

# PURETECH

GIVING LIFE TO SCIENCE®

Corporate Presentation  
February 2024



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

Such statements are based on currently available operating, financial and competitive information and are subject to various risks, uncertainties and assumptions that could cause actual results to differ materially from those anticipated or implied in our forward-looking statements due to a number of important factors including, but not limited to, those risks that are described in the Company's most recent Annual Report and Accounts which can be found on the Company's website at <https://investorspuretechhealth.com/financials-filing/s-reports> and in the Company's Annual Report on Form 20-F for the year ended December 31, 2022 filed with the Securities and Exchange Commission.

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, we assume no obligation to update these forward-looking statements publicly, or to revise any forward-looking statements to reflect events or developments occurring after the date of this document, even if new information becomes available in the future.

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Our Founded Entities are comprised of our Controlled Founded Entities and our Non-Controlled Founded Entities, all of which are incorporated in the United States. References to our "Controlled Founded Entities" refer to Follica, Incorporated, and Entrega, Inc., for all periods prior to March 1, 2023, Vedanta Biosciences, Inc., for all periods prior to May 25, 2022, Sonde Health Inc., and for all periods prior to June 10, 2021, Alivio Therapeutics, Inc. References to our "Non-Controlled Founded Entities" refer to Akili Interactive Labs, Inc., Karuna Therapeutics, Inc., Vor Bio, Inc., Gelesis, Inc., for all periods following May 25, 2022, Sonde Health, Inc., for all periods following March 1, 2023, Vedanta Biosciences, Inc., and, for all periods prior to December 18, 2019, restORbio, Inc. We formed each of our Founded Entities and have been involved in development efforts in varying degrees. In the case of our Controlled Founded Entities Follica, Incorporated and Entrega, Inc., we continue to maintain majority voting control. With respect to our Non-Controlled Founded Entities, we may benefit from appreciation in our minority equity investment as a shareholder of such companies.

# PureTech Team Has a Track Record of Outperforming

Oversaw R&D of therapeutics with 11 regulatory approvals; created several multibillion \$ companies



**Daphne Zohar**

Founder & Chief Executive Officer

Built team, scientific network & pipeline; Recognized as a top leader in biotech by EY, Fierce Pharma, Scientific American, BioWorld; BIO Board Member & Strategy & Policy Committee co-chair



**Bharatt Chowrira, PhD, JD**

President

Former COO Auspex (acq. by Teva \$3.5B), COO Nektar, GC SIRNA (acq. by Merck \$1.1B); Board Member



**Eric Elenko, PhD**

Co-founder & Chief Innovation & Strategy Officer

Co-inventor of KarXT & other key PureTech programs; McKinsey, UCSD



**Julie Krop, MD**

Chief Medical Officer

Former CMO at Freeline, AMAG (oversaw 3 FDA approvals; acquired by Covis group \$647M); Previously at Vertex, Millennium, Pfizer



**Robert Lyne**

Chief Portfolio Officer

Former CEO at Arix Bioscience (acq. by RTW Biotech \$250M); Previously at Touchstone Innovations, Bird & Bird

# World Class Board of Directors Provides Strong Governance

Our board contributed to regulatory approvals of approximately 20 drugs, led multi-billion-dollar strategic transactions & co-founded multiple companies



Raju Kucherlapati, PhD

Interim Board Chair

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



John LaMatta, PhD

Board

Former President of Pfizer Global R&D, Forbes Contributor



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



Robert Horvitz, PhD

Board Observer & Chair of R&D Committee

Nobel Prize in Medicine, MIT, HHMI, neurobiologist at MGH, Former Novartis Scientific Advisory Board Member



