3</sup> **Regulatory &** 

\$18.5M

Total PRTC spend<sup>1</sup>

~\$1.5B

Potential Upside Value<sup>2</sup>



total PureTech principal investment in Karuna; 2 Represents the amounts described in footnote 3 plus the amounts described in footnote 4:3 Represents the \$400 million in potential milestone payments included in PureTech's transaction with Royalty PureTech also may not receive the totality of the milestone payments under its transaction with Royalty Pharma; "A Represents cash generated to date through sales of KRTX common stock and the \$100 million in upfront consideration from PureTech's transaction with Royalty Pharma; 5 As of March 22, 2023, PureTech has sold its right to receive a 3% royalty from Karuna to Royalty Pharma on net sales up to \$2 billion annually, after which threshold PureTech will receive 67% of the royalty payments and Royalty

Additional economics

payments from Karuna/BMS

commercial milestones

under Royalty Pharma

Cash generated to

date through equity sales, milestone

payment from the Royalty Pharma transaction

payments, and upfront

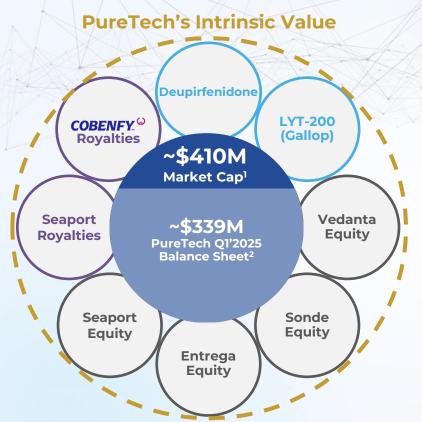
and 2% royalty on annual sales

including milestone

above \$2B<sup>5</sup>

transaction

## Significant Upside Potential Across PureTech's Portfolio



## WHOLLY-OWNED PROGRAMS

**Deupirfenidone (LYT-100):** Potential new SOC for IPF in a >\$10B TAM<sup>3</sup>

**LYT-200:** First-in-class monoclonal antibody for AML and other leukemias in a >\$5B TAM<sup>4</sup>

on analyst estimates of \$4-11B<sup>5</sup> peak sales through 2033)

## FOUNDED ENTITIES EQUITY STAKES

Substantial equity holdings across 4 Founded Entities

## **ROYALTIES, MILESTONES & SUBLICENSE INCOME**

- Up to \$400M in milestone payments from Royalty Pharma
  2% royalties on annual sales > \$2B (up to \$125M/year based)
- Milestone payments on certain Cobenfy<sup>™</sup> regulatory approvals
- **3-5% royalties** on Glyph product sales
- Milestone and sublicense payments
- 35.6% equity stake following >\$325M raised in 2024



## 2025 Capital Allocation Overview

Our hub-and-spoke model enables self-funding operation & disciplined capital allocation



## WHOLLY-OWNED PROGRAMS<sup>1</sup>

## Deupirfenidone (LYT-100) (Phase 3 Ready)

- Exploring various financing mechanisms to support funding the Phase 3 trial (e.g., spinout, project/royalty-based financing, strategic partnerships)
- PureTech will continue to fund the program in the interim

## LYT-200 (Phase 1b ongoing)

• Pursuing external financing; PureTech will continue to fund the program in the interim

#### **FOUNDED ENTITIES<sup>2</sup>**

 Continued support for Founded Entities to the extent helpful with their financing, as well as to maintain certain equity ownership

#### **NEW INNOVATIONS**

Initial expenditures on any new innovation/sourcing to be relatively low

## **OPERATIONAL & TAX EXPENSES**

Continued public company operating expense & US tax obligations

Additionally, potential capital returns to maximize shareholder value



SOC = Standard of care; IPF = Idiopathic pulmonary fibrosis; AML = Acute myeloid leukemia. 1 Wholly-Owned Programs are comprised of the Company's current and future therapeutic candidates and technologies that are developed by the Company's wholly-owned subsidiaries including PureTech LYT, Inc., PureTech LYT100, Inc. and Gallop Oncology, Inc. and included primarily the programs deupirferiadone (LYT-100) and LYT-200; Founded Entities represent companies founded by PureTech in the maintains ownership of an equity interest and, in certain cases, is eligible to receive subliciense income and royalties on product sales. Relevant ownership of an activation of a partially diluted basis (as opposed to a voting basis) as of December 3, 1,2024, including outstanding shares, options and warrants, but excluding unallocated shares authorized to be issued pursuant to equity incentive plans. PureTech and Royalty Pharmar will receive 33% additionally, under its license agreement with Karuna, PureTech retains the right to also receive ecrtain when the solid provided in the product of the product of the provided provided in the provided p

## Our Key Components of Value MAXIMIZING STAKEHOLDER VALUE CAPITAL ROYALTIES, **MILESTONES AND RETURNS** STRONG WHOLLY-OWNED **FOUNDED ENTITY OUR PEOPLE. SUBLICENSE BALANCE SHEET PROGRAMS EQUITY VALUE R&D ENGINE** INCOME 3 FDA approvals



cash, cash equivalents and short-term investments is a non-IFRS measure.

Wholly-Owned Program

Deupirfenidone (LYT-100)

100% Equity

Successful completion of Phase 2b ELEVATE IPF trial

Initiation of Phase 3 trial by YE 2025



## 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



# Unmet Needs in IPF PURETECH

## 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 function<sup>2</sup>



~2-5 years

Life expectancy of IPF without treatment<sup>3</sup>



Two

FDA-approved agents to treat IPF<sup>4</sup>

For most patients, tolerability challenges outweigh suboptimal efficacy



~25%

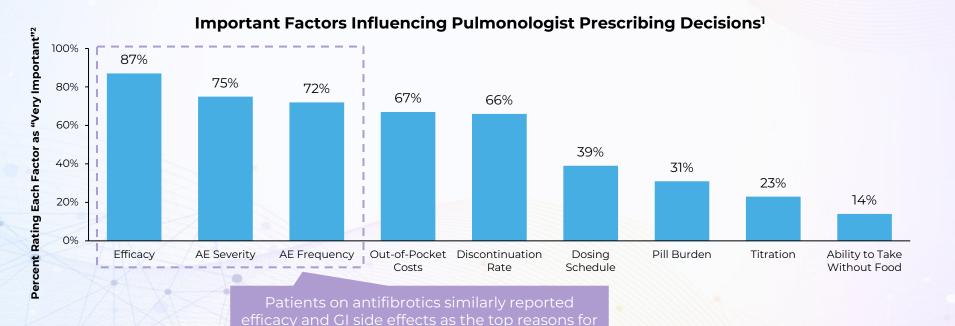
IPF patients ever start antifibrotic treatment

...of which >40% eventually discontinue⁵



# Pulmonologists Ranked Efficacy as the Top Driver for Prescribing Decisions in IPF, Followed By Tolerability

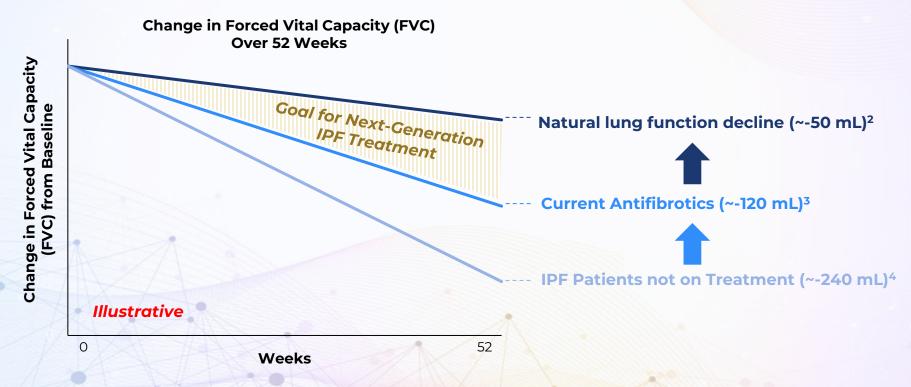
Balancing efficacy with tolerability is key to achieving improved disease management





## Stabilization of Lung Function is the Ideal Treatment Goal in IPF

Pulmonologists and patients seek improved efficacy without sacrificing tolerability<sup>1</sup>



PURETECH

GIVING LIFE TO SCIENCE

## IPF Patients Need Better Treatment Options

Current standard-of-care treatments offer suboptimal efficacy with tolerability challenges

## CHALLENGES WITH CURRENT SOC TREATMENTS

## **X** SUBOPTIMAL EFFICACY

Current treatments only modestly slow lung function decline (by ~50%) and **do not stabilize lung function** 

## **X POOR TOLERABILITY**

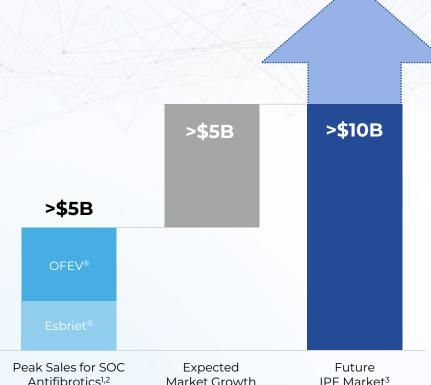
For most patients and providers, tolerability challenges outweigh suboptimal efficacy

## **DEUPIRFENIDONE POTENTIAL**

- Potential to serve as a new standard-of-care treatment
- ✓ Lung function stabilization
- Favorable tolerability



## IPF Market Has the Potential for Substantial Market Growth



## **Global IPF Market:**

- Despite only ~25% of IPF patients ever starting therapy<sup>4</sup> 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

IPF Market<sup>3</sup> (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.

