# **PURETECH** GIVING LIFE TO SCIENCE®

**Corporate Presentation** July 2025

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We report certain financial information using non-IFRS financial measures, as we believe these measures provide information that is useful to management and investors to assess financial performance. These non-IFRS financial measures do not have any standardized meaning and may not be comparable with similar measures used by other companies. For certain non-IFRS financial measures, there are no directly comparable amounts under IFRS. These non-IFRS financial measures should not be viewed as alternatives to measures of financial performance determined in accordance with IFRS. Please see slides 103-104 for a reconciliation of these measures to the most comparable IFRS measure.

This document and the Presentation contain statements that are or may be forward-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," should," "continue," "potential," "likely," "opportunity" and similar expressions or variations of such words are intended to identify forwardlooking 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.

Each forward-looking statement speaks only as at the date of this document. Except as required by law and regulatory requirements, we disclaim any obligation to update or revise these forward-looking statements, whether as a result of new information, future events or otherwise.

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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 ClassHouse 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.

PURETECH



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



Sharon Barber-Lui Interim Board Chair 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



John LaMattina, PhD Board Former President of Pfizer Global R&D, Forbes Contributor



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

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



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



Daphne Zohar 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



FDA approval

PURETECH



Founded Entities<sup>2</sup>

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

Cash Equivalents and Short-term

Investments as of March 31, 2025<sup>1</sup>

PureTech Level Cash,

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

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SEAP⊕RT

\$397.5M **COBENFY** 

\$327.4M

Note: Certain third-party trademarks are included here; PureTech does not claim any rights to any third-party trademarks.

PureTech level cash, cash equivalents and short-term investments excludes cash and cash equivalents at non-wholly owned subsidiary of \$0.4m. PureTech level cash, cash equivalents and short-term investments is a non-IFRS measure; <sup>2</sup> Founded Entities represent companies founded by PureTech in which PureTech maintains ownership of an equity interest and/or, in certain cases, is eligible to receive sublicense income, milestone payments and royalties on product sales. References to Founded Entities include PureTech's ownership interests in Gallop Oncology, Inc., Seaport Therapeutics, Inc., Vedanta Biosciences, Inc., Vor Bio, Inc., Entrega, Inc., Sonde Health, Inc., for all dates prior to July 2, 2024, Akili Interactive Labs, Inc., for all dates prior to March 18, 2024, Karuna Therapeutics, Inc., for all dates prior to October 30, 2023, Gelesis, Inc., for all dates prior to December 21, 2023, Follica, Incorporated, and for all dates prior to December 18, 2019, resTORbio, <sup>3</sup> In 2024, we generated cash proceeds of approximately \$327 million from the acquisitions of two of our Founded Entities (Karuna Therapeutics and Akili Interactive) and milestone payments related to the FDA approval of Cobenfy.

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





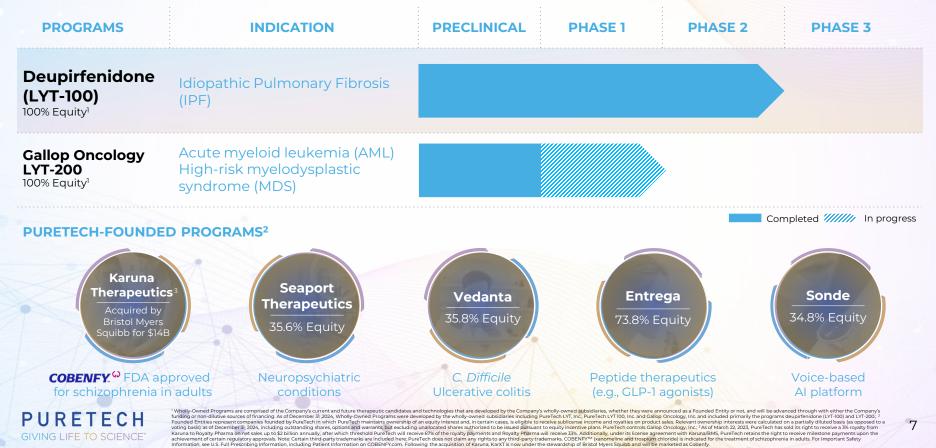
Note: Certain third-party trademarks are included here; PureTech does not claim any rights to any third-party trademarks.

COBENFY<sup>TM</sup> (xanomeline and trospium chloride) is indicated for the treatment of schizophrenia in adults. Fo' 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.

<sup>1</sup>The percentage includes number of successful trials out of all trials run for all therapeutic candidates advanced through at least Phase 1 by PureTech or its Founded Entities from 2009 onward.

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

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



### Karuna Therapeutics Case Study

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

- ► COBENFY <sup>Q</sup> (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

# **\$18.5M**

Total PRTC spend<sup>1</sup>



~\$400M<sup>3</sup>

L1B4

#### Potential Upside Value<sup>2</sup>

#### Additional economics

including milestone payments from Karuna/BMS and 2% royalty on annual sales above \$2B<sup>5</sup>

- Regulatory & commercial milestones under Royalty Pharma transaction
- Cash generated to date through equity sales, milestone payments, and upfront payment from the Royalty Pharma transaction

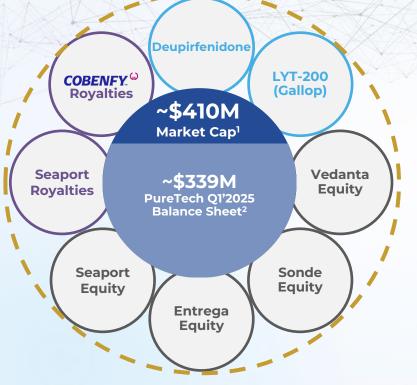


Note: Certain third-party trademarks are included here; PureTech does not claim any rights to any third-party trademarks. COBENFY<sup>IM</sup> (xanomeline and trospium chloride) is indicated for the treatment of Schlzophrenia in adults. For Important Safety Information, see U.S. Full Prescribing Information, including Patient Information on COBEN KaXT is now under the stewardship of British Wares Souibb and will be marketed as Cobenfy

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# Significant Upside Potential Across PureTech's Portfolio

#### **PureTech's Intrinsic Value**



#### WHOLLY-OWNED PROGRAMS

Deupirfenidone (LYT-100): Potential new SOC for IPF in a >\$10B TAM3

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

#### FOUNDED ENTITIES EQUITY STAKES

Substantial equity holdings across 4 Founded Entities

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

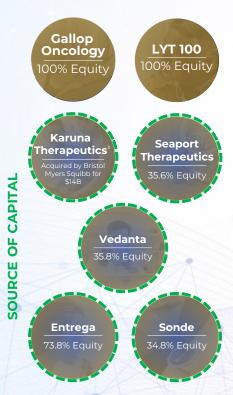
- Up to \$400M in milestone payments from Royalty Pharma
- 2% royalties on annual sales > \$2B (up to \$125M/year based on analyst estimates of \$4-11B<sup>5</sup> peak sales through 2033) OB
  - Milestone payments on certain Cobenfy<sup>™</sup> regulatory approvals
- 3-5% royalties on Glyph product sales
  - Milestone and sublicense payments
- 35.6% equity stake following >\$325M raised in 2024 Ш. Н

# PURFTFCH

SOC = Standard of care: IPF= Idiopathic pulmonary fibrosis; PPF = Progressing pulmonary fibrosis; AML = Acute myeloid leukemia; Note: Certain third-party trademarks are included here; PureTech does not claim any rights to any third-party trademarks, COBENFY<sup>TM</sup> (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.<sup>1</sup> As of June 2025;<sup>2</sup> PureTech level cash, cash equivalents and short-term investments excludes cash and cash equivalents at non-wholly owned subsidiary of \$0.4m. PureTech level cash, cash equivalents and short-term investments is a non-IFRS measure. <sup>3</sup> 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 Research and Markets; Aute Mveloid Leukemia Market Report 2025; 5 Based on various equity research as of December 31, 2024.

# 2025 Capital Allocation Overview

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



PURFTFCH

#### 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

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#### **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

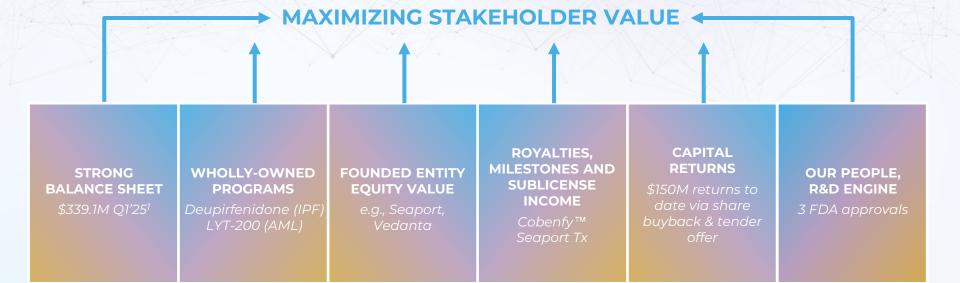
#### **OPERATIONAL & TAX EXPENSES**

• 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.<sup>1</sup> Wholly-Owned Programs are comprised of the Company's funding or non-dilutive therapeutic candidates and technologies that are developed by the Company's wholly-owned subsidiaries; whether they were announced as a Founded Entity or not, and will be advanced through with either the Company's funding or non-dilutive Sources of financing. As of December 31, 2024, Wholly-Owned eveloped by the Wholly-owned subsidiaries including PureTech LYT. Inc., PureT

# Our Key Components of Value





Note: Certain third-party trademarks are included here; PureTech does not claim any rights to any third-party trademarks.