Kiran Mazumdar-Shaw, PhD

Board

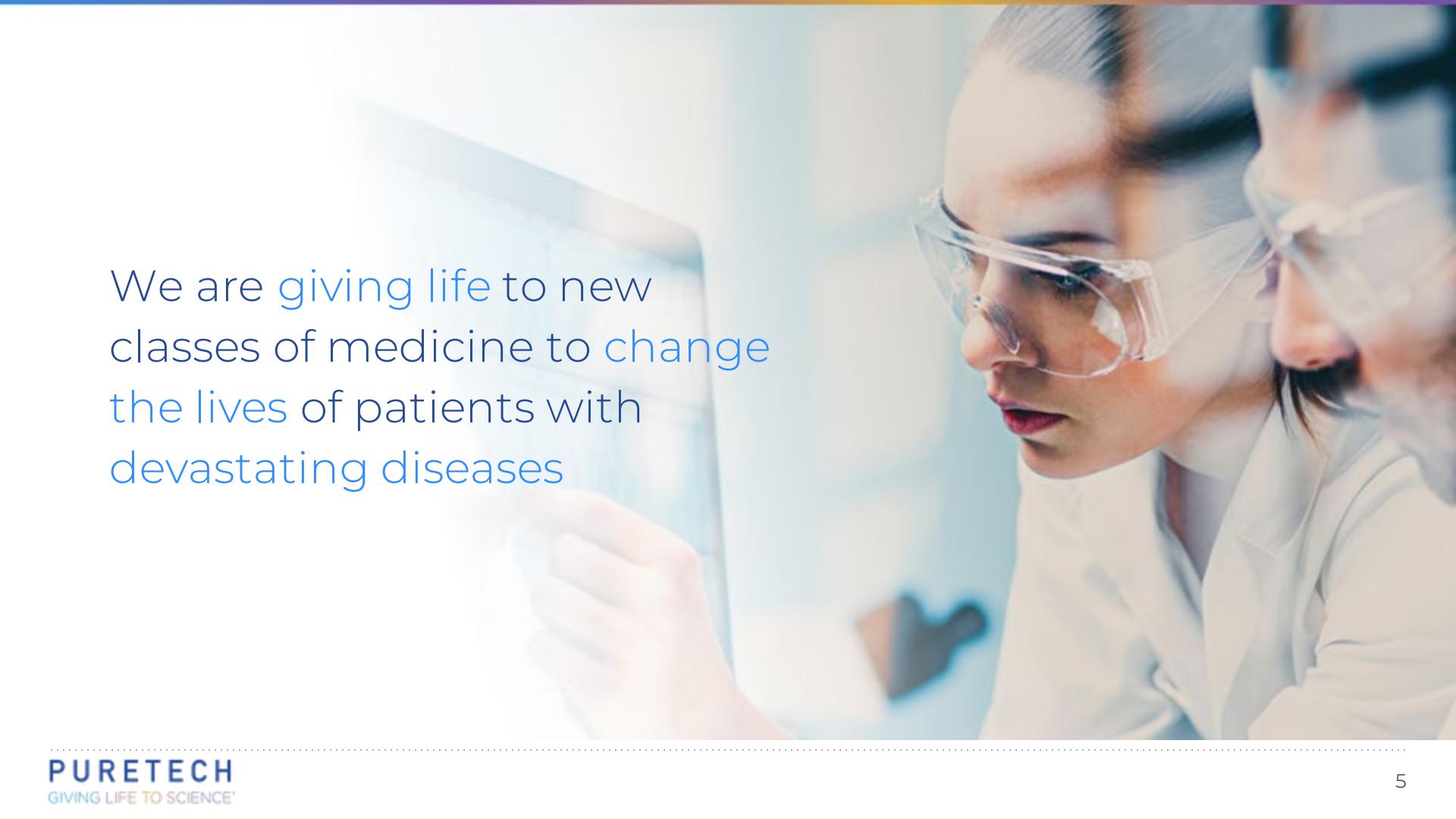
Founder & Chairperson of Biocon, Board of Trustees Member at MIT, Member of National Academy of Engineering



Sharon Barber-Lui, PhD

Board

CFO & Senior VP of Teva Pharma, Former CFO of Merck & Co. Inc. U.S. Oncology & Senior VP of EQRx

A female scientist in a white lab coat and clear safety goggles is looking down at a test tube she is holding. She is in a laboratory setting with other equipment visible in the background. The image is slightly blurred, suggesting motion or a focus on the scientist's face and the test tube.