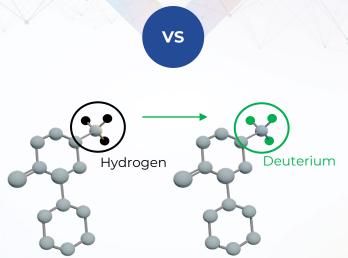
## Introduction to Deupirfenidone



# Deupirfenidone Enables Greater Drug Exposure Relative to Pirfenidone, Driving Improved Efficacy and Favorable Tolerability

## PIRFENIDONE

- Clinically validated efficacy
- Higher exposure, and potentially greater efficacy, limited by tolerability



## DEUPIRFENIDONE

- Strategically replaced hydrogen with deuterium (heavy hydrogen) at site of metabolism
- Enhances the beneficial pharmacology and clinically-validated efficacy of pirfenidone with a favorable tolerability profile



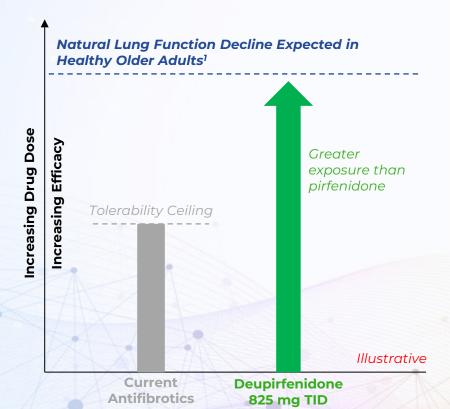
# Deupirfenidone Phase 1 Studies Established the Exposure of the Two Doses, 550 mg TID and 825 mg TID, Chosen for the Phase 2b Trial

## **KEY FINDINGS FROM PHASE 1 STUDIES**<sup>1</sup>

- ▶ Deupirfenidone 550 mg TID had an AUC was ~13% lower than pirfenidone 801 mg TID¹
- ► Deupirfenidone 824 mg² TID had an AUC that was **43% higher** than deupirfenidone 550 mg TID
- Based on the above, deupirfenidone 550mg TID & 825mg TID were chosen to be studied in the Phase 2b ELEVATE trial where the 825mg TID dose demonstrated superior efficacy with a favorable tolerability profile



# 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%					
Rash         30%         Not reported           URTI         27%         7%           Diarrhea         26%         62%	Effects with Use of	Label <sup>2</sup>	Label <sup>3</sup>		
URTI 27% 7%  Diarrhea 26% 62%	Nausea	36%	24%		
Diarrhea 26% 62%	Rash	30%	Not reported		
	URTI	27%	7%		
Fatigue 26% <5%	Diarrhea	26%	62%		
Tatigue 20%	Fatigue	26%	<5%		
Abdominal Pain 24% 15%	Abdominal Pain	24%	15%		
Liver enzyme elevation <5% 14%	Liver enzyme elevation	<5%	14%		
Vomiting 26% 12%	Vomiting	26%	12%		

<sup>\*</sup>Select, non-exhaustive list



## Deupirfenidone Hypothesis: Enable Higher Dose Exposure

Deuteration will enable higher dose exposure, in pursuit of better efficacy, with favorable tolerability

Deupirfenidone 825 mg TID arm demonstrates **improved efficacy** relative to pirfenidone, with favorable tolerability

Patients can tolerate **higher drug exposure** and **retain more lung function** 

Potentially achieve better patient outcomes without compromising tolerability



# ELEVATE Clinical Data



## Key Takeaways from Successful Phase 2b ELEVATE IPF Trial

Deupirfenidone slowed lung function decline in people with IPF; achieved primary & key secondary endpoints

## POTENTIAL FOR LUNG FUNCTION STABILIZATION

Deupirfenidone 825 mg TID achieved -21.5 mL decline in lung function as a monotherapy, approaching natural 6-month lung function decline (~-15 to ~-25 mL¹) expected in healthy adults >60 years old

## ► ENHANCED EFFICACY

Deupirfenidone 825 mg TID demonstrated strong, consistent and durable efficacy with ~50% greater treatment effect (80.9%) than pirfenidone (54.1%) vs placebo

## DOSE-DEPENDENT RESPONSE

Both doses of deupirfenidone (550 mg TID<sup>2</sup> & 825 mg TID) successfully demonstrated dose-dependent response

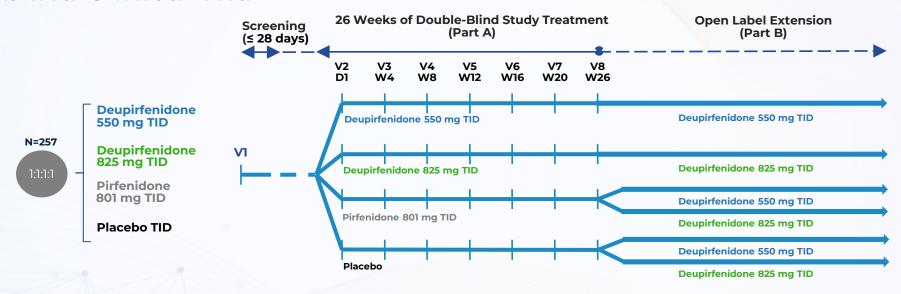
## ► FAVORABLE TOLERABILITY

Both doses of deupirfenidone demonstrated favorable tolerability

Data support potential for deupirfenidone to deliver improved efficacy vs current standard-of-care treatment for IPF



## 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** 

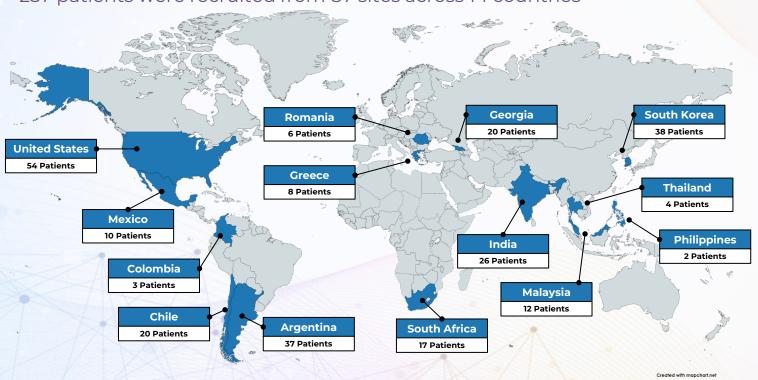
(pooled deupirfenidone arms)

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 Bayesian<sup>1</sup> and frequentist analyses were applied

## **BAYESIAN STATISTICS**

Used for Primary and Key Secondary Endpoints

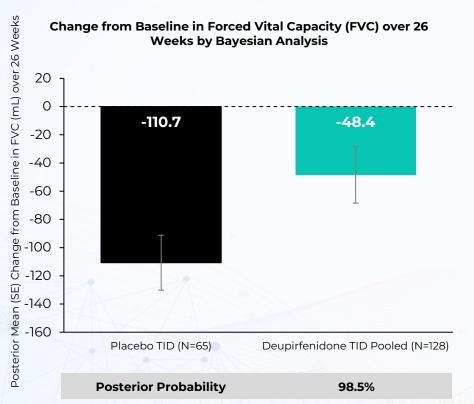
## FREQUENTIST ANALYSIS

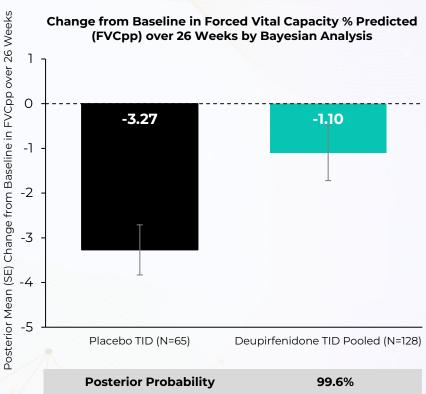
Used for Primary and Key Secondary Endpoints

- ▶ 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



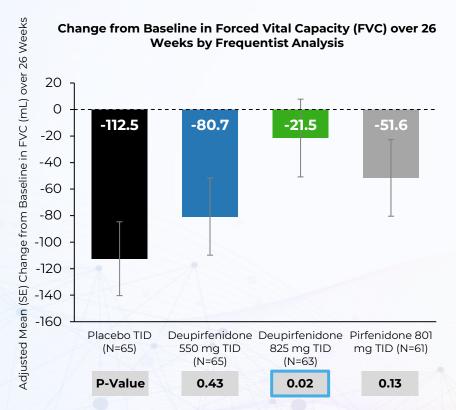
## **ELEVATE Achieved Primary and Key Secondary Endpoints**

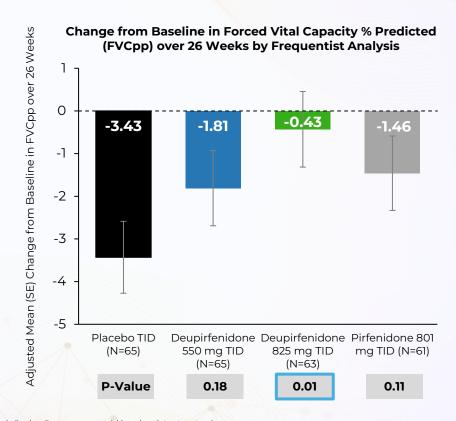






# Deupirfenidone Demonstrated Potential to Serve as a New Standard-of-Care Treatment for IPF





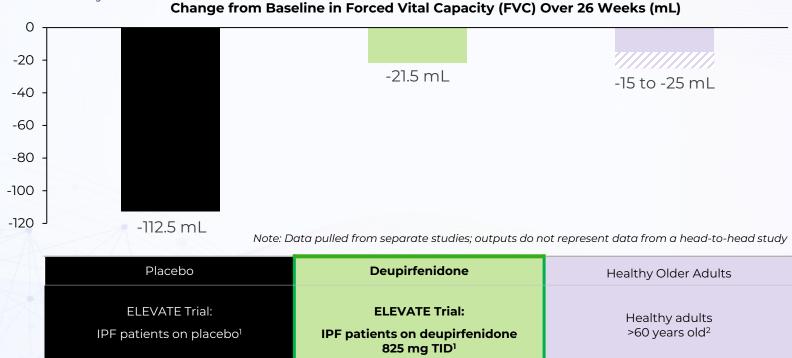


Efficacy analyses used a random coefficient regression model with absolute FVC or FVCpp including baseline as response variable and week, treatment and interaction between week and treatment as fixed effect. The analyses were performed based on the predefined Full Analysis Set. p values are two-sided 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 Significantly Slowed Decline and Stabilized Lung Function