COBENFY<sup>TM</sup> (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.

<sup>1</sup> PureTech level cash, cash equivalents and short-term investments as of March 31, 2025, is an unaudited figured and excludes cash and cash equivalents at non-wholly owned subsidiary of \$0.4m. PureTech level cash, cash equivalents and short-term investments is a non-IFRS measure.

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# Wholly-Owned Program

Deupirfenidone (LYT-100)

100% Equity

Successful completion of Phase 2b ELEVATE IPF trial

Initiation of Phase 3 trial by YE 2025



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, whether they were announced as a Founded Entity or not, and will be advanced through with either the Company's funding or non-dilutive sources of financing. As of December 31,2024, Wholly-Owned Programs were developed by the wholly-owned subsidiaries including PureTech LYT, Inc., PureTech LYT100, Inc. and Gallop Oncology, Inc. and included primarily the programs deupifenidone (LYT-100) and LYT-200.

# 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 doses due to poor tolerability, resulting in suboptimal efficacy		Debilitating, fatal disease; current SOC agents cannot be taken in high doses due to poor tolerability, resulting in suboptimal efficacy					
	đ	Ideal Treatment Goal in IPF	Stabilization of lung function without compromising on safety and tolerability					
	Ē	Robust Deupirfenidone Data	Potential to set a new standard for IPF treatment: Phase 2b study <b>showed dose</b> <b>dependent lung function stabilization</b> with a <b>favorable tolerability profile</b>					
	i	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 2043 <sup>1</sup>					
	Initiation of pivotal Phase 3 trial expected by the end of 2025							
PU	URETECH							

SOC = standard-of-care; IPF = idiopathic pulmonary fibrosis; PPF = progressive pulmonary fibrosis <sup>1</sup> Independent of possible adjustments or extensions.

# Unmet Needs in IPF



# Idiopathic Pulmonary Fibrosis (IPF) Overview

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



# >232,000

#### IPF patients in the US & EU5<sup>1</sup>

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



#### IPF patients ever start antifibrotic treatment

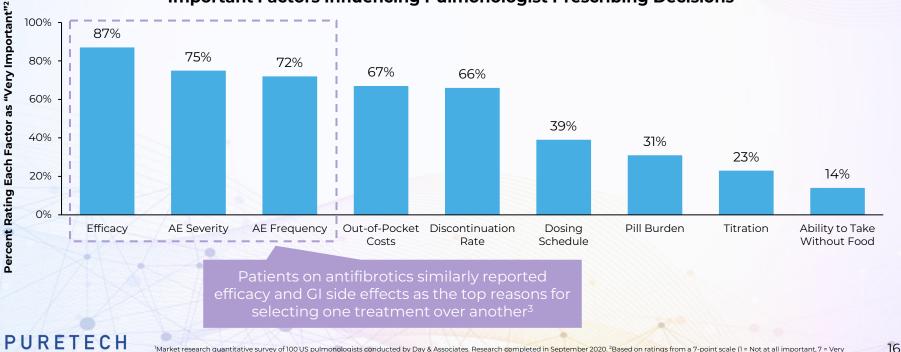
...of which >40% eventually discontinue⁵



<sup>1</sup> GlobalData Epidemiology and Market Size Search, EUS=United Kingdom, France, Germany, Italy and Spain; <sup>2</sup> Barratt SL, Creamer A, Hayton C, Chaudhuri N. Idiopathic Pulmonary Fibrosis (IPF): An Overview. J Clin Med. 2018 Aug 67(8):201; <sup>3</sup> 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. <u>https://doi.org/10.18553/jmcp.2017.23.3-bs17</u>; 4 ESBRIET (pirfenidone) and OFEV (nintedanib) were approved in 2014; <sup>5</sup> 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.

## 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

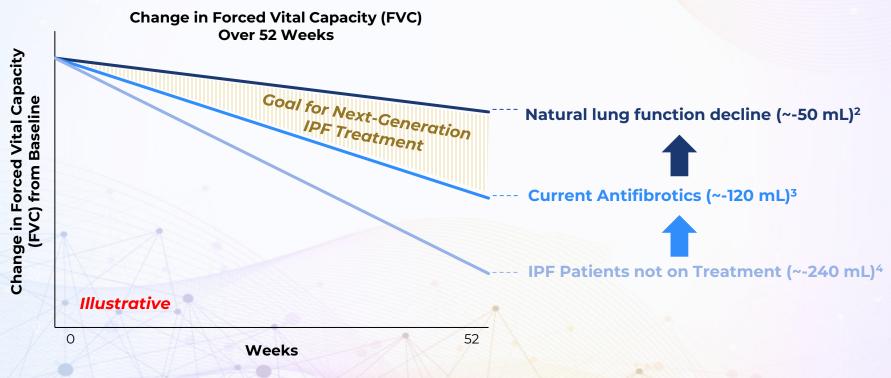


#### Important Factors Influencing Pulmonologist Prescribing Decisions<sup>1</sup>

<sup>1</sup>Market research quantitative survey of 100 US pulmonologists conducted by Day & Associates. Research completed in September 2020.<sup>2</sup>Based on ratings from a 7-point scale (1 = Not at all important, 7 = Very important);<sup>3</sup>Market research quantitative survey of 90 participants with IPF conducted by Sago. Research completed in April 2024. AE = adverse event

### 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 <sup>1</sup>Per 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; <sup>2</sup>Per Valenzuela. Boehringer Ingelheim. ERS 2024 and Luoto. Eur Respir J. 2019. <sup>3</sup> Based on pirfenidone and nintedanib's pivotal studies. <sup>4</sup>Raman, Lavanya et al. "Nintedanib for non-IPE progressive pulmonary fibrosis: 12-month outcome data from a real-world multicentre observational study." ERJ open research vol. 9,2 00423-2022. 20 Mar. 2023, doi:10.1103/23120541.00423-2022.

# **IPF** Patients Need Better Treatment Options

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

#### CHALLENGES WITH CURRENT SOC TREATMENTS

#### **×** SUBOPTIMAL EFFICACY

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

#### × POOR TOLERABILITY

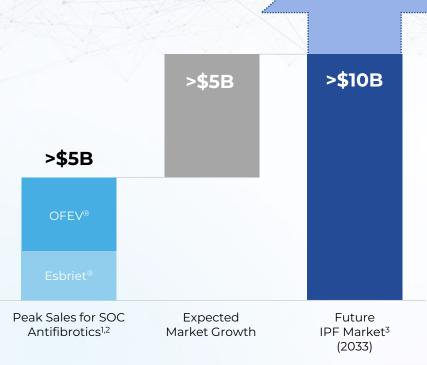
For most patients and providers, tolerability challenges outweigh suboptimal efficacy

#### **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



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. <sup>1</sup> 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). <sup>2</sup> Roche 2021 Financial Results. Esbriet peak sales (2020). <sup>3</sup> Straits Research Report, Idiopathic Pulmonary Fibrosis Market Size, Share & Trends Analysis Report By Drug Type (Nintedanib, Pirfendone, 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; <sup>4</sup> 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 Sco. 2021 Juli8(17):112-1128.

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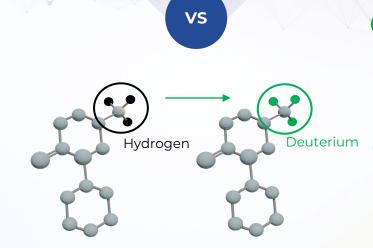
# Introduction to Deupirfenidone



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 TID<sup>1</sup>
- Deupirfenidone 824 mg<sup>2</sup> 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

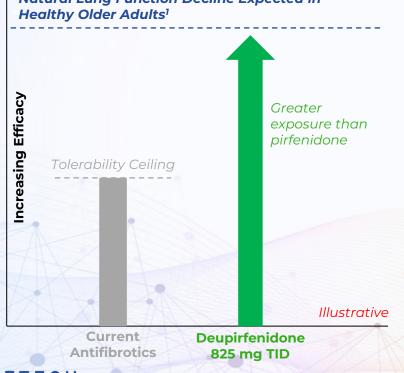


TID = three times a day; AUC = Area Under the Curve Toby M. Maher, Michael C. Chen, Chris C. Korth, Eric Elenko, Mark D. Harnett, Varun Garg, Camilla S. Graham, Wassim H. Fares, Julie Krop (2023), Deupirfenidone (LYT-100) dose-selection rationale for a Phase 2b idiopathic pulmonary fibrosis study — ELEVATE IPF; <sup>2</sup> Deupirfenidone 824 mg TID was used in PureTech's Phase 1 studies, whereas deupirfenidone 825 mg TID was used in PureTech's Phase 2b study.