We are giving life to new  
classes of medicine to change  
the lives of patients with  
devastating diseases

# We Are Delivering on Our Mission to Change Patients' Lives

Outstanding track record of R&D productivity & clinical success

28



new therapeutics &  
therapeutic candidates  
generated to date

2



taken from inception to  
FDA & EU regulatory  
clearances

1

filed for FDA approval

>80%

of trials have been  
successful<sup>1</sup>

6x

better probability of clinical  
success compared to the  
industry average<sup>2</sup>

# Distinctive Approach

R&D engine is repeatable and scalable

## VALIDATED EFFICACY



Advancing new medicines with proven clinical **efficacy** previously held back by limitations

## CLEAR PATIENT BENEFIT



Applying **proprietary technologies** to address key limitations and **unlock drug potential** for **patients**

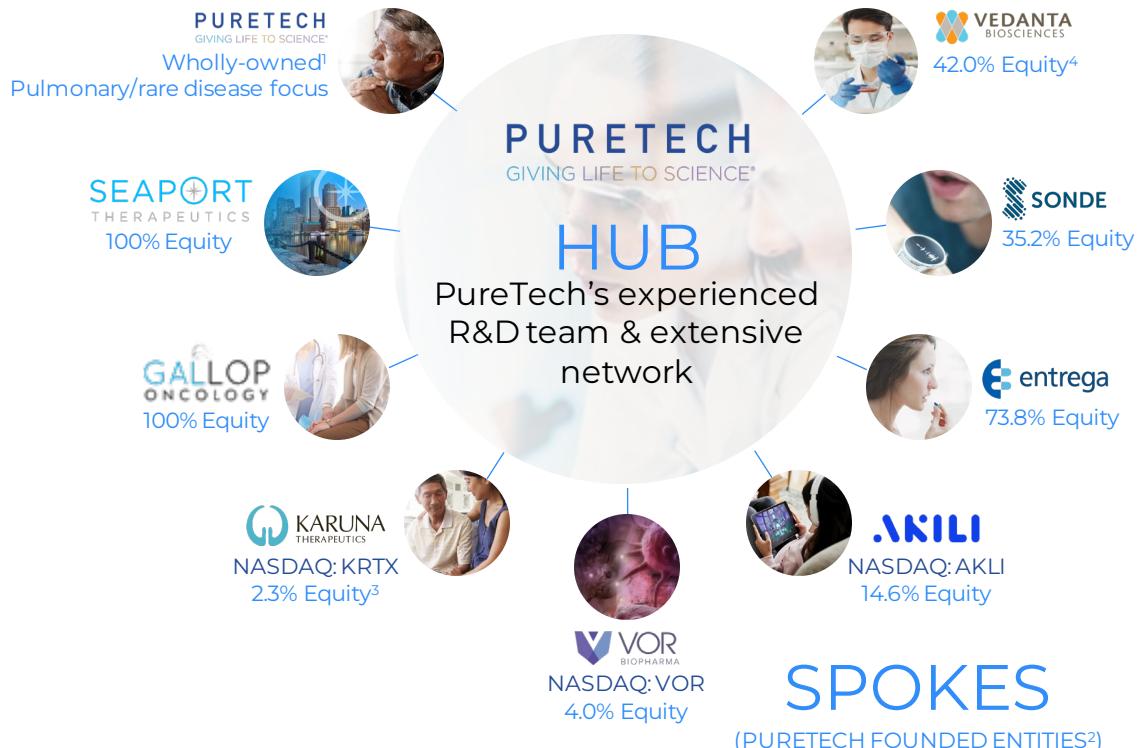
## EFFICIENT & DE-RISKED PATH



Building on **well-defined clinical & regulatory paths** backed by our proven R&D track record

## The PureTech-Pioneered Hub-and-Spoke Model

## Robust pipeline of new medicines poised for tremendous growth



## CAPITAL EFFICIENT MODEL

- ✓ **\$320M** estimated Consolidated Cash, Cash Equivalents & Short-Term Investments<sup>5</sup>; cash figures & capital return strategy to be updated following the closing of the Karuna/BMS transaction. Estimated gross proceeds from PureTech's KRXT equity holdings is ~\$294M.
- ✓ Operational runway into **2027**
- ✓ PureTech has not needed to raise capital in **~7 years**
- ✓ **\$3.8B** raised by Founded Entities since July 2018, of which 96% was from 3<sup>rd</sup> parties