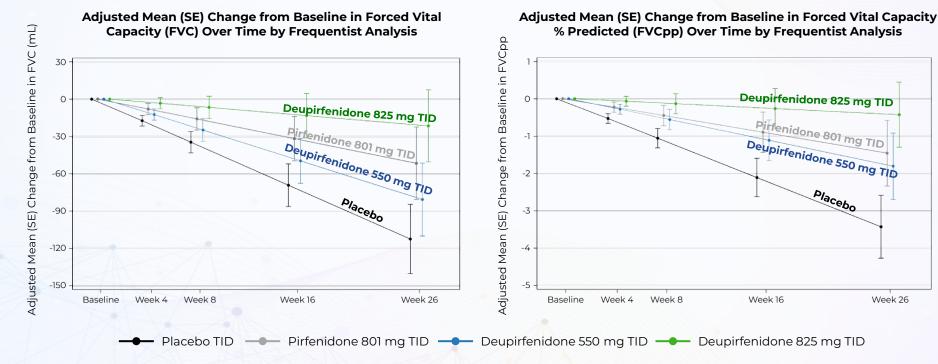
FVC decline for deupirfenidone 825 mg TID at 26 weeks in ELEVATE approached the level of natural decline expected in healthy adults





## Deupirfenidone Demonstrated a Clear Dose-dependent Effect

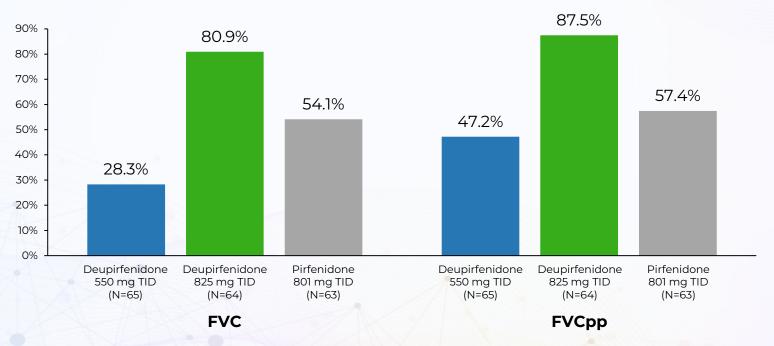
Change from baseline in FVC and FVCpp (Mixed Model Repeated Measure with Random Slope Regression)





# 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





## Deupirfenidone Had Favorable Tolerability in ELEVATE Trial

Meaningful reduction in key GI-related adverse events

Key Predefined Gastrointestinal AEs from ELEVATE Study	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 <sup>1</sup>	3 (4.6)	5 (7.9)	4 (6.2)	9 (14.1)
Constipation	1 (1.5)	4 (6.3)	1 (1.5)	3 (4.7)
Vomiting	0 (0)	2 (3.2)	5 (7.7)	1 (1.6)

BOLD: Met our pre-defined safety threshold relative to pirfenidone 801 mg TID arm, per market research and KOL feedback (25% less than the proportion of patients reporting in the pirfenidone arm)

Key GI AEs were predefined prior to unblinding data, based on market research and KOL feedback



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

Deuteration PK
Differentiation

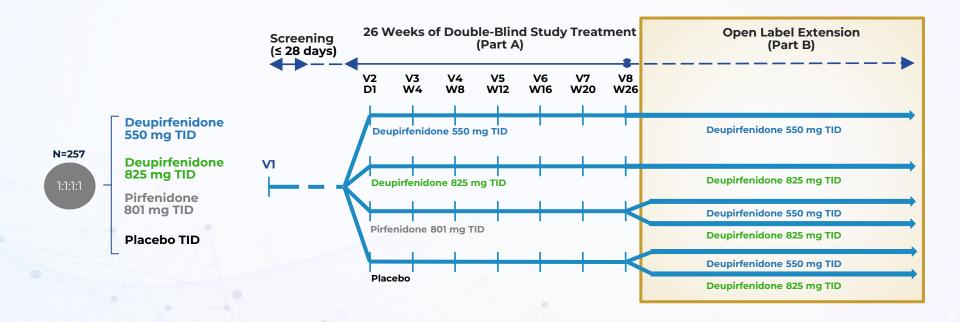
Favorable
Tolerability
Profile

Higher
Dose & Higher
Exposure

Greater
Efficacy

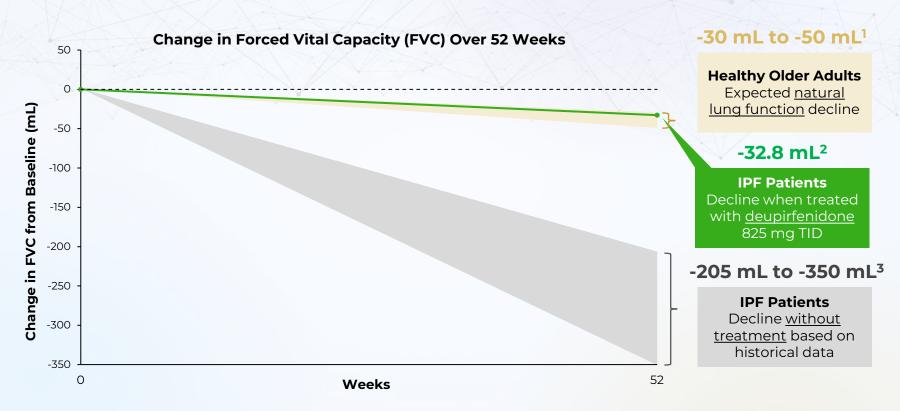


#### >90% of Patients Opted to Enroll in the Ongoing Open-label Extension





# 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\*

<sup>&</sup>lt;sup>1</sup> Per Valenzuela. Boehringer Ingelheim. ERS 2024 and Luoto. Eur Respir J. 2019.

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 data<sup>1</sup>

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 <sup>2</sup>	-32.8 mL <sup>3</sup>	-70.4 mL; -79.2 mL <sup>4,5</sup>	

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



# Historic IPF Trial Failures and PureTech Differentiation



#### Reasons for Historic IPF Trial Failures & PureTech Differentiation

#### **Reasons for Trial Failure**

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

Most Phase 2 IPF studies are 12-week trials that are not 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

Biogen Galápagos PLIANT HORIZON



● Galecto FibroGen Roche Promedior

#### PureTech Differentiation

Deupirfenidone efficacy builds on over a decade of established human efficacy data of pirfenidone

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

Deupirfenidone 825 mg TID arm had an adequate number of patients to achieve statistical significance

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)

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# Commercial Opportunity for Deupirfenidone



# Broad and Layered Intellectual Property (IP) Coverage<sup>1</sup>, Including Various Doses, Formulations, Methods of Treatment, and more

Composition of Matter Patent exclusivity up to 2033 with PTE; Additional IP coverage to ~2043

Active patents acquired from Auspex (exclusivity up to 2033 with PTE)

6 Issued US patents

In-licensed US patent from Auspex

- 26 Issued foreign patents
- US patent application in-licensed from Auspex; directed to formulation of deuterated pirfenidone (exp. 2035)

#### Additional patents filed:

- 13 Pending US patent applications
- **39** Foreign applications

For the use of deuterated pirfenidone, including for the treatment of a range of conditions



#### 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



# 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 treatment<sup>1</sup>

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



#### 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 date<sup>1</sup>



Additional data from Phase 2b to be presented at ATS

✓ Preliminary 52-week OLE data demonstrate durable treatment effect



Before the end of Q3 2025

Potential meeting with the FDA



YE 2025

Phase 3 Initiation



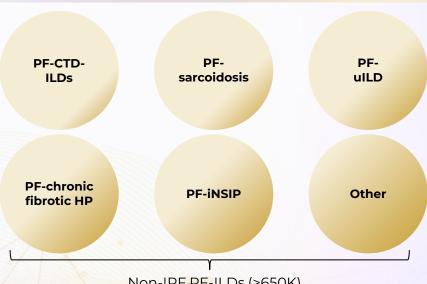
#### Potential to Expand into Other Progressive, Fibrotic Diseases with High Unmet Need

Progressive pulmonary fibrosis (PPF), also termed progressive fibrotic ILD (PF-ILD), is estimated to affect >1.3M patients in the US and 15 major markets<sup>1,2,3</sup>

**CURRENT ADDRESSABLE MARKET: >720K** 

**FUTURE ADDRESSABLE MARKET: >1.3M** 

IPF



Non-IPF PF-ILDs (>650K)



Wholly-Owned Program

Gallop Oncology

100% Equity

LYT-200

Topline results from Phase 1b trial in AML expected in Q3 2025

Phase 1b trial in solid tumors successfully completed



#### Gallop Oncology: Advancing Galectin-9 Targeting mAb, LYT-200

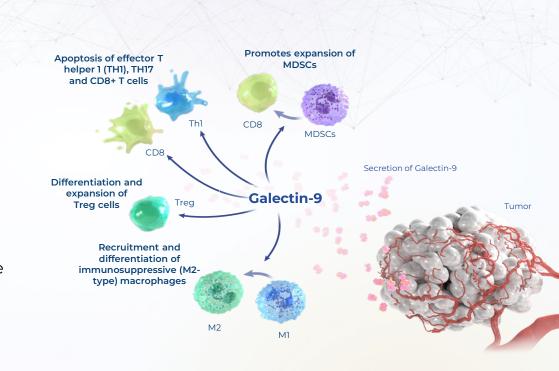
Driving immunosuppression through multiple pathways

# HEMATOLOGIC MALIGNANCES (Phase 1b ongoing)

- ► Received **Orphan Drug designation** from the FDA for the treatment of AML
- ► Received **Fast Track designation** from the FDA for the treatment of AML
- ► Topline results from Phase 1b trial in AML expected in Q3 2025

# SOLID TUMORS (Phase 1b completed)

- Received Fast Track designation from the FDA for the treatment of head and neck cancers
- Phase 1b trial in solid tumors successfully completed







#### LYT-200 Clinical Data to Date in AML & Solid Tumors

# AML/MDS DOSE ESCALATION COHORTS<sup>1</sup> (ONGOING)

Favorable safety profile demonstrated to date, with no dose limiting toxicities

**Monotherapy arm:** 30 evaluable patients dosed, 2.0 mg/kg - 16.0 mg/kg

- At 7.5mg/kg and above: 1 patient achieved CR, 3 patients achieved PRs, and >50% of patients achieved SD
- o Average treatment duration of 3.5 months