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



Dose ncreasing Drug



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

\*Select, non-exhaustive list

# PURETECH

Per Valenzuela. Boehringer Ingelheim. ERS 2024 and Luoto. Eur Respir J. 2019; <sup>2</sup> Side effects for prifenidone reported in 3 randomized, double-blind, placebo-controlled trials (ASCEND, CAPACITY 004, and CAPACITY 006) in which a total of 623 patients received 2403 mg/day of pirfenidone; <sup>3</sup> Side effects for nintedanib reported in 3 randomized, double-blind, placebo-controlled trials in which a total of 723 patients received 150 mg/twice/day of nintedanib. URTI = upper respiratory tract infection

# 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 mL<sup>1</sup>) 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

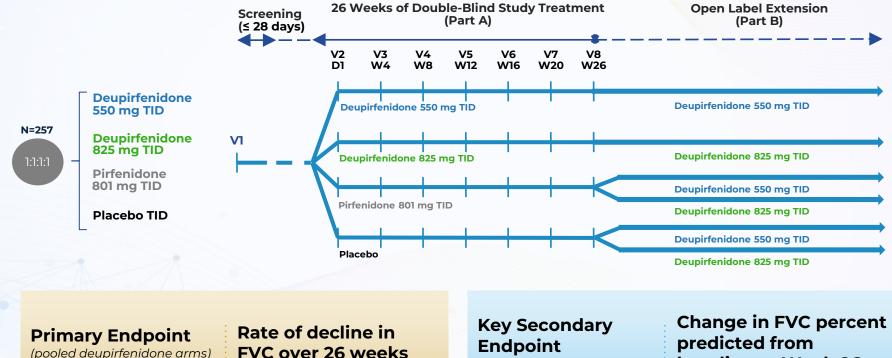
Both doses of deupirfenidone demonstrated favorable tolerability

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

#### PURETECH GIVING LIFE TO SCIENCE"

<sup>1</sup> 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 (PPF) compared with healthy references. Poster presented at the European Respiratory Society International Congressi, 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), 1701812. <u>https://doi.org/10.1183/13993003.01812-2017</u>; Approximately equivalent exposure to pitfenidone dos-election rationale for a Phase 2b idiopathic pulmonary fibrosis study — ELEVATE IPF. Poster presented at the CHEST Annual Meeting, Honolulu, HI). Deupirfenidone doss-election rationale for a Phase 2b idiopathic pulmonary fibrosis study — ELEVATE IPF. Poster presented at the CHEST Annual Meeting, Honolulu, HI).

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



(pooled deupirfenidone arms)

baseline to Week 26

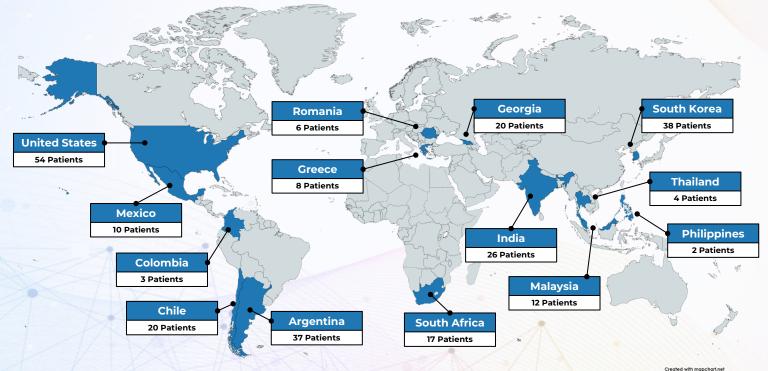
#### FVC = Forced Vital Capacity; TID = three times a day Note: Patients in all arms were permitted to decrease and re-increase their assigned dose as tolerated

PURETECH

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

257 patients were recruited from 87 sites across 14 countries

PURETECH



#### 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

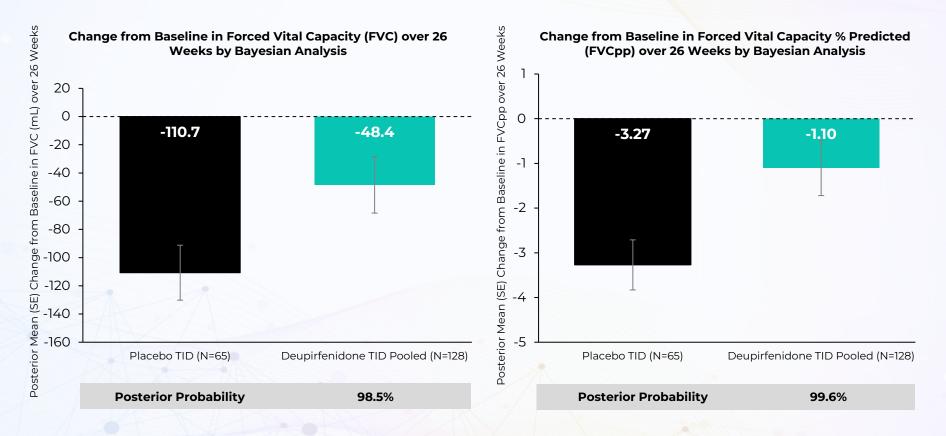
PURFT

- 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

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<sup>1</sup> Bayesian is a method that has been used by large pharmaceutical companies in the IPF space. The FDA has also acknowledged the benefits of this approach. 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. FVC = forced vital capacity

# ELEVATE Achieved Primary and Key Secondary Endpoints

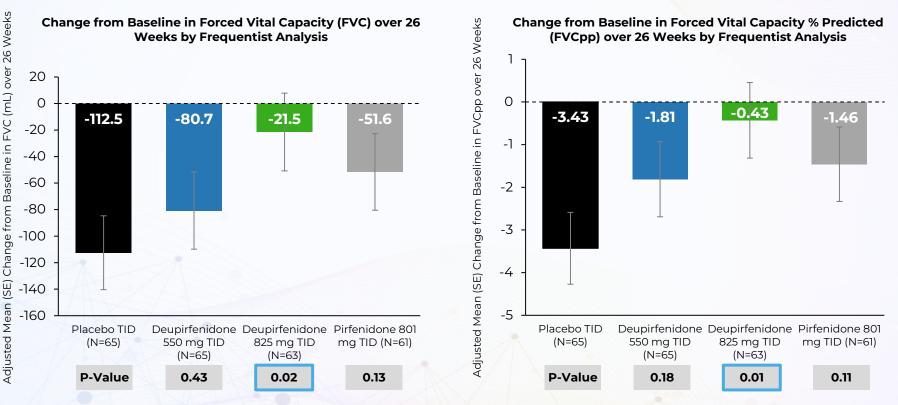




Efficacy analyses used a random coefficient regression model with absolute FVC or FVCpp including baseline as response variable and week, treatment (placebo, pirfenidone, deupirfenidone pooled arm) and interaction between week and treatment as fixed effect. The analyses were performed based on the predefined Full Analysis Set; Change from baseline FVC is not adjusted for patient characteristics such as height, age, race or sex. TID = 3 times per day

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# 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

Statistically Significant

# 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

#### 0 -20 -21.5 ml -15 to -25 ml -40 -60 -80 -100 -120 -112.5 ml Note: Data pulled from separate studies; outputs do not represent data from a head-to-head study Placebo Deupirfenidone Healthy Older Adults **ELEVATE Trial: ELEVATE Trial:** Healthy adults

#### Change from Baseline in Forced Vital Capacity (FVC) Over 26 Weeks (mL)



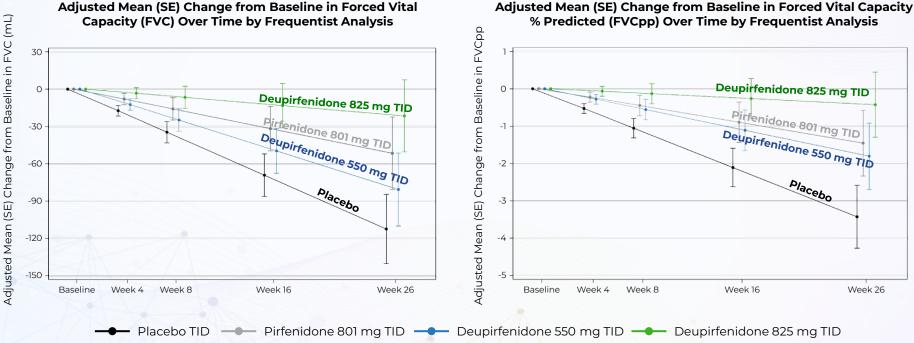
IPF patients on placebo<sup>1</sup>

<sup>1</sup> Reflects outputs obtained via frequentist analysis; <sup>2</sup>Per Valenzuela. Boehringer Ingelheim. ERS 2024 and Luoto. Eur Respir J. 2019 (6-month decline in general population aged 60-102 years, estimated by taking reported 1-year decline and dividing by 2). Change from baseline FVC is not adjusted for patient characteristics such as height, age, race, or sex.

IPF patients on deupirfenidone 825 mg TID<sup>1</sup> >60 years old<sup>2</sup>

# Deupirfenidone Demonstrated a Clear Dose-dependent Effect

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

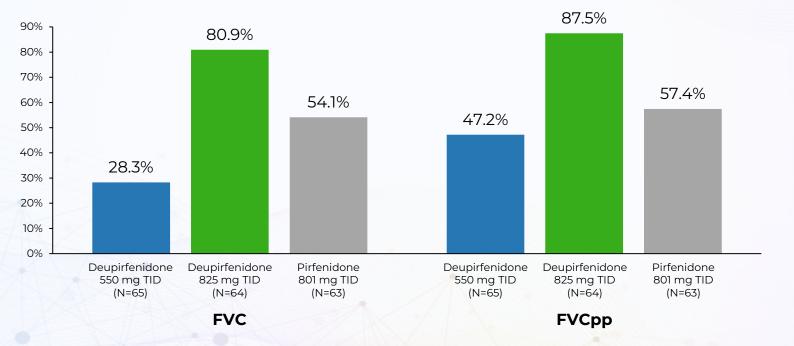




Efficacy analysis is based on pre-defined Full Analysis Set using a random coefficient regression model with absolute FVC as a response, including baseline. MMRM = mixed model for repeated measure; SE = standard error; TID = 3 times per day. Baseline is defined as the last available measurement performed before the first study drug administration in Part A. Adjusted mean (SE) by frequentist analysis is estimated based on a random coefficient regression model with absolute FVC over time, including baseline, as a response, and fixed effects for treatment(placebo, pirfenidone, deupirfenidone 550 mg or deupirfenidone 825 mg), visit (week), and treatment by visit interaction, as well as participant-level random effects for the intercept and slope.