1. References to "Wholly Owned Pipeline" refer to the Company's five pre-clinical candidates for LY-170, LY-200, LY-370, LY-390 and LY-370. Certain of the Wholly Owned Pipeline and certain assets within the Wholly Owned Pipeline are being advanced through the newly formed Ruchatech, Inc. and Gallo Chirologix, Inc. As of March 22, 2023, PurTech has sold its right to receive a 3% royalty from Royalty Pharma in net sales up to \$1 billion annually, after which the total PurTech will receive 6% of the royalty payments and Royalty Pharma will receive 3%. PurTech retains its equity ownership in Karuna. Additionally, under its license agreement with Karuna, PurTech retains the right to receive milestone payments upon the achievement of certain regulatory approvals and 20% of sublicense income. Vedanta's \$65 million recent financing round was structured as convertible debt. PurTech ownership reflects ownership as of June 30, 2023, and does not take into account any potential future dilution, if applicable, as a result of conversion of the debt amount. \*Founded Entities represent companies founded by PurTech in which PurTech maintains ownership in an equity interest and, in certain cases, is eligible to receive milestones in connection with product sales. As of the date of this release, PurTech maintained control over Enteq, Inc. by virtue of its majority ownership and the right to elect a majority of the Board of Directors. PurTech also controls Seprat, Seprat, Inc. and Gallo Chirologix, Inc. As of the date of this release, PurTech did not have a controlling interest in Karuna Therapeutics, Inc., Akin, Inc., Sonde Health, Inc., Vedanta Biosciences, Inc. and Vor Biopharm, Inc. The preliminary selected financial results reported by the Company are unaudited, subject to adjustment, and provided as an approximation in advance of the Company's annual report of financial results.

# KarXT Case Study – Invented & Advanced by PureTech

1st new mechanism for treating schizophrenia in over 50 years

## PATIENT NEED

**~2.7M** living with schizophrenia in the US

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

Current antipsychotics **have significant side effects and poor adherence**

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



## PURETECH ROLE

Built top team of CNS experts & leaders

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



**Xanomeline**  
CNS active agonist

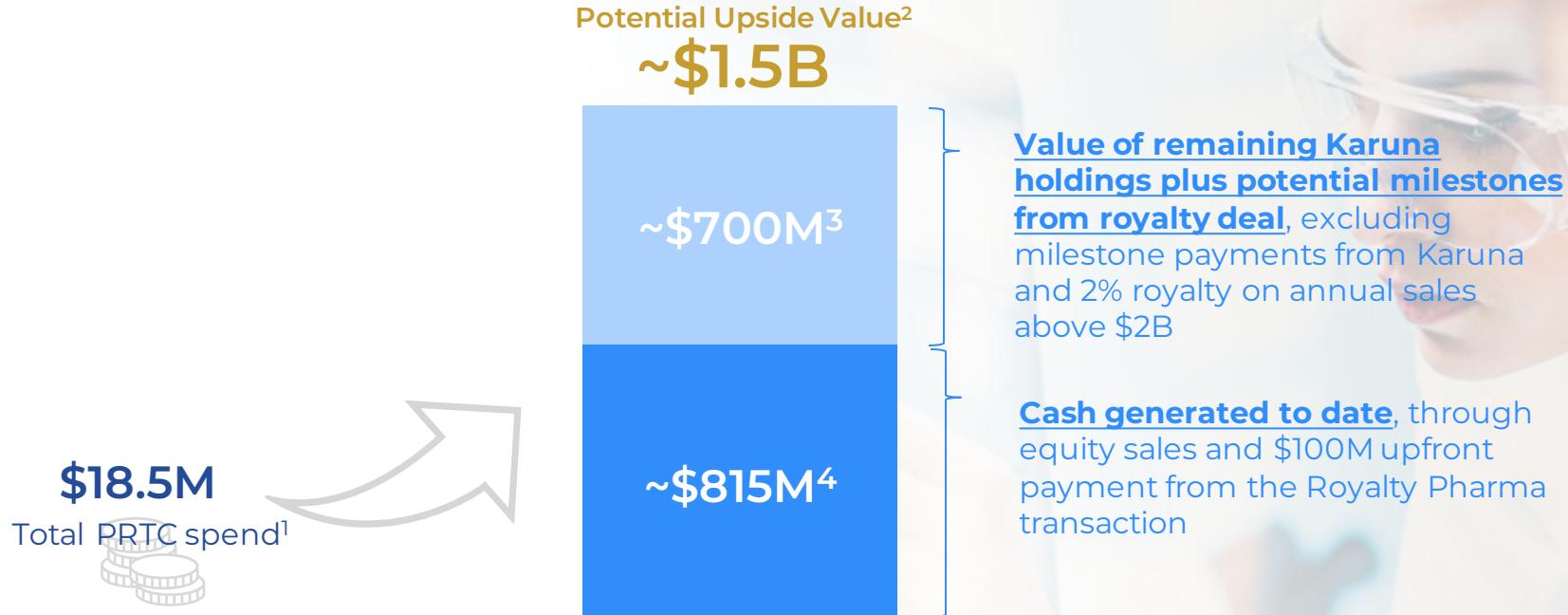
**Trospium chloride**  
Peripheral antagonist  
blocks side effects of agonist