**Combination arm:** 29 evaluable patients dosed, 4.0 mg/kg, 7.5mg/kg, and 12.0 mg/kg, with venetoclax/HMA

- 6 patients achieved CRs, 1 patient achieved MLFS, and >50% of patients achieved SD
- o Average treatment duration of 4 months

# SOLID TUMORS ALL COHORTS (COMPLETED; N=44)

Favorable safety profile demonstrated in all cohorts, with no dose limiting toxicities; showed disease control & initial efficacy signals

**Monotherapy cohorts:** 20 patients dosed, 0.2 – 16.0 mg/kg every two weeks or 10 mg/kg every week

o 3 patients achieved SD

**Combination cohorts:** 24 patients dosed, 6.3mg/kg or 16mg/kg every week, with tislelizumab

- o In urothelial cancer patients, 2 patients achieved SD
- In head and neck cancer patients, 1 patient achieved CR lasting >2 years, 2 patients achieved PRs, 2 patients achieved SD
- o 33% Overall Response Rate
- 50% and 43% disease control rate at 6.3mg/kg and 16mg/kg, respectively





### Our Portfolio



# Neuropsychiatric medicines

Advancing SPT-300 into potentially registration-enabling Phase 2b study

Advancing SPT-320 into Phase 1 studies

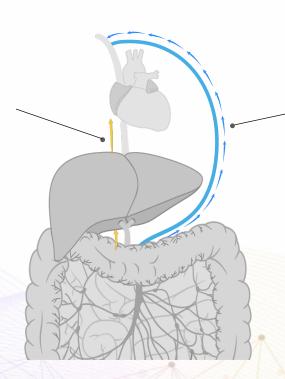


#### Glyph™: Leveraging the Lymphatic System to Unlock New Medicines

Proprietary platform advances active drugs previously limited by low oral bioavailability/hepatotoxicity

#### CONVENTIONAL

Oral drugs with high firstpass metabolism can have low bioavailability & hepatotoxicity



#### **GLYPH™**

Employ the lymphatic system's natural lipid absorption and transport process to bypass the liver, as a result:

- Enhances oral bioavailability
- Reduces dose
- Reduces first-pass hepatotoxicity
- Provides novel composition IP

#### Pipeline of First & Best-in-Class CNS Medicines

PROGRAMS <sup>1</sup>	GLYPH™ BENEFIT	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2
<b>SPT-300</b> Glyph Allopregnanolone	Overcome lack of oral bioavailability	Major depressive disorder (MDD)			
<b>SPT-320</b> Glyph Agomelatine	Negate need for liver function testing	Generalized anxiety	disorder, MDD		
SPT-348 Non-hallucinogenic neuroplastogen	Improve PK & tolerability	Mood & neuropsychiatric disorders			

Multiple discovery/preclinical programs underway leveraging the Glyph™ platform





Completed ////// In progress

Received Fast Track Designation for AML (012025)

Topline results from Phase 1b trial in AML (032025)



Gallop Oncology 100% Equity Deupirfenidone (LYT-100)

100% Equity

Additional details from the Phase 2b trial to be presented at ATS (May 2025)

FDA meeting to discuss the Phase 2b data (before the end of Q3 2025)

Initiation of Phase 3 trial in IPF (By YE 2025)

Topline results from Phase 1b trial in solid tumors (mid-2025)

Advancing SPT-320

into Phase 1 studies

(e.g., GLP-1 agonists)

validation (2025)

Additional pre-clinical

Developing oral administra-

tion of peptide therapeutics



Seaport **Therapeutics** 

Multiple Near-Term Key Catalysts Across

Portfolio

Advancing SPT-300 into potentially registrationenabling Phase 2b study

Entrega

Karuna Therapeutics

COBENFY. 60

PureTech retains rights to royalty and milestone payments upon the achievement of Cobenfy<sup>™</sup> sales and certain regulatory approvals

Sonde

Continue development of the voice-based artificial intelligence platform to detect changes in health

Topline results from Phase 2b clinical trial of VE202 in ulcerative colitis (2025) IND filing for VE707 (2025)

Vedanta

Topline results from Phase 3 pivotal RESTORATIVE303 trial (2026)

PURETECH

AML = acute myeloid leukemia; ATS = American Thoracic Society. Founded Entities represent companies founded by PureTech in which PureTech maintains ownership of an equity interest and, in certain cases, is eliqible to receive sublicense income and royalties on product sales. Relevant ownership interests were calculated on a partially diluted basis (as opposed to a voting basis) as of December 31, 2024, including outstanding shares, options and warrants, but excluding unallocated shares authorized to be issued pursuant to equity incentive plans. PureTech controls Gallop Oncology, Inc.; As of March 22, 2023, PureTech has sold its right to receive a 3% royalty from Karuna to Royalty Pharma on net sales up to \$2 billion annually, after which threshold PureTech will receive 67% of the royalty payments and Royalty Pharma will receive 33%. Additionally, under its license agreement with Karuna, PureTech retains the right to also receive certain sublicense income. Note: Certain third-party trademarks are included here; PureTech does not claim any rights to any third-party trademarks. COBENFYIM (xanomeline and trospium chloride) is indicated for the treatment of schizophrenia in adults. For Important Safety Information, see U.S. Full Prescribing Information, including Patient Information on COBENFY.com. Following the acquisition of Karuna, KarXT is now under the stewardship of Bristol Myers Squibb and will be marketed as Cobenfy.

Nasdaq Global Market & LSE Main Market / FTSE-indexed: PRTC

**Headquartered in Seaport, Boston** 

**240,254,449** outstanding shares as of June 30, 2025

**\$339.1M** PureTech Level Cash, Cash Equivalents & Short-Term Investments as of March 31, 2025<sup>1</sup>

#### ANALYST COVERAGE

**Leerink Partners LLC** 

**Peel Hunt LLP** 

Faisal Khurshid

Miles Dixon

**Jefferies** 

Benjamin Jackson

Substantial shareholders include Invesco Asset Management, Baillie Gifford & Co., Lansdowne Partners LLP, Citigroup, Vanguard Group, Recordati S.p.A.





#### **Appendix Contents**

#### APPENDIX A: INTERNAL PROGRAM

- ▶ Deupirfenidone Clinical Advisory Board
- ▶ Deupirfenidone Preclinical Data
- ► Deupirfenidone Clinical Data
- Deupirfenidone Market Research
- Pirfenidone Data
- ► Case Study for Deuterium Benefits
- ► Case Study for Success in Genericized Markets

#### **APPENDIX B: FOUNDED ENTITIES**

- ▶ Gallop Oncology
- Seaport Therapeutics
- ▶ Sonde
- Vedanta
- ▶ Entrega

#### **APPENDIX C: SUPPLEMENTAL MATERIALS**

- ► PureTech's Proven Expertise
- ▶ PureTech is Executing & Delivering Results
- ► Financial Highlights/Non-IFRS Measures



#### Accelerating Momentum & Delivering Results

Key milestones in recent years



PureTech completes successful Phase 2b trial of deupirfenidone in IPF





BMS/Karuna received FDA Approval for Cobenfy™



PureTech's Founded Entity Karuna Therapeutics **acquired by BMS for \$14B** 

#### ROYALTY PHARMA

PureTech and Royalty Pharma entered into Cobenfy (KarXT) royalty transaction for **up to \$500M** 



PureTech's LYT-200 granted **Orphan Drug and Fast Track** Designations



PureTech's Founded Entity Vedanta Biosciences **initiated Phase 3 trial** of VE303



PureTech launched Founded Entity Seaport Therapeutics; \$325M raised in 2024



# Appendix A: Wholly-Owned Program Deupirfenidone



#### Registration-enabling Program in IPF Guided by Leading Experts

PureTech's clinical advisory board for IPF & related lung disorders



**BILL BRADFORD, MD, PHD** Former SVP InterMune: developed pirfenidone for the treatment of IPF



VINCENT COTTIN, MD Professor at Université Claude Bernard Lyon; Coordinator of Center for Rare Pulmonary Diseases at Louis Pradel Hospital: Section Editor of the European Respiratory Journal



**KEVIN FLAHERTY, MD** Professor at University of Michigan; PhIII trial of nintedanib in pfILD (NEJM)



TOBY MAHER, MD, PHD Professor & Director of ILD at Keck School of Medicine, USC; PhII trial of pirfenidone in uILDs (Lancet RM)



Chair, Department of Medicine, Cedars-Sinai; results of two latestage studies evaluating the effect of pirfenidone in patients w/ IPF (Lancet)

**PAUL NOBLE, MD** 



MD, PHD Chair of Erasmus Medical Center ILD program; PI on study to identify disease progression in patients with newly diagnosed pfILDs

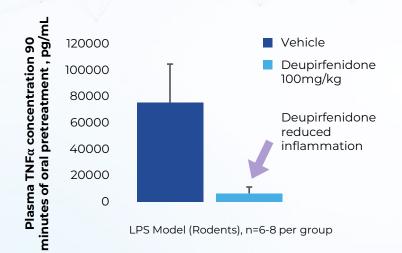
# Deupirfenidone Preclinical Data

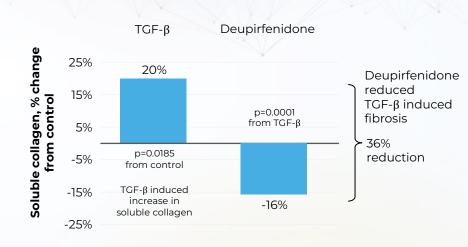


#### Deupirfenidone: Preclinical POC Demonstrates Antiinflammatory & Anti-fibrotic Pharmacology

PRECLINICAL PLASMA
CONCENTRATIONS OF TNFA WITH
DEUPIRFENIDONE VERSUS CONTROL

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



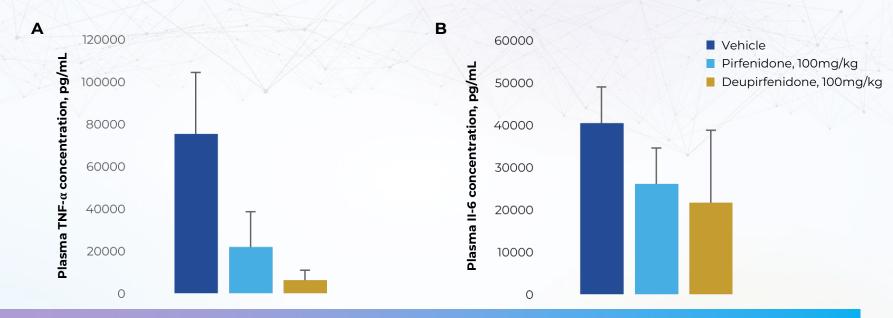




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#### Deupirfenidone Preserves Pharmacologic Effect of Pirfenidone