## 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



<sup>1</sup>25% of patients in pirfenidone pivotal trials and 15% in nintedanib pivotal trials reported abdominal pain; AE= adverse event; TID = three times a day Note: Differences between groups are determined by the difference between percentage of incidences observed.

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

Deuteration PK Differentiation

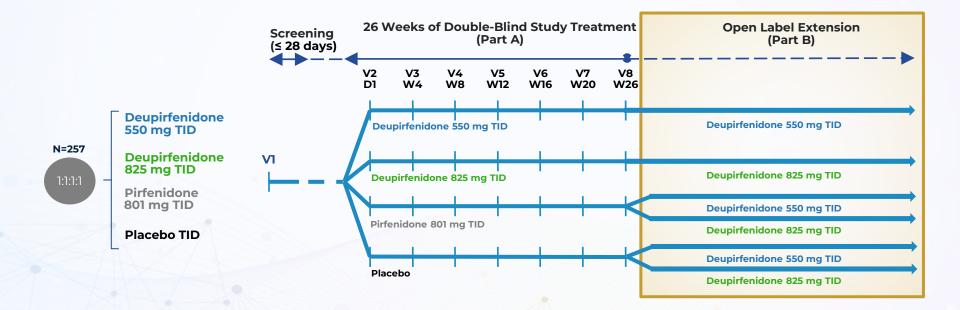


Favorable Tolerability Profile Higher Dose & Higher Exposure

Greater Efficacy

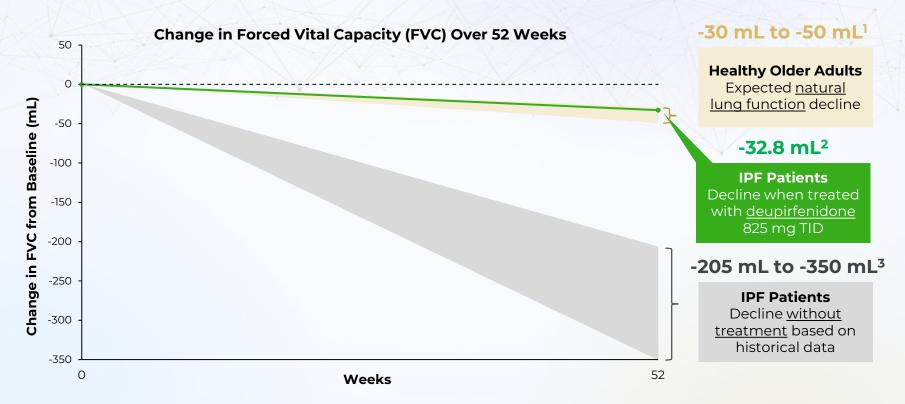


## >90% of Patients Opted to Enroll in the Ongoing Open-label Extension





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



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

<sup>2</sup>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.

<sup>3</sup> Per placebo arm 48-week decline in pirfenidone CAPACITY 004 and CAPACITY 006 trials (Noble. Lanct. 2011.) and 52-week decline in nintedanib INPULSIS-1 and INPULSIS-2 trials (Richeldi. N Engl J Med. 2014)

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



TID = Three times a day; BID = Twice a day;<sup>1</sup> Cross-trial comparisons are inherently limited, as these data are from separate studies with differing designs, patient populations, and methodologies. No direct, head-tohead trials have been conducted; <sup>2</sup>Per Valenzuela. Boehringer Ingelheim. ERS 2024 and Luoto. Eur Respir J. 2019;<sup>3</sup> Integrated analysis of double-blind (26 weeks) 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; <sup>4</sup> Per FIBRONEER-IPF trial (Richeldi. N Engl J Med. 2025); <sup>5</sup>The FIBRONEER-IPF trial placebo arm without background treatment showed a 52-week FVC change from baseline of -148.7 mL (per Richeldi. N Engl J Med. 2025), vs. a historical placebo arm change from baseline of -205 mL to -350 mL in the pirfenidone CAPACITY 004 and CAPACITY 006 trials (Noble, Lanct. 2011), and nintedanib INPULSIS-1 and INPULSIS-2 trials (Richeldi. N Engl J Med. 2014).

# Historic IPF Trial Failures and PureTech Differentiation



## Reasons for Historic IPF Trial Failures & PureTech Differentiation

	Reasons for Trial Failure	PureTech Differentiation		
Idiopathic Nature of Disease	Evaluating a new mechanism of action for an idiopathic disease is inherently risky	Deupirfenidone efficacy builds on over a decade of established human efficacy data of pirfenidone		
Short Phase 2 Trial Duration	Most Phase 2 IPF studies are 12-week trials that are not predictive of a 52-week trial (treatment duration required for pivotal)	Robust 26-week ELEVATE trial with deupirfenidone, with additional durable 52-week OLE data		
Small Study Size	Smaller Phase 2 trials may not be representative of Phase 3 population	Deupirfenidone 825 mg TID arm had an adequate number of patients to achieve statistical significance		
Study Quality	Variability (e.g., outliers, decentralized FVC) in Phase 2 lead to false assumptions for Phase 3	No outliers observed in ELEVATE study. Phase 3 trial will include rigorous QC systems employed in ELEVATE		
Lack of Active Control	IPF studies have not historically used an active control arm	First trial to compare an investigational drug to an approved antifibrotic; pirfenidone and placebo performed as expected, increasing data confidence		
Deviation from Phase 2 Design	Phase 3 studies that deviate from their Phase 2 design (e.g., change in dosing or background SOC use) increase technical risk	Phase 3 design will recapitulate key aspects of ELEVATE (e.g., dose)		
Examples:	Biogen Galápagos PLIANT HORIZON Galecto FibroGen Roche / Martin Promedior	<b>PURETECH</b> GIVING LIFE TO SCIENCE*		
	Phase 2 IPF Trial Failures: Biogen, Galecto, Horizon, Pliant; Example Phase 3 IPF Trial Failures: FibroGen, Galar	pagos, Roche/Promedior		

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

## Commercial Opportunity 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

- 32 Active patents acquired from Auspex (exclusivity up to 2033 with PTE)
  - In-licensed US patent from Auspex

6 Issued US patents26 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%)

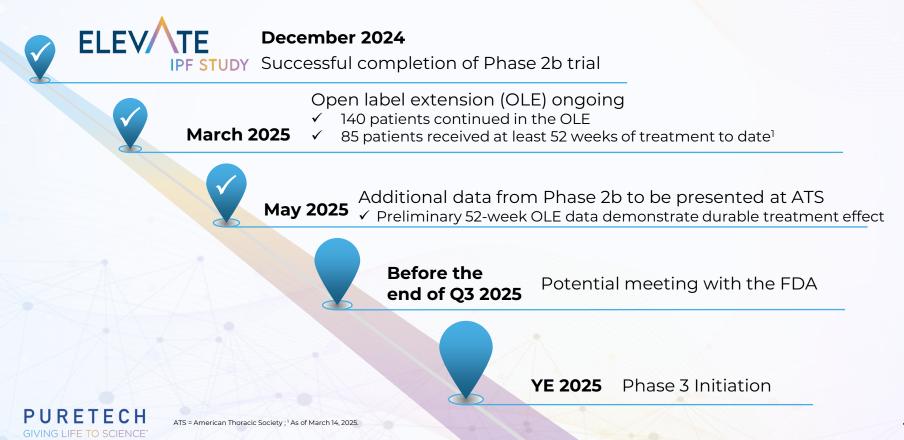


 Deupirfenidone has the potential for significantly improved efficacy without sacrificing tolerability, making it a treatment option for a wide range of IPF patients



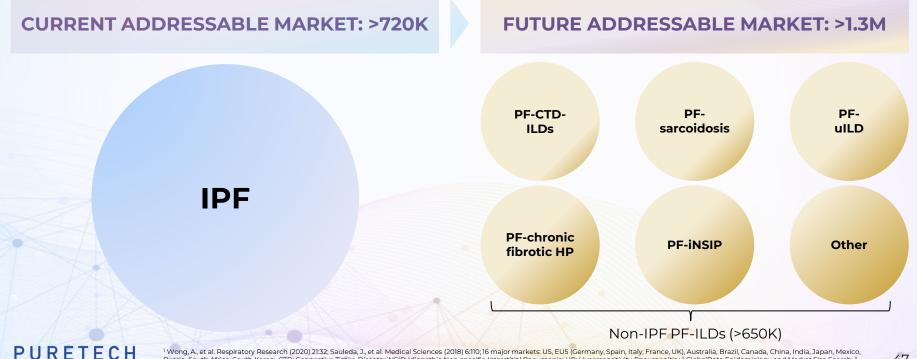
SOC = standard of care. Retrospective cohort analysis using claims data for individuals enrolled in private and Medicare Advantage health plans from OptumLabs Data Warehouse (N=21,444,770); Dempsey TM, Payne S, Sangaralingham L, Yao X, Shah ND, Limper AH. Adoption of the Antifibrotic Medications Pirfenidone and Nintedanib for Patients with Idiopathic Pulmonary Fibrosis. Ann Am Thorac Soc. 2021;18(7):1121-1128.