## 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
- ✓ NDA submission completed in September 2023; PDUFA date, September 26, 2024
- ✓ Ongoing Phase 3 programs in **psychosis in Alzheimer's disease**
- ✓ Karuna Therapeutics is expected to be acquired by Bristol Myers Squibb for **\$14B**

# Generating Value for Patients and Shareholders

## KarXT Case Study Part 2



<sup>1</sup> Represents total PureTech principal investment in Karuna. <sup>2</sup> Represents the amounts described in footnote 3 plus the amounts described in footnote 4. <sup>3</sup> Represents the value of PureTech's holdings of KRTX common stock following the anticipated BMS acquisition of Karuna announced on December 22, 2023, plus the \$400 million in potential milestone payments included in PureTech's transaction with Royalty Pharma. The value of KRTX common stock may vary over time. PureTech also may not receive the totality of the milestone payments under its transaction with Royalty Pharma. <sup>4</sup> Represents cash generated to date through sales of KRTX common stock and the \$100 million in upfront consideration from PureTech's transaction with Royalty Pharma. Please see slide 80 for additional information regarding PureTech's sales of KRTX common stock.

# Wholly Owned Pipeline<sup>1</sup>

Certain assets to be advanced by new Founded Entities

## OUR PROGRAMS<sup>2</sup>

## DISCOVERY

## PRECLINICAL

## PHASE 1

## PHASE 2

## PHASE 3

**LYT-100<sup>3</sup>**  
Deuirfenidone

Idiopathic pulmonary fibrosis (IPF)