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



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



# Deupirfenidone Clinical Data



#### Deupirfenidone Phase 1 Clinical Trials

1. Initial PK studies

#### FOUNDATIONAL PK DATA

Multiple-dose safety, tolerability, and PK

MAD 1.0



Tolerable up to 1000mg BID, linear PK

Determine dose with same exposure as pirfenidone

PK



800 – 850 mg BID matches pirfenidone AUC 2. Head-to-head tolerability TOLERABILITY ADVANTAGE VS. PIRFENIDONE

**550 mg TID** deupirfenidone vs. pirfenidone: **Comparable AUC**<sup>1</sup>

Adult



Demonstrated tolerability advantage over pirfenidone

3. High-dose studies

EXPLORE FEASIBILITY OF

HIGHER EXPOSURES

Safety and tolerability > 1000 mg BID

MAD 2.0



Tolerable up to 2000mg BID with no dose limiting toxicity



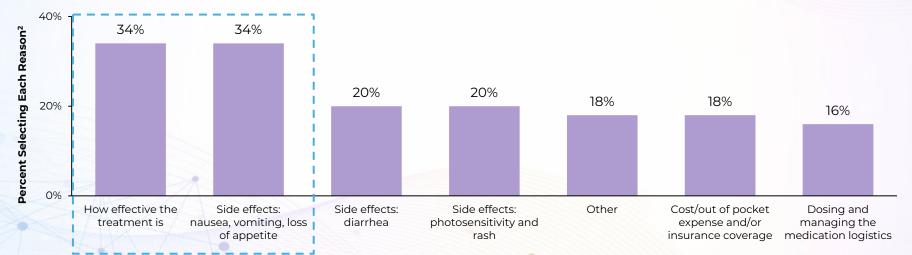


# Market Research PURETECH 65

#### IPF Patients Reported Efficacy and Tolerability as the Top Reasons for Selecting their Antifibrotic Treatment

Efficacy and GI tolerability were weighed equally when considering antifibrotic treatment

#### Reasons for Starting Treatment with One Antifibrotic Over Another<sup>1</sup>

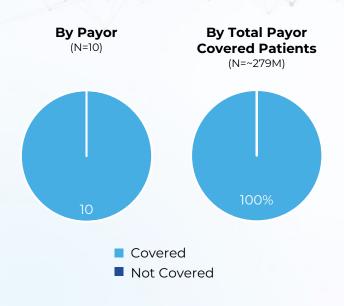




#### Deupirfenidone Payor Market Research

Independent research indicates payors in favor of profile<sup>1</sup>

# DEUPIRFENIDONE COVERAGE EXPECTATIONS<sup>2</sup>



- ► Ten out of ten payors would put deupirfendone on formulary if "clinically meaningful" differences compared to current SOC are demonstrated<sup>3</sup>
- ▶ Payers would view 20 50% improvement in FVC decline over current SOCs as clinically meaningful, consistent with KOL perspectives that PureTech has received



#### Deupirfenidone in The Face of Generics & Novel MOAs

#### **DEUPIRFENIDONE VS. GENERICS**

- The safety/tolerability of deupirfenidone remains attractive and meaningful to pulmonologists and payers even in the face of generic competition<sup>1</sup>
- Current SOC agents cannot be taken in high doses due to poor tolerability; Only ~25% of patients in the U.S. have ever initiated antifibrotic treatment; Presence of generics is not likely to drive a dramatic increase in adoption
- Even if all US payers require step edits through a generic antifibrotic, ~50% of IPF patients will still be eligible for deupirfenidone due to the significant tolerability challenges with current standard-of-care

# OF ACTIONS (MOAS)

- There are several Phase 3 & a handful of notable Phase 2 programs evaluating novel MOAs in IPF. If successful, nearly all of these programs are expected to be used on top of or after current SOC
- There is potential for deupirfenidone to be positioned as the preferred backbone antifibrotic for future combination regimens
- Development of novel MOAs in IPF has proved difficult, with many recent failures of late-phase programs. For many ongoing programs, it remains to be seen if early Ph2 data can be replicated in Ph3 studies

#### Deupirfenidone in The Face of Generics & Novel MOAs (Cont'd)

Base Case: deupirfenidone at equivalent dose to pirfenidone with favorable safety/tolerability

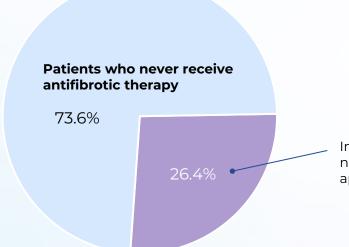
COMPETITOR	OVERVIEW	POSITIONING OF DEUPIRFENIDONE
Generic pirfenidone and nintedanib	<ul> <li>Both generic pirfenidone and generic nintedanib are expected to be on the market at time of deupirfenidone launch<sup>1</sup></li> <li>Assume all payers add generics to generic Tier<sup>2</sup>; some payers require step edits<sup>3</sup> of generics before allowing treatment with branded agents</li> </ul>	<ul> <li>Deupirfenidone will compete for new patient starts in plans without step edits</li> <li>In plans with step edits, deupirfenidone will be used as second line of treatment for patients who fail on generic antifibrotics</li> <li>Even if all payers require step edits, ~50% of patients will be eligible for deupirfenidone</li> </ul>
Reformulated pirfenidone and nintedanib	<ul> <li>A few reformulated pirfenidone and nintedanib approaches, including inhaled and sustained release, are in early development</li> </ul>	<ul> <li>Deupirfenidone will offer oral systemic delivery of the medication, without the AEs associated with inhaled (e.g., cough) and other reformulations of the currently approved drugs</li> <li>None of the localized delivery candidates have demonstrated the same evidence of efficacy as systemic therapies</li> </ul>
Novel Mechanisms	<ul> <li>Nearly all new mechanisms are being studied on top of/or after the standard-of- care (currently pirfenidone &amp; nintedanib)</li> </ul>	<ul> <li>Potential for deupirfenidone to be the backbone standard-of-care for future combination regimens</li> <li>Pirfenidone and nintedanib remain key competitors for deupirfenidone</li> </ul>



# Only ~25% of IPF Patients in the U.S. Have Ever Initiated Antifibrotic Treatment

OPTUM Study of 11,000 Patients with IPF<sup>1</sup> October 2014 to July 2019

10,996 patients with IPF in a US health claims database (OPTUM)



Over 40% of patients eventually discontinue antifibrotic therapy

Experienced nausea, diarrhea, or myalgias
Switched to the other antifibrotic

Discontinued therapy

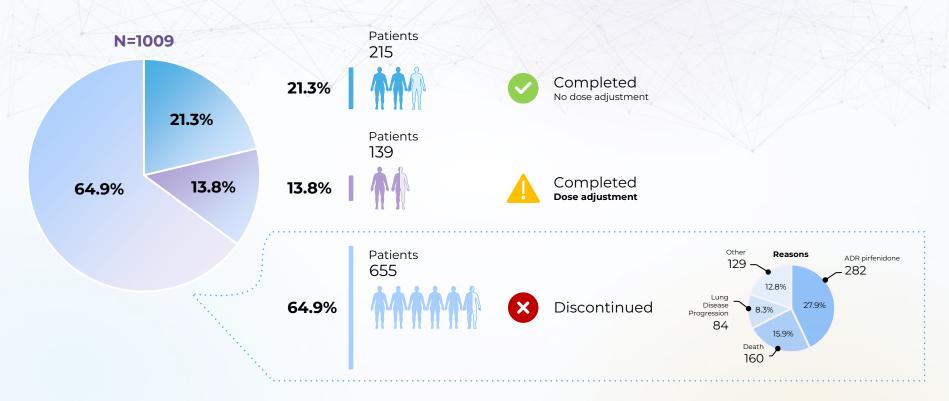
0% 10% 20% 30% 40% 50%
Patients %

Initiated pirfenidone or nintedanib since FDA approval in 2014





#### Prospective Registry Found Only 21% of Patients Who Started Pirfenidone Remained on Full Dose After 2 Years



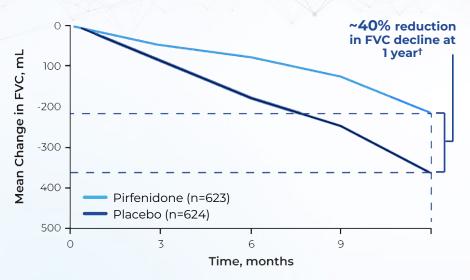


## Pirfenidone: A Clinically Validated Treatment for IPF



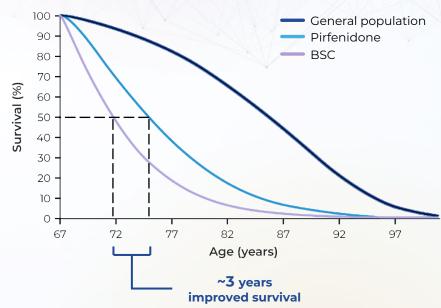
#### Pirfenidone: A Clinically Validated Treatment for IPF with Beneficial Effects on FVC and Survival

POOLED MEAN CHANGE FROM BASELINE IN FVC FROM THE **ASCEND** AND **CAPACITY** TRIALS<sup>1\*</sup>



\*FVC assessed at weeks 12, 24, 36, and 48 in CAPACITY and weeks 13, 26, 39, and 52 in ASCEND. †Mean change from baseline in FVC.