## Accelerating Program Advancement for Patients in Need



## 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>



<sup>1</sup> Wong, A., et al. Respiratory Research (2020) 21:32; Sauleda, J., et al. Medical Sciences (2018) 6:110; 16 major markets: US, EUS (Germany, Spain, Italy, France, UK), Australia, Brazil, Canada, China, India, Japan, Mexico, Russia, South Africa, South Korea; CTD; Connective Tissue Disease; iNSIP: Idiopathic Non-specific Interstitial Pneumonia; HP; Hypersensitivity Pneumonitis; 2 GlobalData Epidemiology and Market Size Search; 3 Nintedanib is approved for PPF, also known as PF-ILD, in addition to IPF and SSc-ILD, Additional pipeline agents have demonstrated that mechanisms to treat IPF could also work for treating PPF.

# 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



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, whether they were announced as a Founded Entity or not, and will be advanced through with either the Company's funding or non-filituitive sources of financing. As of December 31,2024, Wholly-Owned Programs were developed by the wholly-owned subsidiaries including PureTech LYT, Inc, PureTech LY

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

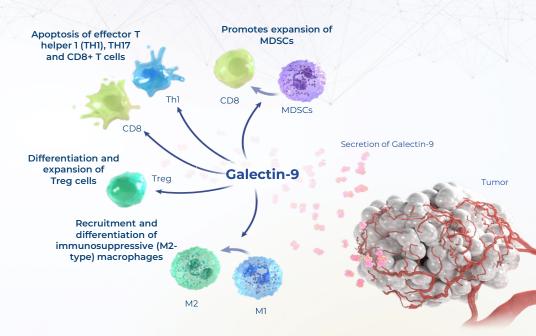
Driving immunosuppression through multiple pathways

### 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 is an investigational drug not approved by any regulatory authority. mAb = monoclonal antibody; AML = acute myeloid leukemia; Treg = T regulatory cell; MDSC = myeloid derived suppressor cell; MI/M2 = tumor associated macrophage (TAMI) (immunoactive) and 2 (immunosuppressed) cell; TAI = T helper1 cell https://www.nature.com/articles/s41573-023-00636-2; https://pubmed.ncbinlm.nih.qov/27038510/; https://www.nature.com/articles/s41538-020-1186-7.



## 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
- 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

- 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



AML = Acute myeloid leukemia; MDS = Myelodysplastic syndromes; PR = Partial response; CR = Complete response; SD = Stable disease; PD = Progressive disease; MLFS = Morphological leukemia-free state; ORR = Overall response rate; ELN (European Leukemia Network) guidelines 2017: for response assessment: <a href="https://www.ncbi.nlm.nih.go/pmc/articles/PMCS291965;">https://www.ncbi.nlm.nih.go/pmc/articles/PMCS291965;</a> 'Data as of 4/28/25.



# **Our** Portfolio

Seaport Therapeutics

35.6% Equity

# Neuropsychiatric medicines

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

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Advancing SPT-320 into Phase 1 studies

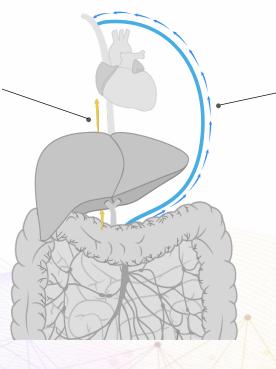


## Glyph™: Leveraging the Lymphatic System to Unlock New Medicines

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





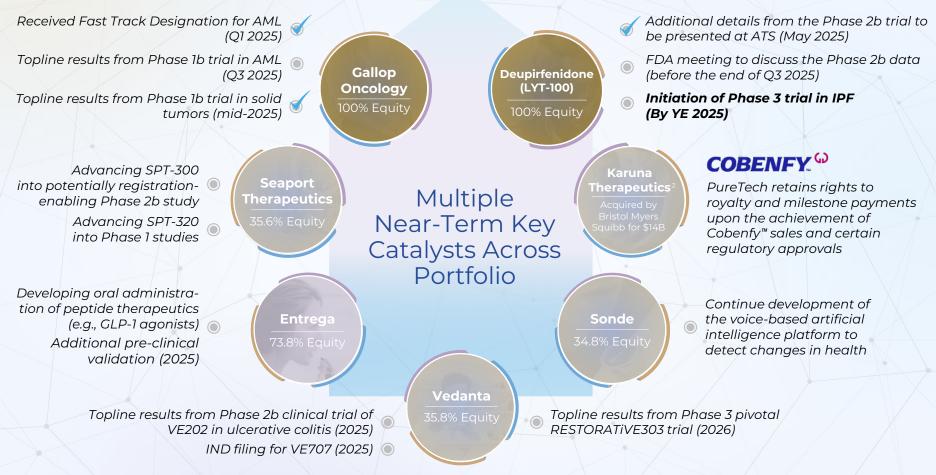
## Pipeline of First & Best-in-Class CNS Medicines

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		
<b>SPT-348</b> Non-hallucinogenic neuroplastogen	Improve PK & tolerability	Mood & neuropsychiatric disorders			
			Con	npleted //////// In progre	SS
M	ultiple discovery/pre	eclinical programs u	Inderway leveraging	g the Glyph™ pl	atform



<sup>1</sup> The FDA and corresponding regulatory authorities will ultimately review Seaport's clinical results and determine whether their therapeutic candidates are safe and effective. No regulatory agency has made any such determination that our therapeutics are safe or effective for use by the general public for any indication.





PURETECH GIVING LIFE TO SCIENCE 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 eligible to receive sublicense income and royatiles 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 outstances, but exploiting unalicated hore but be issued pursuant to equity incentive plans. PureTech controls Gallop Oncology, Inc; <sup>2</sup> As of March 22, 2023, PureTech has sold its right to also creative a 3% royatly from Karuna to Royatly Pharma on net sales up to \$2 billion annually, after which threshold PureTech will receive 67% of the royatly payments and Royatly Pharma will receive 3%. Additionally, under its license agreement with Karuna, PureTech retains the right to also creative certain sublicinese income. Next: Certain third-party trademarks are included here? PureTech will receive 67% of the royatly tademarks. COBENFY<sup>M</sup> (namenline and trospium chloride) is indicated for the treatment of schizophrenia in adults. For Important Safety Information, see US. Full Prescribing Information, including Patient Information on COBENFY.com. Following the acquisition of Karuna, RaX's in sow under the stewardship of Bristol Myers Squibb and will be marketed as Cobenfy.

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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.



**PURETECH** GIVING LIFE TO SCIENCE <sup>1</sup>PureTech level cash, cash equivalents and short-term investments excludes cash and cash equivalents at non-wholly owned subsidiary of \$0.4m. PureTech Level Cash, cash equivalents and short-term investments is a Non-IFRS measure



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### **APPENDIX A: INTERNAL PROGRAM**

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- Case Study for Deuterium Benefits
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- Vedanta
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- PureTech is Executing & Delivering Results
- Financial Highlights/Non-IFRS Measures

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## Accelerating Momentum & Delivering Results

IPF STUDY

Key milestones in recent years

ELEV



## **COBENFY**

BMS/Karuna received FDA Approval for Cobenfy™ (<sup>III</sup> Bristol Myers Squibb<sup>™</sup>

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 completes

successful Phase 2b trial of

deupirfenidone in IPF

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



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

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



Note: Certain third-party trademarks are included here; PureTech does not claim any rights to any third-party trademarks.

COBENFY<sup>IM</sup> (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.

# 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



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)* 



### PAUL NOBLE, MD

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



### MARLIES WIJSENBEEK, MD, PHD

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

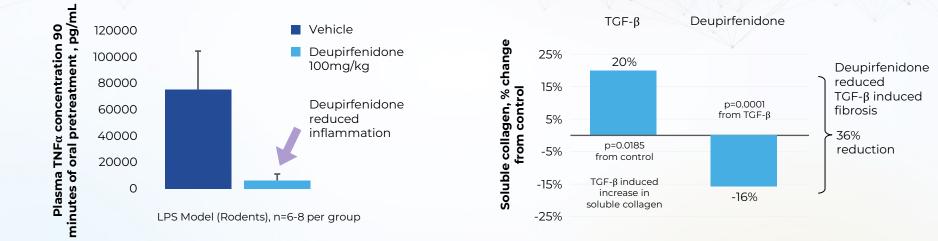


# Deupirfenidone Preclinical Data



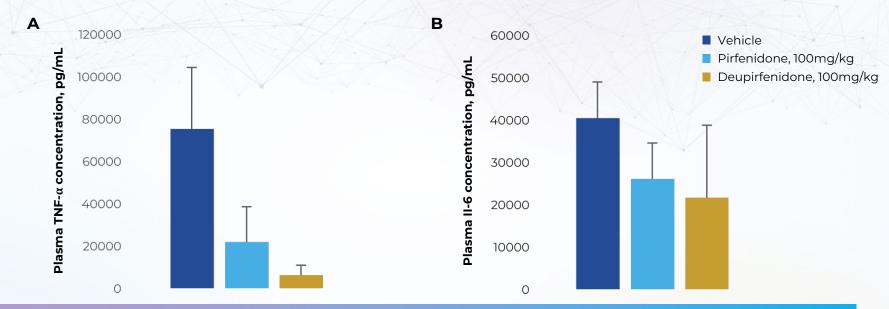
Deupirfenidone: Preclinical POC Demonstrates Antiinflammatory & Anti-fibrotic Pharmacology

PRECLINICAL PLASMA CONCENTRATIONS OF TNFA WITH DEUPIRFENIDONE VERSUS CONTROL IN VITRO REDUCTION OF TGF-B INDUCED SOLUBLE COLLAGEN PRODUCTION (MOUSE FIBROBLASTS)



## 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 µg/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



matches pirfenidone AUC

2. Head-to-head tolerability TOLERABILITY ADVANTAGE VS. PIRFENIDONE

.....