Topline results  
expected in Q4 2024

**LYT-200**  
Anti-Galectin-9 mAb

Solid tumors & hematological  
malignancies



**LYT-300**  
Glyph Allopregnanolone

Neuropsychiatric & rare CNS conditions



**LYT-310**  
Glyph Cannabidiol

Epilepsies & other neurological  
indications



**LYT-320**  
Glyph Agomelatine

Anxiety & mood  
disorders



Undisclosed

Undisclosed



Undisclosed

Undisclosed



Completed

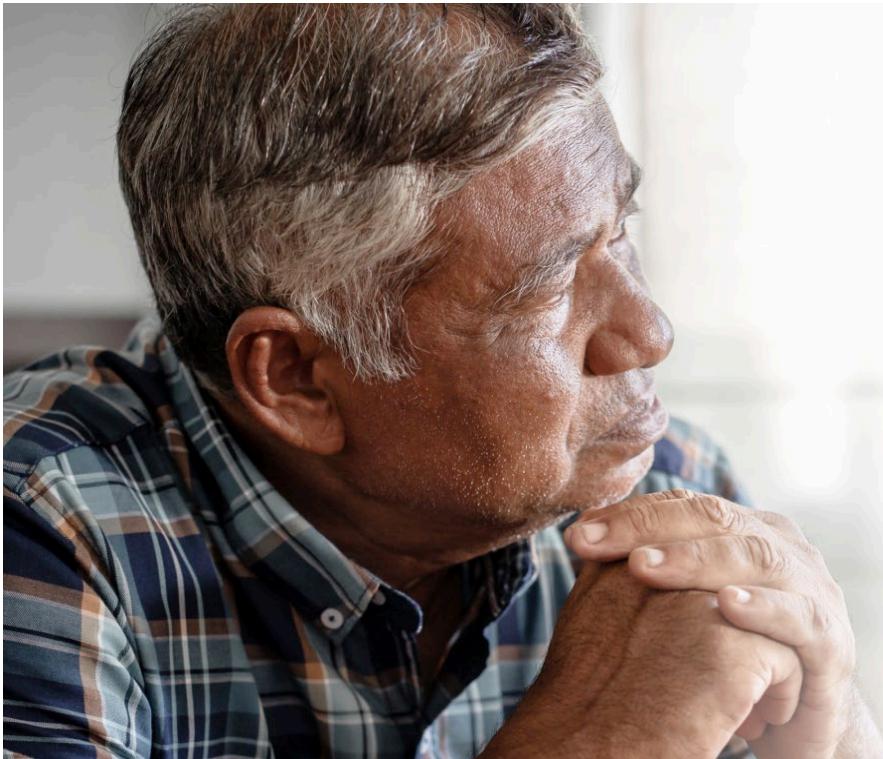
Phase-ready

In progress

<sup>1</sup> References to "Wholly Owned Programs" refer to the Company's five therapeutic candidates (LYT-100, LYT-200, LYT-300, LYT-310 and LYT-320), Glyph platform and potential future therapeutic candidates and platforms that the Company may develop or obtain. References to "Wholly Owned Pipeline" refer to LYT-100, LYT-200, LYT-300, LYT-310 and LYT-320. Certain of the Wholly Owned Programs and certain assets within the Wholly Owned Pipeline are being advanced through the newly announced Founded Entities Seaport Therapeutics, Inc. and Gallop Oncology, Inc. <sup>2</sup>The FDA and corresponding regulatory authorities will ultimately review our clinical results and determine whether our wholly-owned therapeutic candidates are safe and effective. No regulatory agency has made any such determination that our wholly-owned therapeutic candidates are safe or effective for use by the general public for any indication. <sup>3</sup> Also being advanced for medical countermeasures under the FDA Animal Rule; plans underway to study LYT-100 in progressive fibrotic interstitial lung disease (PF-ILDs) and exploring LYT-100 in additional opportunities where pirfenidone has shown human efficacy signals e.g. heart failure with preserved ejection fraction (HFpEF) and focal segmental glomerulosclerosis (FSGS).

# LYT-100 for Idiopathic Pulmonary Fibrosis (IPF)

ORPHAN DESIGNATION: ~120,000 patients in the US, ~110,000 in the EU<sup>1</sup>



## FATAL & PROGRESSIVE

Causes scar tissue in the lungs, leading to **shortness of breath and loss of lung function<sup>2</sup>**

Median survival 2 – 5 years<sup>3</sup>

## UNMET MEDICAL NEED

2 standard of care treatments proven to slow disease progression, but **have significant side effects, including nausea, vomiting and diarrhea<sup>4,5</sup>**

# Pirfenidone:

Clinically validated anti-fibrotic & anti-inflammatory

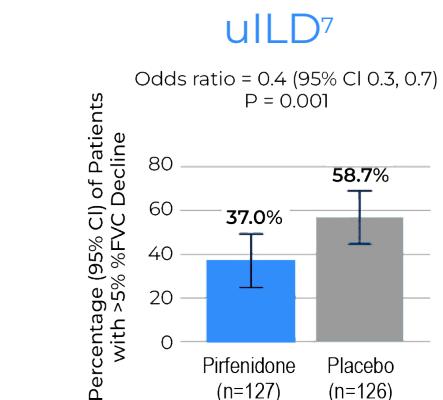
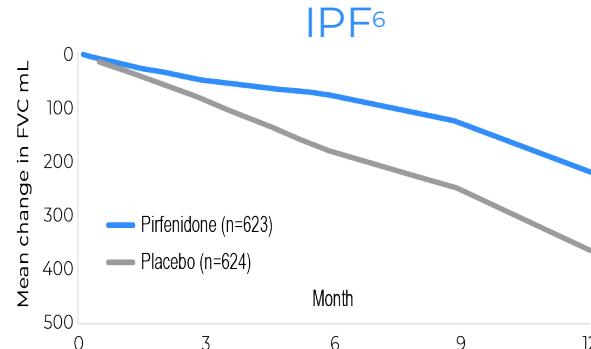
## VALIDATED EFFICACY

- ✓ Pirfenidone FDA-approved for IPF with breakthrough designation for Unclassifiable Interstitial Lung Disease (uILD); has been shown **to extend life in patients with IPF by an average of ~2.5 years<sup>1</sup>**

- ✓ Over a **dozen late-stage & real-world efficacy studies** demonstrate **efficacy in IPF<sup>2</sup>**