~3 YEAR IMPROVEMENT IN SURVIVAL WITH PIRFENIDONE VS BEST SUPPORTIVE CARE IN A MATCHED POPULATION FROM THE UK<sup>2</sup>



#### Design & Tolerability Findings of Pirfenidone Studies

Pirfenidone discontinuations often related to gastrointestinal (GI) adverse events (AEs)1

#### Pirfenidone GLAEs:

- ▶ Require titration in IPF and other studies
- ▶ More common in women²

#### PIRFENIDONE FOOD EFFECT/ANTACID STUDY2

PIRFENIDONE FOOD EFFECT AND BIOEQUIVALENCE STUDY<sup>3</sup>

PIRFFNIDONF PHASE 3 STUDIES

Design

801mg single-dose in healthy older adults, 44% women

801mg single-dose in healthy adults, 36% women

2403mg per day, IPF patients 26% women

Most common AEs	Pirfenidone N=16
Nausea	43.8%
Dizziness	37.5%

AEs	N=16
Nausea	43.8%
Dizziness	37.5%

Most common **AEs** 

AEs more frequent in the fasted state AE rate higher in women

Most common AEs	Pirfenidone N=44
Nausea	29.5%
Dizziness	18.2%
Headache	9.1%
Constipation	9.1%
Vomiting	4.5%
Dyspepsia	4.5%
J.	

AEs more frequent in the fasted state

Most common GI AEs^	Pirfenidone N=623	Placebo N=624
Nausea	36%	16%
Rash	30%	10%
Ab. pain	24%	15%
Diarrhea	26%	20%
Headache	22%	19%
Dyspepsia	19%	7%
Dizziness	18%	11%
Vomiting	13%	6%
Anorexia	13%	5%

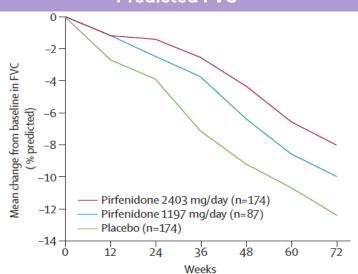
Other most common AEs observed in the Phase 3 studies (pirfenidone vs. placebo) include upper resp. infect (27% vs. 25%), fatique (26% vs. 19%), GERD (11% vs. 7%), sinusitis (11% vs. 10%), insomnia (10% vs. 7%), weight decrease (10% vs. 5%), arthalgia (10% vs. 7%)



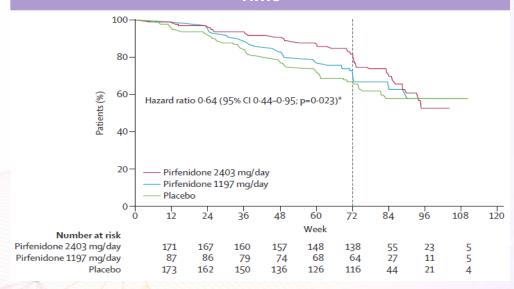
# Full-dose Pirfenidone Produces Greatest Effect on FVC Decline and Survival in IPF

Analysis From Study 004 From CAPACITY Study Program

#### Mean Change from Baseline in Percent Predicted FVC



#### Kaplan-Meier Distribution of Progression-free Survival Time

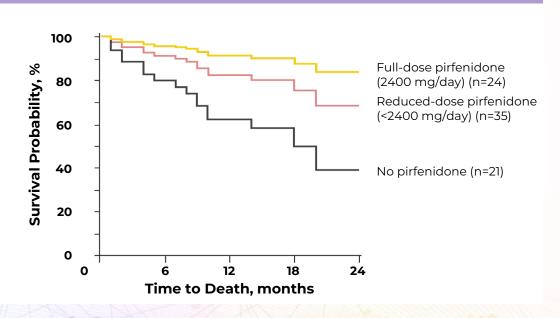


#### Maximal Survival Benefit With Full-dose Pirfenidone

Real-world Study of the Dosing and Tolerability of Pirfenidone

#### **Three-group Analysis**

The hazard for death was reduced only with the use of full-dose pirfenidone (HR [IQR], 0.19 [0.04-0.96]; P=0.045)

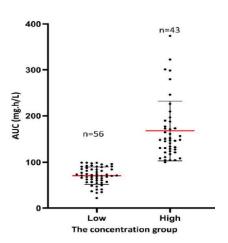




# Higher Plasma Concentrations of Pirfenidone are Associated with Improved Clinical Outcomes

Used the natural distribution in plasma levels to assign patients to "low" versus "high" concentrations of pirfenidone

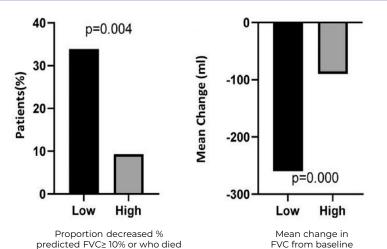
#### Distribution for two different pirfenidone concentrations\*

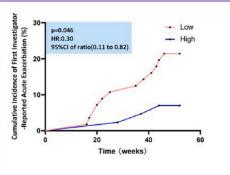


\*Patients treated with pirfenidone ≥1,200 mg/day

Horizontal red lines represent the mean value, and the lower and upper black lines represent the SD value, respectively.

#### Efficacy Outcomes during the 52-Week Study Period



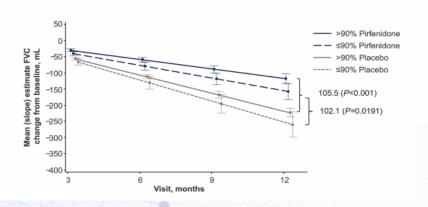


Time to First Investigator-Reported Acute Exacerbation

#### Lower Dose Intensity of Pirfenidone Leads to Worse Outcomes

In pirfenidone registration studies, IPF patients who took <90% pirfenidone had faster FVC decline

**CAPACITY Study 004, 006 and ASCEND:** Modelled mean (SEM) observed forced vital capacity (FVC) volume change from baseline (mL) over time by dose intensity (>90%, ≤90%)¹



- Patients' change from baseline in FVC
  was stratified by dose intensity (i.e.,
  patients who took >90% of their intended
  dose of pirfenidone vs patients who took
  <90%)</li>
- Patients who took <90% of their intended dose of pirfenidone had faster decline in FVC as compared to patients who took >90%



# Case Study for Deuterium Benefits PURETECH

# A Case Study for Deuterium Benefits: Austedo®, a Deuterated Tetrabenazine

#### **TETRABENAZINE**

- Tetrabenazine is a generic drug indicated for the treatment of chorea associated with Huntington's disease
- Side effects prevent patients from achieving optimal dosing and efficacy

VS

The introduction of deuterium into the tetrabenazine molecule led to the creation of Austedo® by Teva Pharmaceuticals<sup>1</sup>

#### **DEUTETRABENAZINE**

- Significant efficacy and tolerability benefits due to the achievement of higher drug exposure
- Increased treatment rates and treatment duration
- ✓ Significant expansion of prescriber base; Teva predicts
   ∼\$2.5B in Austedo® sales by

   2027²



# Case Study for Success in Genericized Markets



#### Case Studies of Blockbuster Brands in Genericized Markets

Branded drugs that demonstrate clinically meaningful differentiation can achieve blockbuster commercial success, despite generic competition

#### **PULMONARY ARTERIAL HYPERTENSION (PAH) MARKET**

#### Opsumit® (macitentan)

**Endothelin Receptor Antagonists** 

Opsumit® (macitentan) gained FDA approval in 2013

Tracleer® (bosentan) and Letairis® (ambrisentan) lost patent exclusivity in 2019

Opsumit® (macitentan) \$2.4B sales in 2024<sup>1</sup> despite generic entrants

#### **Uptravi®** (selexipag)

**Prostacyclins** 

Generic versions of Flolan® (epoprostenol) available

Remodulin® (IV treprostinil) lost patent exclusivity in 2019

Uptravi® (selexipag) \$2.2B sales in 2024<sup>1</sup> despite generic competition

#### Winrevair™ (sotatercept)

Activin Signaling Inhibitors

Winrevair™ (sotatercept) gained FDA approval in 2024 as an add-on to background SOC therapies

Winrevair™ (sotatercept)
Peak sales estimate of \$3-5B²
despite its primary use as a
combination therapy with generics



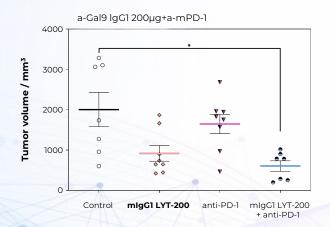
# Appendix A: Wholly-Owned Program LYT-200



#### Gallop Oncology: LYT-200

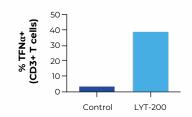
Multiple lines of preclinical data supporting therapeutic potential

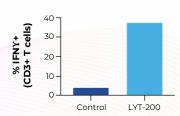
#### SINGLE AGENT ACTIVITY IN B16F10 MELANOMA MODEL



n = 8 / arm: \*p < 0.001: \*\*p < 0.05: NS = not significant

#### T CELL ACTIVATION WITH LYT-200 IN PATIENT-DERIVED ORGANOID<sup>1</sup> MODEL





#### LYT-200 DRUG PROPERTIES MAKE IT AN EXCELLENT CLINICAL CLONE:

#### High affinity & specificity for galectin-9 Robust activity in preclinical studies:

- Single agent causes tumor reduction in pancreatic models where anti-PDls don't work
- ➤ ~50% tumor reduction with LYT-200 vs. ~22% tumor reduction with anti-PD-1 in melanoma model
- ► Increase in intra-tumoral CD8 T cells in combination with anti-PD-1
- Activation of intra-tumoral immunity in patient-derived tumor models



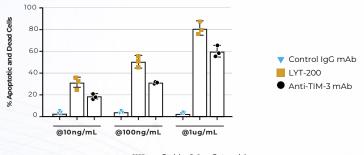


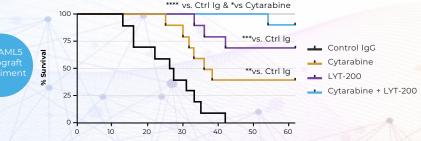
#### LYT-200

Administration induces apoptosis of leukemia cells & extends survival of leukemia cell engrafted animals