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

Older 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



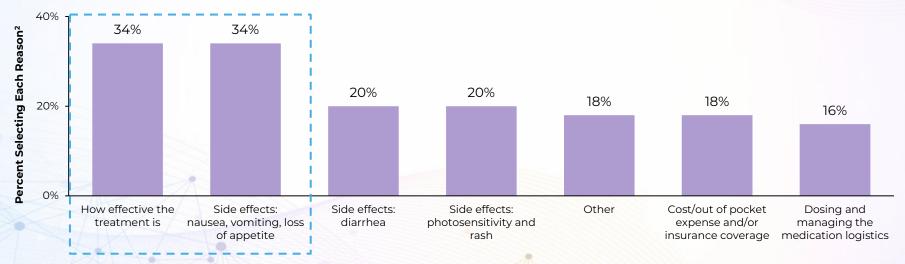


# Market Research



## 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>

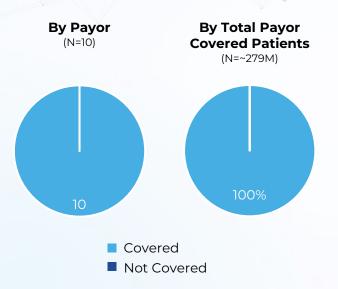
### **PURETECH** GIVING LIFE TO SCIENCE

<sup>1</sup>Market research quantitative survey of 90 participants with IPF conducted by Sago. Research completed in March 2024. <sup>2</sup>This question was asked of N=44 participants who had ever taken an antifibrotic medication to manage their IPF. Participants were specifically asked about the decision for starting treatment with pirfenidone or nintedanib. Participant were allowed to select all reasons that applied to them.

## 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



<sup>11</sup>D payors (mix of regional, national, PBM, and IDN) were qualitatively interviewed by a third party; Research completed in QI 2023 based on a product profile using the results of the Phase 1 healthy older adult crossover study; the results here based on the UPSIDE product profile where LYT-100 results in improved efficacy; <sup>2</sup> Payors were asked: "how would your organization manage Product X"; <sup>3</sup> All payors expect to cover LYT-100 if LYT-100 result in improved efficacy outcomes for IPF patients.

## Deupirfenidone in The Face of Generics & Novel MOAs

### **DEUPIRFENIDONE VS. GENERICS**

- The safety/tolerability of deupirfenidone remains attractive and meaningful to pulmonologists and payers <u>even in the face of</u> <u>generic competition<sup>1</sup></u>
- 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

### DEUPIRFENIDONE VS. NOVEL MODE 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

#### Generic pirfenidone and nintedanib

### **OVERVIEW**

- Both generic pirfenidone and generic nintedanib are expected to be on the market at time of deupirfenidone launch<sup>1</sup>
- 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

### **POSITIONING OF DEUPIRFENIDONE**

- Deupirfenidone will compete for new patient starts in plans without step edits
- In plans with step edits, deupirfenidone will be used as second line of treatment for patients who fail on generic antifibrotics
- Even if all payers require step edits, ~50% of patients will be eligible for deupirfenidone

Reformulated pirfenidone and nintedanib  A few reformulated pirfenidone and nintedanib approaches, including inhaled and sustained release, are in early development

- 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
- None of the localized delivery candidates have demonstrated the same evidence of efficacy as systemic therapies

- **Novel Mechanisms**
- Nearly all new mechanisms are being studied on top of/or after the standard-ofcare (currently pirfenidone & nintedanib)

- Potential for deupirfenidone to be the backbone standard-of-care for future combination regimens
- Pirfenidone and nintedanib remain key competitors for deupirfenidone



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

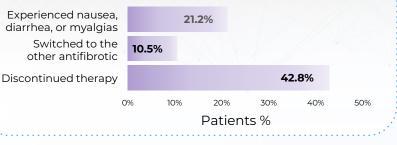
OPTUM Study of 11,000 Patients with IPF<sup>1</sup> October 2014 to July 2019

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

## Patients who never receive antifibrotic therapy

73.6%

Initiated pirfenidone or nintedanib since FDA approval in 2014 Over 40% of patients eventually discontinue antifibrotic therapy

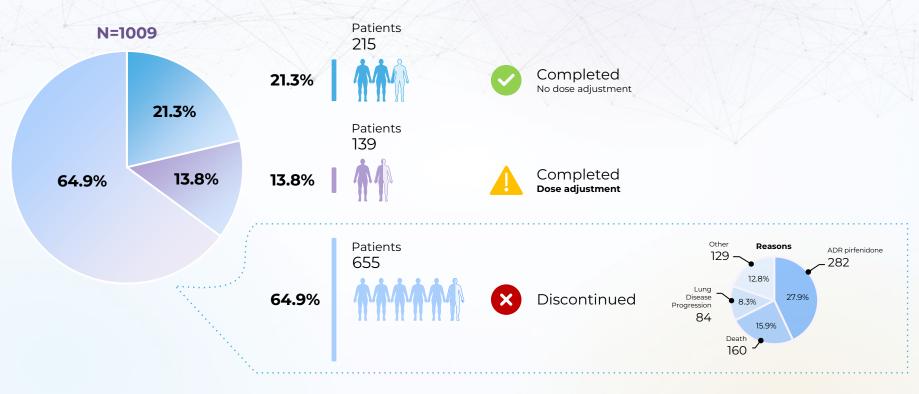




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\*Retrospective cohort analysis using claims data for individuals enrolled in private and Medicare Advantage health plans from OptumLabs Data Warehouse (N=2),444,770).
<sup>1</sup> Dempsey TM, Payne S, Sangaralingham L, Yao X, Shah ND, Limper AH. Adoption of the Antifibrotic Medications Pirfenidone and Nintedanib for Patients with Idiopathic Pulmonary Fibrosis. Ann Am Thorac Soc. 2021;8(7):112-1128.

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



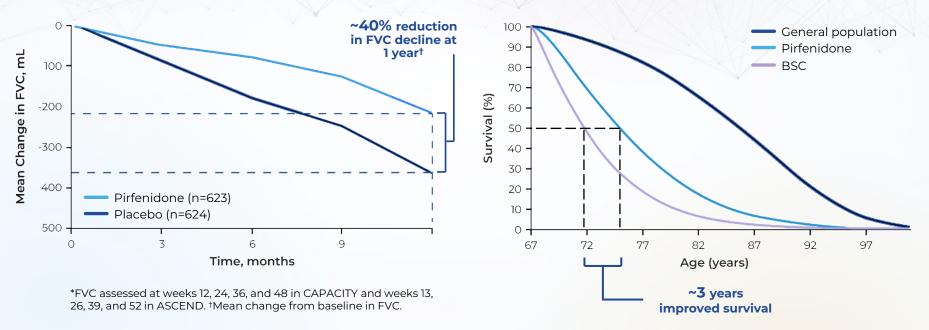


## Pirfenidone: A Clinically Validated Treatment for IPF



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



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# Design & Tolerability Findings of Pirfenidone Studies

Pirfenidone discontinuations often related to gastrointestinal (GI) adverse events (AEs)<sup>1</sup>

### Pirfenidone GI AEs:

- Require titration in IPF and other studies
- More common in women<sup>2</sup>

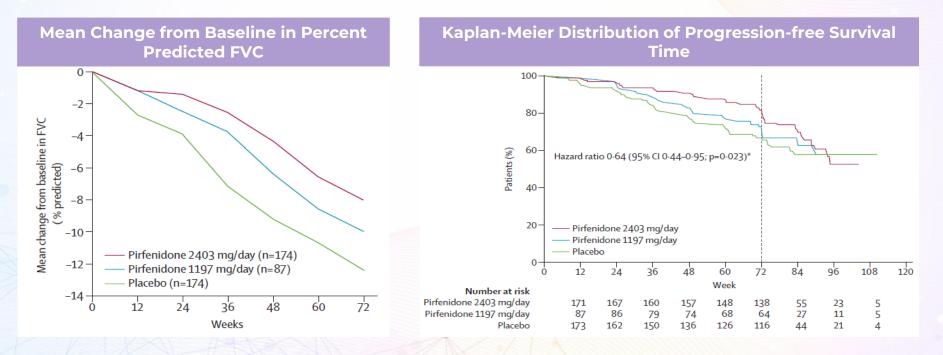
	PIRFENIDONE FOOD EFFECT/ANTACID STUDY <sup>2</sup>		PIRFENIDONE FOOD EFFECT AND BIOEQUIVALENCE STUDY <sup>3</sup>		PIRFENIDONE PHASE 3 STUDIES <sup>1</sup>		
Design	801mg single-dos adults, 44		801mg single-dose in healthy adults, 36% women		2403mg per day, IPF patients 26% women		
	Most common AEs	Pirfenidone N=16	Most common AEs	Pirfenidone N=44	Most common GI AEs^	Pirfenidone N=623	Placebo N=624
	Nausea	43.8%	Nausea	29.5%	Nausea	36%	16%
	Dizziness	37.5%	Dizziness	18.2%	Rash	30%	10%
Most	AEs more frequent in the fasted state AE rate higher in women		Headache	9.1%	Ab. pain	24%	15%
common					Diarrhea	26%	20%
AEs			Constipation	9.1%	Headache	22%	19%
			Vomiting	4.5%	Dyspepsia	19%	7%
			Dyspepsia	4.5%	Dizziness	18%	11%
			AEs more frequent in the fasted state		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%), fatigue (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



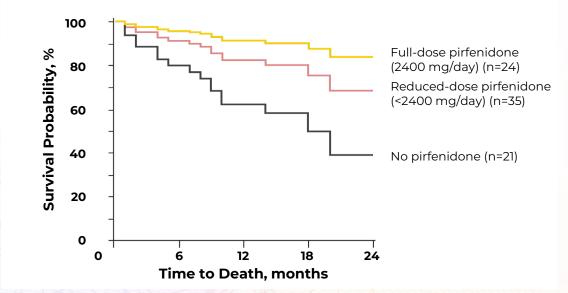


95% CIs were only calculated for absolute differences for the week 72 time point in study 004 (0.7 to 9.1) and study 006 (-3.5 to 4.7). ANCOVA, analysis of covariance; CI, confidence interval; FVC = forced vital capacity; IPF = idiopathic pulmonary fibrosis. Noble PW, et al. Lancet. 2011;377:1760-1769.