- ✗ **BUT** GI-related tolerability issues significantly limit its usage resulting in **~50% who discontinue, dose adjust, or switch<sup>3</sup> & 3 out of every 4 patients are not on standard of care<sup>4</sup>**

Despite drawbacks, 2022 sales of both SOC treatments combined were ~\$4B<sup>5</sup>



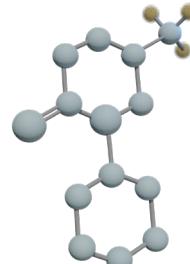
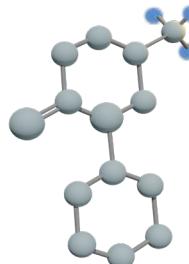
<sup>1</sup>Fisher, M., Nathan, S. D., Hill, C., Marshall, J., Dejonckheere, F., Thureson, P., & Maher, T. M. (2017). Predicting Life Expectancy for Pirfenidone in Idiopathic Pulmonary Fibrosis. *Journal of Managed Care & Specialty Pharmacy*, 23(3-b Suppl), S17-S24. [https://doi.org/10.18553/jmcp.2017.723\\_3-b\\_a7](https://doi.org/10.18553/jmcp.2017.723_3-b_a7) <sup>2</sup>Saad, M. I., Mcleod, L., Hodges, C., Vlahos, R., Rose-John, S., Ruwampura, S., & Jenkins, B. J. (2021). ADAM17 Deficiency Protects against Pulmonary Emphysema. *American Journal of Respiratory Cell and Molecular Biology*, 64(2), 183-195. doi:10.1165/crmb.2020-0214oc. <sup>3</sup>Cottin, V., et al. *ERJ Open Research* (2018); Dempsey, et al. *Annals of the American Thoracic Society*, 18(7), 1121-1128. <https://doi.org/10.1163/A.annalsATS.202.0007> <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 Soc*. 2021 Jul;18(7):1121-1128. <sup>5</sup>IPF & PF-ILD SOC 2022 annual sales. <sup>6</sup>Noble, P., et al. *European Respiratory Journal* (2016) 47:243-253. <sup>7</sup>ERS 2019: <http://bit.ly/219WCC>

# LYT-100:

A potential game changer for IPF patients

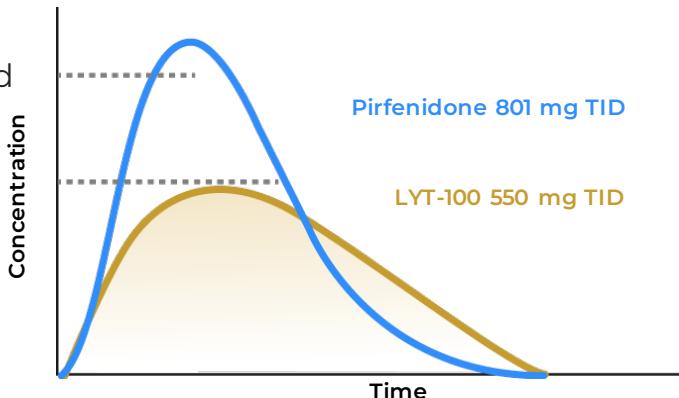
## PIRFENIDONE

- Clinically validated efficacy
- Associated with GI AEs
- Higher exposure limited by tolerability



## LYT-100

- Substantially improved adverse event profile<sup>1</sup>
- Pharmacology (activity) maintained
- Higher dose could improve efficacy; maximum tolerated dose not determined



# LYT-100: Efficient & De-risked Path

- ✓ **Composition of Matter Patent** exclusivity up to 2033 with PTE
- ✓ **Additional IP coverage** to ~2044
- ✓ Potential for **Orphan Drug Exclusivity for IPF** & other indications
- ✓ **Streamlined development program** using the same endpoints that have supported past approvals
- ✓ Potential to become the **frontline therapy for IPF**

# LYT-100:

Data to date (N>400)<sup>1</sup> demonstrate favorable safety & tolerability profile