#### AML MODEL

LYT-200 cause apoptosis of AML cells and is superior to anti-TIM-3 mAb

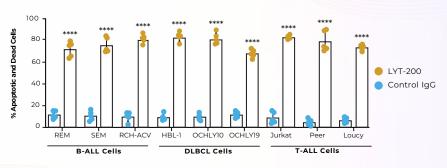


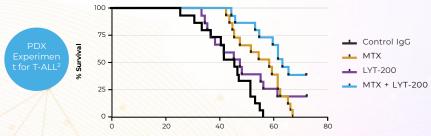


**Days Post-Transplation** 

#### T-ALL, B-ALL & DLBCL MODEL

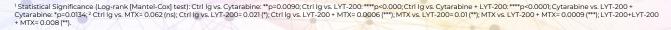
LYT-200 cause apoptosis of B-ALL, T-ALL and DLBCL cells





**Days Post-Transplation** 







#### Phase 1b Clinical Trial in AML/MDS Ongoing

#### DOSE ESCALATION TRIAL

Safety, tolerability, PK/PD, RP2D, Safety & efficacy + exploratory endpoints

#### PATIENT POPULATION

AML R/R to at least one line of prior therapy with or without allogeneic system cell transplant

OR

Patients with a document-ed diagnosis of R/R, high-risk MDS after at least one line of treatment

#### AND

For whom no standard therapy that may provide clinical benefit is available

#### DOSE FINDING (4+2 DESIGN)



If clinical benefit is observed & safety is maintained in any cohort, patients may be added to cohort(s) to further expand on safety/efficacy

(Up to additional 6 patients)

Topline results from Phase 1b trial in AML in Q3 2025

#### Phase 1b Clinical Trial in Solid Tumors Completed

#### SOLID TUMOR DOSE ESCALATION & DOSE **EXPANSION TRIAL**

Dose Finding (CRM) (all comers), safety, tolerability, RP2D, PK/PD, exploratory

Up to 26 patients

- Completed bi-monthly, monotherapy dose escalation portion of Phase 1b/2a trial (no dose limiting toxicities)
- Completed evaluation of weekly dosing

#### CLINICAL INVESTIGATORS























Other sites: Mayo, START, Sarah Cannon

# Appendix B: Founded Entities



#### Karuna Case Study

Wholly owned subsidiary of Bristol Myers Squibb as of March 18, 2024 1st new mechanism for treating schizophrenia in over 50 years

#### PATIENT NEED

~2.8M living with schizophrenia in the US

~3.2M with Alzheimer's disease psychosis in the US

Current antipsychotics have significant side effects and poor adherence

Xanomeline: clinical efficacy but was sitting on a shelf at Eli Lilly

#### PURETECH ROLE

Built top team of CNS experts & leaders

- ✓ PureTech invented & filed patents to cover the agonist/antagonist concept
- √ Completed tolerability POC
- ✓ Planned Phase 2 EMERGENT-1 study



**Xanomeline**CNS active agonist

**Trospium chloride**Peripheral antagonist
blocks side effects of
agonist

and Royalty Pharma will receive 33%. Additionally, under its license agreement with Karuna, Pure Tech retains the right to also receive certain sublicense income

(PureTech entitled to Milestone Payments/ Royalties & up to \$400M in milestone payments from agreement w/Royalty Pharma<sup>1</sup>)

#### VALUE REALIZATION

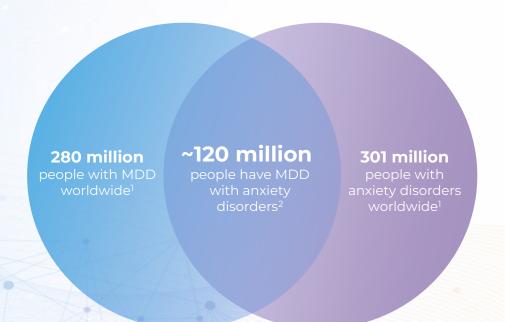
- ✓ Phase 2 EMERGENT- 1, Phase 3 EMERGENT-2 & Phase 3 EMERGENT-3 trials met primary endpoint with clinically meaningful & significant reduction in PANSS total score vs. placebo
- ✓ Ongoing Phase 3 programs in **psychosis in**Alzheimer's disease
- ✓ Karuna Therapeutics acquired by Bristol Myers Squibb for \$14B
- √ Cobenfy™ (formerly known as KarXT) FDA approval on September 26, 2024



PURETECH GIVING LIFE TO SCIENCE

#### Seaport Therapeutics: SPT-300, First Tailored Treatment for MDD

Large unmet need for new therapies to address multiple mental health disorders



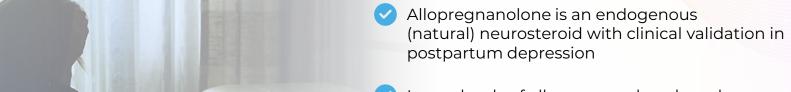
#### MDD WITH ANXIETY

- ► MDD patients with anxiety, compared with MDD patients without anxiety<sup>3</sup>:
  - ► Less likely to achieve remission
  - ► Slower to respond to treatment
  - ▶ Poorer quality of life



#### SPT-300 (Glyph Allopregnanolone)

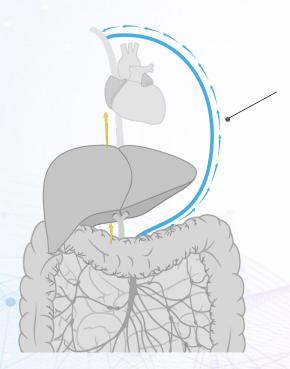
For major depressive disorder



- Lower levels of allopregnanolone have been documented in patients with mood disorders
- ...BUT method of administration (IV form) significantly limits patient uptake
- Oral chemical analogs have different composition than endogenous (natural) allopregnanolone and may not capture its full therapeutic potential
- SPT-300 retains the activity & potency of endogenous allopregnanolone in an oral form



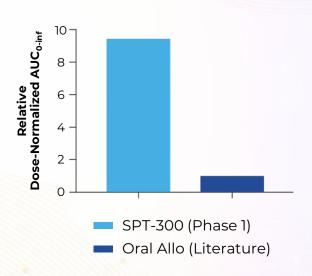
#### SPT-300 (Glyph Allopregnanolone)



#### GLYPH SPT-300 PHASE 1

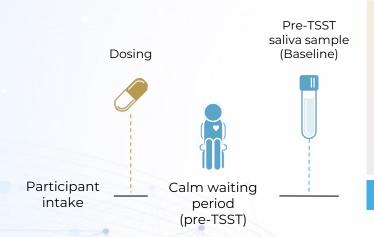
- >9X drug delivery to target vs. oral allopregnanolone<sup>1</sup>
- Generally well-tolerated, AEs generally mild and transient
  - ✓ Most common AE was somnolence (on-target effect of GABA<sub>A</sub>)
- No treatment-related severe or serious AEs
- No sudden loss of consciousness observed

# SPT-300 ORAL SYSTEMIC EXPOSURE (HUMAN) VS LITERATURE DATA<sup>1,2</sup>



#### Phase 2a Trial Design in Acute Anxiety

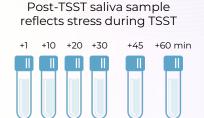
Randomized, placebo-controlled trial in the Trier Social Stress Test (TSST)



- 1. Anticipation: prepare a speech
- 2. Public speaking to a panel
- 3. Live math test to a panel



**Trier Social Stress Test** 



\_ Recovery \_\_\_ period

#### PRIMARY AIM:

To characterize pharmacology of SPT-300 for potential anxiety indications

#### PRIMARY ENDPOINT:

Reduction in salivary cortisol, a stress hormone

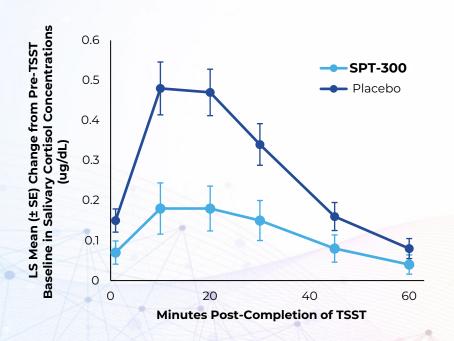
#### TRIAL DESIGN:

N=80 randomized to SPT-300 or placebo



#### Positive Phase 2a Study for SPT-300 in The Trier Social Stress Test

SPT-300 achieved primary endpoint (p=0.0001) in stress hormone response



#### POSITIVE DATA

- SPT-300 had an effect size (Cohen's d = 0.72)<sup>2</sup>
- Generally well tolerated: All treatmentrelated adverse effects were transient, mild or moderate

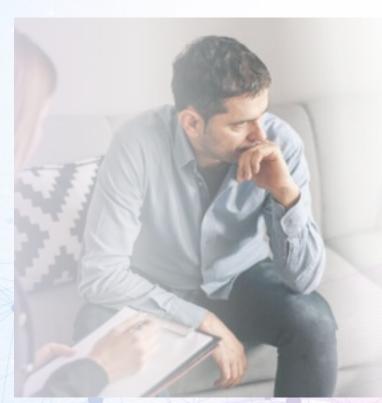
#### VALIDATION

- Further supports the potential of SPT-300 for anxiety disorders
- Further validates the Glyph platform



#### SPT-320 (Glyph Agomelatine)

For generalized anxiety disorder



- Clinically validated and approved for MDD in the EU and MDD & GAD in Australia
- Oifferentiated mechanism of action
- Consistent and statistically significant against placebo in GAD (4/4 studies)
- Superior efficacy and tolerability vs. standard-of-care<sup>1,2</sup>
- ...BUT it has low oral bioavailability and is associated with hepatoxicity necessitating liver function monitoring
- SPT-320 has the potential to greatly reduce the risk of clinically significant liver enzyme elevations<sup>3</sup>

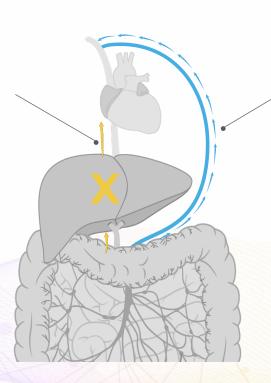


#### SPT-320: First-In-Class Potential for GAD & MDD

#### **AGOMELATINE**

- Low oral bioavailability (~1%)
- Most of the drug does not reach the brain
- Liver enzymes increase likely linked to hepatic first-pass metabolism:

 $\sim$ 1.0% – 1.4% agomelatine vs. 0.7% with placebo<sup>1</sup>



#### SPT-320

SPT-320 potential for therapeutic exposure with reduced risk of liver enzyme elevations

#### Vedanta

Developing a new class of drugs to modulate the human microbiome

#### INNOVATION

Rationally-defined consortia of **gut bacteria**; manufactured from **pure cell banks** to produce drug product of **known bacterial isolates; orally administered** to modulate microbial communities and immune responses

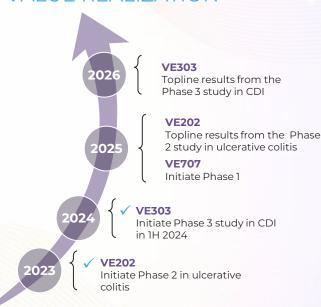


#### VALIDATION

- ► Four clinical-stage programs in development
- VE303 (C. difficile) demonstrated accelerated gut microbiota restoration after antibiotics in a Phase la/lb study
- ➤ VE202 (IBD) demonstrated durable & dose dependent colonization in Phase 1 trial in healthy volunteers
- ► VE416 (food allergy) being evaluated in Phase 1/2 study
- ► Strong IP portfolio
- ▶ \$71.1M in total Series C

(PRTC Ownership: 35.8%1)

#### UPCOMING MILESTONES & VALUE REALIZATION



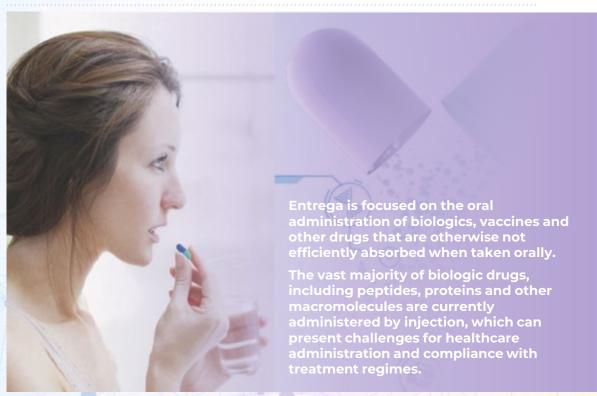
VE303 & VE202 received Fast Track designation from the U.S. FDA



#### Entrega

(PRTC Ownership: 73.8%1)

Engineering hydrogels to enable the oral administration of peptide therapeutics (e.g., GLP-1 agonists)



#### MILESTONES ACHIEVED

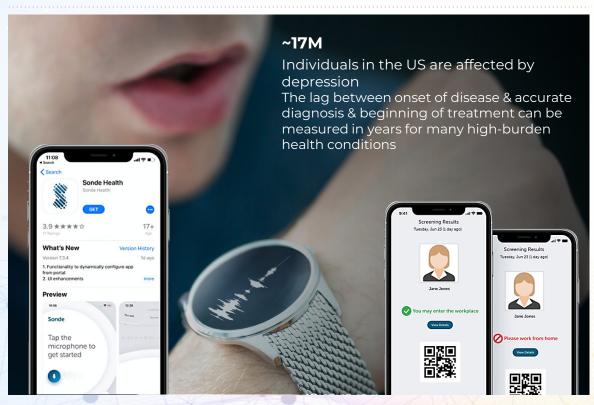
➤ To validate its technology, Entrega generated preclinical proof-of-concept data demonstrating administration of therapeutic peptides into the bloodstream of large animals.



#### Sonde

#### (PRTC Ownership: 34.8%1)

Voice-based artificial intelligence (AI) platform with the potential to transform how we monitor health



#### SONDE

Developing proprietary technology to sense & analyze subtle changes in the voice to create a range of persistent brain, muscle & respiratory health measurements that provide a more complete picture of health in just seconds

#### **KEY HIGHLIGHTS**

- Technology has demonstrated the potential to screen & monitor for disease in individuals from brief samples of speech
- ► Ongoing collaborations with multiple US & ex-US hospitals, clinics & academic medical centers
- Partnership with Qualcomm Technologies for vocal biomarker technology
- ► Collected **voice data** from over 80,000 subjects as part of ongoing validation of platform
- Expanded development of its proprietary technology into respiratory & other health & wellness conditions, including mental health



### Appendix C: Supplemental Materials



#### PureTech's Proven Expertise

We give life to classes of medicine with proven efficacy by addressing key limitations

allopregnanolone

PROGRAM	VALIDATED EFFICACY	PROBLEM	PURETECH INSIGHT/IP	
BMS's Cobenfy (fka KarXT) FDA approved for schizophrenia in adults	Xanomeline is highly effective in reducing psychosis	Xanomeline has GI tolerability issues	restricted muscarinic antagonist	ccarinic A Xanomeline Scarinic Trospium Chloride
LYT-100 for inflammation and fibrosis, including IPF	Pirfenidone extends life in patients with IPF by an average of ~2.5 years <sup>1</sup>	GI tolerability issues negatively impact patient compliance & efficacy	Retain clinically-validated activity of pirfenid w/ favorable tolerability & potential for improefficacy	
SPT-300 for neuropsychiatric & rare CNS conditions	Allopregnanolone has demonstrated efficacy in mental health conditions	Marketed allopregnanolone requires 60-hr IV infusion & chemical analogs may have different pharmacological effects than endogenous	Using proprietary Glyph technology, achieve levels of allopregnanolone at/above those as w/ therapeutic effect & demonstrated expos dependent target engagement w/ GABA <sub>A</sub> receptors <sup>2</sup> . Approach may have advantages	ssociated sure-



oral chemical analogs

#### PureTech is Executing & Delivering Results

#### REGULATORY

COBENFY (KarXT)

**FDA Clearance** 

**Endeavor** (AKL-T01) Plenity •

(Gelesis100)

#### **R&D & DATA PRESENTATIONS**

- Phase 2b results for deupirfenidone
- Phase 2 & Phase 3 results for Karuna's KarXT
- Phase 1 results for Vedanta's VE303 & VE202
- Phase 2 results for Vedanta's VE303
- Pivotal data for AKL-T01 ADHD study published in Lancet Digital Health
- Vedanta's IO candidate selected & being advanced with BMS
- PureTech programs published in *Nature* & *Nature* Neuroscience
- POC study for Vor published in PNAS
- Presentations on PureTech's LYT-200 at ESMO & ASH & SITC & AACR
- Presentations on PureTech's deupirfenidone at CHEST & ATS & ERS
- PureTech's deupirfenidone MAD study published in **Clinical Pharmacology in Drug Development**

#### PARTNERSHIPS

- PureTech's partnership with Imbrium Therapeutics to advance LYT-503/IMB-150 \$6.5 million in upfront payment and eliaible to receive up to \$53 million in additional development milestone payments for this program as well as royalties on product sales
- PureTech's royalty agreement with Royalty Pharma for up to \$500M \$100 million up front and up to \$400 million in additional payments for PureTech's 3% royalty in BMS's Cobenfy (formerly known as KarXT). After \$2 billion sales threshold, PureTech to retain 67% of royalty payments

#### **FINANCINGS**

- Seaport's \$100M Series A financing; \$225M Series B financing Key investors include ARCH Venture Partners. Sofinnova Investments. Third Rock Ventures. General Atlantic with participation from T. Rowe Price Associates, Foresite Capital, Invus Capital, Goldman Sachs, Canada Pension Plan Investment Board (CPP Investments)
- Karuna's \$124M Series A+B financings; \$103M IPO; \$14B acquisition by BMS Key investors include ARCH Venture Partners. Fidelity. Eventide. Pivotal bioVenture Partners. Partner Fund
- Vor's \$153M Series A+B financings; \$203.4M IPO Key investors include RA Capital Management, Fidelity Management & Research Company, Pagliuca Family Office, Alexandria Venture Investments, 5AM Ventures, Johnson & Johnson Innovation—JJDC, Inc. (JJDC). Osage University Partners, Novartis Institutes for BioMedical Research
- Vedanta's \$71M Series C financing; \$68M Series D financing Kev investors include Bill & Melinda Gates Foundation, Bristol-Myers Sauibb, Rock Sprinas Capital, affiliates of Magnetar Capital
- Sonde's \$16M Series A financing Key investors include M Ventures, MP Healthcare Venture Management, Neoteny 4
- Vedanta's \$106.5M financing Syndicate led by new investors AXA IM Alts and The AMR Action Fund along with existing investors Bill & Melinda Gates Foundation, Skyviews Life Science, and others



#### Financial Highlights

Cash Flow and Liquidity	March 31, 2025 N \$ millions	March 31, 2024 \$ millions
Cash and Cash Equivalents	289.7	453.0
Short-term investments	49.8	121.4
Consolidated Cash, cash equivalents and short-term investments	339.5	574.4
Less: Cash and Cash Equivalents held at non-wholly-owned subsidiaries	(0.4)	(1.1)
PureTech Level Cash, cash equivalents and short-term investments <sup>1</sup>	339.1	573.3



#### Non-IFRS Measures

#### **Reported Performance**

Reported performance considers all factors that have affected the results of our business, as reflected in our consolidated financial statements.

#### **Core Performance**

Core performance measures are alternative performance measures (APM) which are adjusted and non-IFRS measures. These measures cannot be derived directly from our Consolidated Financial Statements. We believe that these non-IFRS performance measures, when provided in combination with reported performance, will provide investors, analysts and other stakeholders with helpful complementary information to better understand our financial performance and our financial position from period to period. The measures are also used by management for planning and reporting purposes. The measures are not substitutable for IFRS financial information and should not be considered superior to financial information presented in accordance with IFRS.

#### Cash flow and liquidity

PureTech Level Cash, cash equivalents and short-term investments

Measure type: Core performance.

**Definition:** Cash and cash equivalents, and Short-term investments held at PureTech Health plc and only wholly-owned subsidiaries.

Why we use it: PureTech Level Cash, cash equivalents and short-term investments is a measure that provides valuable additional information with respect to cash, cash equivalents and short-term investments available to fund the Wholly Owned Programs and make certain investments in Founded Entities.