# 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)

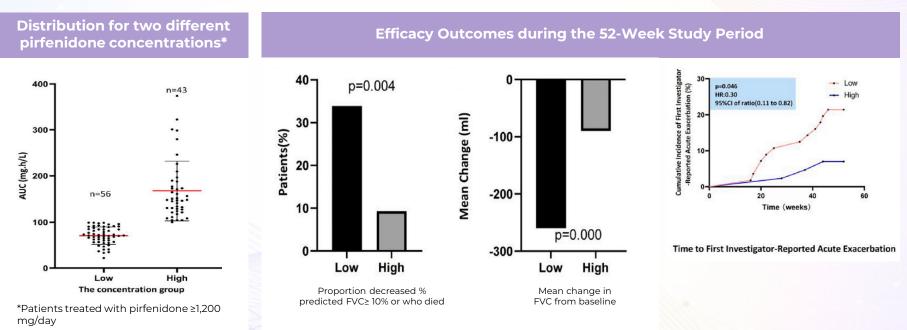




HR, hazard ratio; IQR, interquartile range. Dhooria S, et al. Sarcoidosis Vasc Diffuse Lung Dis. 2020;37:148-157

# 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



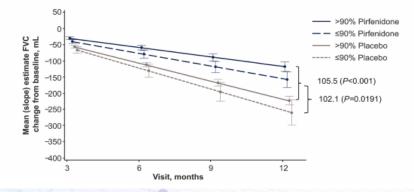
Horizontal red lines represent the mean value, and the lower and upper black lines represent the SD value, respectively.

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# 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%)<sup>1</sup>



- 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 <<u><</u>90%)
- Patients who took <90% of their intended dose of pirfenidone had faster decline in FVC as compared to patients who took >90%

78

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<sup>1</sup> Nathan, S. D., Lancaster, L. H., Albera, C., Glassberg, M. K., Swigris, J. J., Gilberg, F.,... & Noble, P. W. (2018). Dose modification and dose intensity during treatment with pirfenidone: analysis of pooled data from three multinational phase III trials. *BMJ open respiratory research*, 5(1), e000323; Modelled mean (SEM) observed forced vital capacity (FVC) volume change from baseline (mL) over time by dose intensity (>90%, ≤90%), based on actual dose (modified intention-to-treat population). No imputation for missing values and deaths. Months 3, 6, 9 and 12 correspond to weeks (2, 24, 35 and 48 for CAPACITY (004 and 006) studies and weeks 13, 26, 39 and 52 for ASCEND (016), respectively. The annual rate of decline was estimated from the linear mixed-effects model comparing pirfenidone with placebo for each of the dose intensity groups (>90%, <90%), with change from baseline as the outcome variable. Study (CAPACITY 004 and 006 and ASCEND 016), treatment, sex, age and height were evaluated as fixed effects, and patient and assessment time were evaluated as random effects in an unstructured variance-covariance matrix.

# Case Study for Deuterium Benefits



# A Case Study for Deuterium Benefits: Austedo<sup>®</sup>, 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<sup>®</sup> sales by 2027<sup>2</sup>



# 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**

<b>Opsumit® (macitentan)</b> Endothelin Receptor Antagonists	<b>Uptravi® (selexipag)</b> Prostacyclins	Winrevair™ (sotatercept) Activin Signaling Inhibitors	
Opsumit <sup>®</sup> (macitentan) gained FDA approval in 2013	Generic versions of Flolan® (epoprostenol) available	Winrevair™ (sotatercept) gained FDA approval in 2024 as an add-on to background SOC therapies	
	↓	•	
Tracleer® (bosentan) and Letairis® (ambrisentan) lost patent exclusivity in 2019	Remodulin <sup>®</sup> (IV treprostinil) lost patent exclusivity in 2019	Winrevair™ (sotatercept) Peak sales estimate of \$3-5B <sup>2</sup> despite its primary use as a combination therapy with generics	
		·	
Opsumit® (macitentan) \$2.4B sales in 2024 <sup>1</sup> despite generic entrants	Uptravi® (selexipag) \$2.2B sales in 2024 <sup>1</sup> despite generic competition		

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# Appendix A: Wholly-Owned Program LYT-200

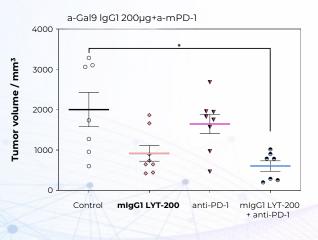


# Gallop Oncology: LYT-200

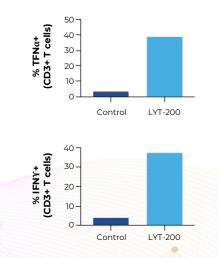
Multiple lines of preclinical data supporting therapeutic potential

#### SINGLE AGENT ACTIVITY IN B16F10 MELANOMA MODEL

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



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



### 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-PD-1s 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



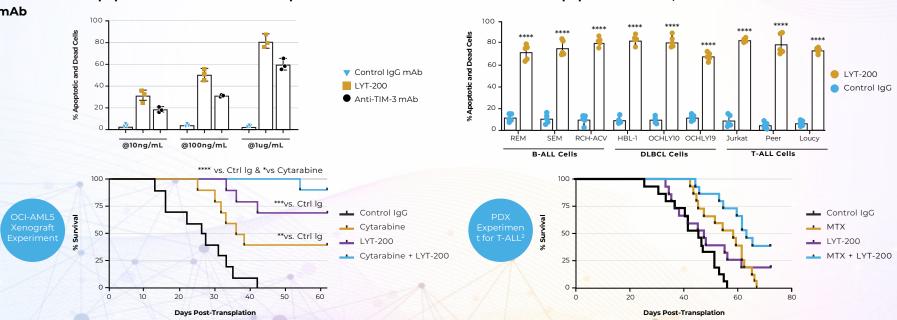
<sup>1</sup> For patient-derived organoids, n = 20 tumor samples; Success defined as: >20% upregulation of at least two out of three T cell activation markers; Success achieved in 60% of tumors with majorit showing >2 fold activation.



# LYT-200

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

## AML MODEL<sup>1</sup>



T-ALL, B-ALL & DLBCL MODEL

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

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

# PURETECH

<sup>1</sup> Statistical Significance (Log-rank [Mantel-Cox] test): Ctrl Ig vs. Cytarabine: \*\*p=0.0090; Ctrl Ig vs. LYT-200: \*\*\*\*p<0.000; Ctrl Ig vs. Cytarabine + LYT-200: \*\*\*\*p<0.000; Cytarabine + LYT-200: \*\*\*\*p<0.0001; Cytarabine vs. LYT-200 + Cytarabine: \* \$ = 0.0134; 2 Ctrl | g vs. MTX = 0.062 (ns); Ctrl | g vs. LYT-200 = 0.021 (1); Ctrl | g vs. LYT-200 + MTX = 0.0006 (\*\*\*); MTX vs. LYT-200 = 0.01 (\*\*); MTX vs. LYT-200 + MTX = 0.0009 (\*\*\*); LYT-200 + LYT-200 + MTX= 0.008 (\*\*).



# 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

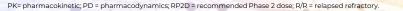
#### DOSE FINDING (4+2 DESIGN)



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

0

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

Completed evaluation of weekly dosing

### CLINICAL INVESTIGATORS





Columbia University Medical Center Manji Gulam

Memorial Sloan Kettering Cancer Center

Eric Sherman

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

with Alzheimer's disease ~3.2M 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



PURFTFCH

### 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



(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 Mvers Sauibb for **\$14B**
- ✓ Cobenfy<sup>™</sup> (formerly known as KarXT) FDA approval on September 26, 2024

Note: Certain third-party trademarks are included here; PureTech does not claim any rights to any third-party trademarks. COBENFY™ (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

ech 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

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

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

## ~120 million

people have MDD with anxiety disorders<sup>2</sup> **301 million** people with anxiety disorders worldwide<sup>1</sup>

# 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

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280 million

<sup>1</sup> Depressive disorder (depressive): World Health Organization; <sup>2</sup> Kessler et al., 2015. Anxious and non-anxious major depressive disorder in the World Health Organization World Mental Health Surveys. Epidemiol Psychiatr Sci. 2015 Jun;24(3):210-26; <sup>3</sup> Compared to patients with MDD without anxiety: Hopwood M. (2023). Anxiety Symptoms in Patients with Major Depressive Disorder: Commentary on Prevalence and Clinical Implications. Neurology and therapy, 12(Suppl 1), 5–12.



# SPT-300 (Glyph Allopregnanolone)

For major depressive disorder



Allopregnanolone is an endogenous (natural) neurosteroid with clinical validation in postpartum depression

Lower levels of allopregnanolone have been documented in patients with mood disorders

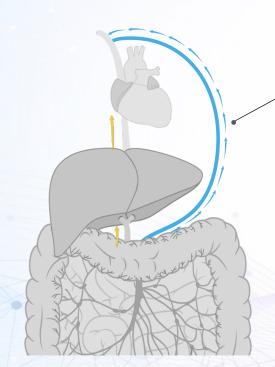
...BUT method of administration (IV form) significantly limits patient uptake

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



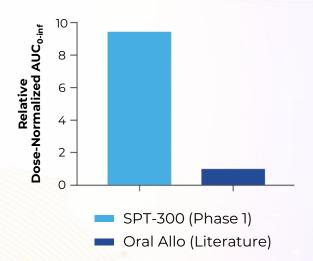
# SPT-300 (Glyph Allopregnanolone)



### 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>



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<sup>1</sup>Not a head-to-head; comparative values from brexanolone NDA 211371 Multi-disciplinary Review and Evaluation, FDA CDER, 2018.<sup>2</sup> AUC(0-inf) of LYT300 and Study 547-CLP-107 (in ref 1: Brexanolone NDA) were divided by mg allopregnanolone dosed, then both values divided by that dose-normalized AUC of 547-CLP-107 to show relative exposure at an equivalent dose.

SEAP RT 92

# Phase 2a Trial Design in Acute Anxiety

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



### PRIMARY AIM:

PURFTFCH

To characterize pharmacology of SPT-300 for potential anxiety indications

### PRIMARY ENDPOINT:

Reduction in salivary cortisol, a stress hormone

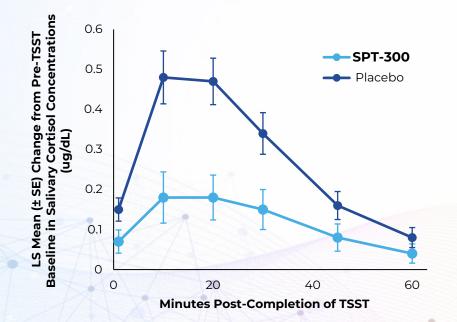
### TRIAL DESIGN:

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<sup>1</sup>



# **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

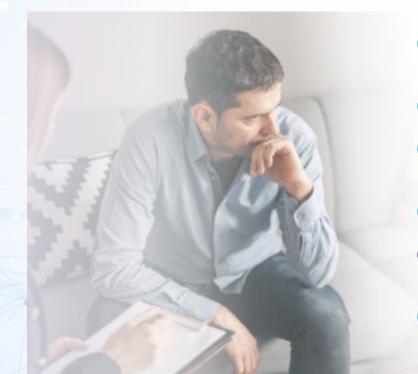


<sup>1</sup> SPT-300 vs. placebo log(10) LS Mean Change from Pre-TSST Baseline to Maximal Salivary Cortisol Concentration (ug/dL);<sup>2</sup> Fries, Eva, et al. (2006). Psychoneuroendocrinology, 31(10), 1278–1288. https://doi.org/10.1016/j.psyneuen.2006.09.009.



# SPT-320 (Glyph Agomelatine)

For generalized anxiety disorder



Clinically validated and approved for MDD in the EU and MDD & GAD in Australia

Differentiated 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>

THERAPEUTICS

**PURETECH** GIVING LIFE TO SCIENCE' MDD=Major depressive disorder. GAD=Ceneralized anxiety disorder 1 Cipriani, A, et al.(2018). Comparative efficacy and acceptability of 21 antidepressant drugs for the acute treatment of adults with major depressive disorder: a systematic review and network meta-analysis. The Lancet, 391(10128),1357–1366. <u>https://doi.org/10.1016/s0140-6736(17)32802-7</u>;<sup>2</sup> Slee, A, et al.(2019). Pharmacological treatments for generalised anxiety disorder: a systematic review and network meta-analysis. The Lancet, 393(10178), 768–777. <u>https://doi.org/10.1016/s0140-6736(18)31793-8</u>; <sup>3</sup> In silico modeling using the FDA-licensed DLISym platform shows potential to greatly reduce risk of clinically significant liver enzyme elevations.

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

## AGOMELATINE

- Low oral bioavailability (~1%)
- X Most of the drug does not reach the brain
  - Liver enzymes increase likely linked to hepatic first-pass metabolism:
    - ~1.0% 1.4% agomelatine vs. 0.7% with placebo1

## 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

effective

### 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

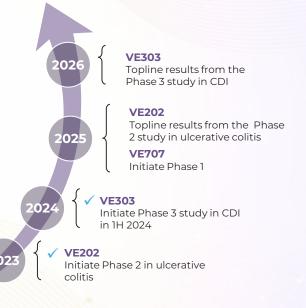
#### ~500K **Treated using antibiotics** which damage the CDI cases microbiome per year in the US ~1M **IBD** interventions limited Ulcerative colitis & by toxicities & systemic Crohn's disease immune suppression patients in the US Allergen avoidance & ~4.6M desensitization therapies Living with peanut may not prove cost-

### 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%<sup>1</sup>)

# UPCOMING MILESTONES & VALUE REALIZATION



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

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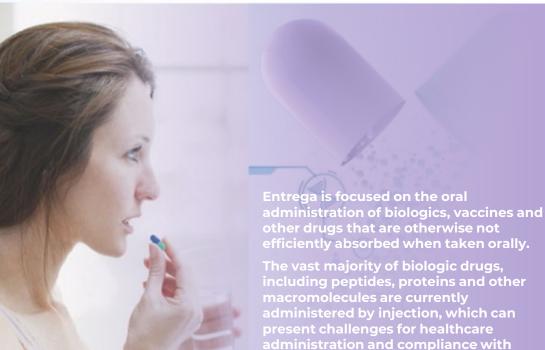
allergy in the US

<sup>1</sup>As of December 31, 2024, PureTech's percentage ownership of Vedanta Biosciences was approximately 35.8 percent on a diluted basis. This calculation includes issued and outstanding shares, options, and warrants, but excludes unallocated shares authorized to be issued pursuant to equity incentive plans. PureTech ownership reflects current ownership and does not take into account any potential future dilution, if applicable, as a result of conversion of that debt amount.

# Entrega

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

### (PRTC Ownership: 73.8%<sup>1</sup>)



### MILESTONES ACHIEVED

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

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<sup>1</sup> As of December 31, 2024, PureTech's percentage ownership of Entrega was approximately 73.8 percent on a diluted basis. This calculation includes outstanding shares, options, and warrants, but excludes unallocated shares authorized to be issued pursuant to equity incentive plans.

# Sonde

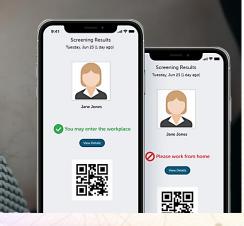
Voice-based artificial intelligence (AI) platform with the potential to transform how we monitor health

### < Search Sonde Health 17+ What's New Version History Version 7.3.4 1d ago 1. Functionality to dynamically configure app from portal 2. Ul enhancement Preview Sonde Tan the microphone to get started

### ~17M

Individuals in the US are affected by depression

The lag between onset of disease & accurate diagnosis & beginning of treatment can be measured in years for many high-burden health conditions



### 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**

(PRTC Ownership: 34.8%<sup>1</sup>)

- 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

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<sup>1</sup>As of December 31, 2024, PureTech's percentage ownership of Sonde was approximately 34.8 percent on a diluted basis. This calculation includes outstanding shares, options, and warrants, but excludes unallocated shares authorized to be issued pursuant to equity incentive plans.

# Appendix C: Supplemental Materials



# PureTech's Proven Expertise

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

PROGRAM	VALIDATED EFFICACY	PROBLEM	PURETECH INSIGHT/IP
<b>BMS's Cobenfy</b> (fka KarXT) FDA approved for schizophrenia in adults	Xanomeline is highly effective in reducing psychosis	Xanomeline has GI tolerability issues	Pairing xanomeline with peripherally- restricted muscarinic antagonist improved AE profile and unlocked Ist new class in 50+ years
<b>LYT-100</b> 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 pirfenidone w/ favorable tolerability & potential for improved efficacy
SPT-300	Allopregnanolone has	Marketed allopregnanolone	Using proprietary Glyph technology, achieved blood

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 allopregnanolone Using proprietary Glyph technology, achieved blood levels of allopregnanolone at/above those associated w/ therapeutic effect & demonstrated exposuredependent target engagement w/ GABA<sub>A</sub> receptors<sup>2</sup>. Approach may have advantages vs. oral chemical analogs



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COBENFY<sup>TM</sup> (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. I 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. <u>https://doi.org/10.18553/jmcp.2017.23.3-b.s17</u>;<sup>2</sup> Brexanolone NDA 211371 Multi-disciplinary Review and Evaluation, FDA CDER, 2018; FXTAS = Fragile X-associated Tremor/Ataxia Syndrome.

# PureTech is Executing & Delivering Results

#### REGULATORY



### **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 eligible 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

Key investors include Bill & Melinda Gates Foundation, Bristol-Myers Squibb, Rock Springs 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

#### **PURETECH** GIVING LIFE TO SCIENCE<sup>\*</sup>

Note: Certain third-party trademarks are included here; PureTech does not claim any rights to any third-party trademarks. COBENFY<sup>M</sup> (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.

# Financial Highlights

Cash Flow and Liquidity	March 31, 2025 \$ 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.