## HEALTHY OLDER ADULT CROSSOVER TRIAL (N=49)

TEAE	LYT-100 550mg TID n (%)	Pirfenidone 801mg TID n (%)
<b>Gastrointestinal</b>	<b>8 (17.4%)</b>	<b>16 (34.0%)</b>
Nausea	7 (15.2%)	14 (29.8%)
Vomiting	2 (4.3%)	3 (6.4%)
Abdominal Pain/Distension	1 (2.2%)	3 (6.4%)
<b>Nervous System</b>	<b>8 (17.4%)</b>	<b>15 (31.9%)</b>
Headache	6 (13.0%)	9 (19.1%)
Dizziness	1 (2.2%)	7 (14.9%)
Somnolence	1 (2.2%)	2 (4.3%)

## LYT-100 DEMONSTRATED IMPROVED TOLERABILITY

Achieved ~50% reduction in healthy older adults experiencing **GI-related AEs compared to pirfenidone** in crossover trial

## IN OTHER LYT-100 STUDIES

Multiple Ascending Dose trial (N=40): without dose titration<sup>2</sup>; well-tolerated at all doses studied<sup>3</sup>; all treatment-related **AEs were mild & transient**

**Higher dose (824mg TID LYT-100)** in the 2<sup>nd</sup> Multiple Ascending Dose (N=24): well-tolerated with no additional incident<sup>4</sup>

Long COVID trial: strong safety & tolerability profile

LYT-100 is an investigational drug not approved by any regulatory authority.  
<sup>1</sup> Across single ascending dose trial, multiple ascending dose trial, healthy older adult crossover trial and additional Deuterium-Containing Drug Candidate for Interstitial Lung Disease and Other Inflammatory and Fibrotic Diseases Clinical Pharmacology in Drug Development. <https://doi.org/10.1101/274910>. TEAE = treatment-emergent adverse event; Discontinuations for AEs 1 during pirfenidone administration, 1 during LYT-100 administration. <sup>3</sup> LYT-100 was administered in doses of 100 mg, 250 mg, 500 mg, 750 mg and 1000 mg BID over five days. <sup>4</sup> Toby M. Maher, Michael C. Chen, Chris C. Korth, Eric Elenko, Mark D. Harnett, Varun Garg, Camilla S. Graham, Wasim H. Fares, Julie Krop (2023), Deupirfenidone (LYT-100) dose-selection rationale for a Phase 2b idiopathic pulmonary fibrosis study — ELEVATE IPF.

# Potential for Higher Dose of LYT-100 Presented at CHEST '23

Higher dose could potentially translate to enhanced efficacy in IPF

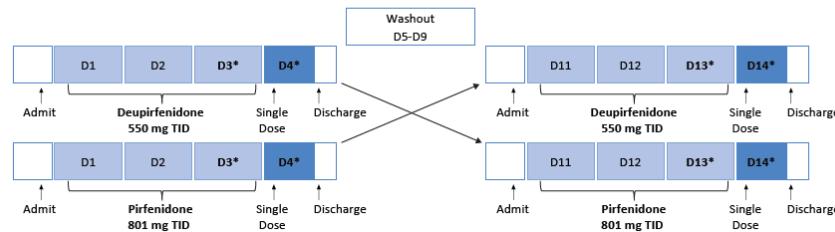
- LYT-100 (824mg TID) achieved a 43% higher exposure level than approved dose of pirfenidone (801 mg TID)<sup>1</sup>
- LYT-100 (824mg TID) well-tolerated with no additional incidence of GI or CNS AEs when titrated up from LYT-100 550 mg TID

## WHAT DOES THIS MEAN?

**LYT-100 can be studied at a higher dose that could provide enhanced efficacy with favorable tolerability in IPF**, based on the pirfenidone Phase 3 CAPACITY trial where approved dose of pirfenidone demonstrated better efficacy than a lower dose

## STUDY DESIGN

Figure 2. Study 1: Randomized, Placebo-controlled, Two-period Crossover Study in Healthy Older Adults Comparing Deupirfenidone 550 mg TID vs Pirfenidone 801 mg TID in Fed and Fasted Conditions

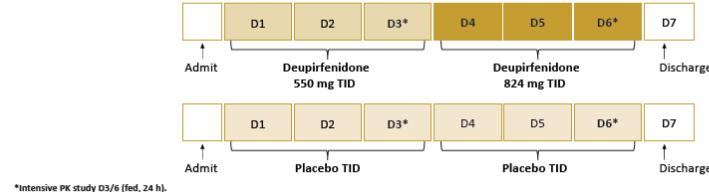


\*Intensive PK study D3/13 (fed, 24 h) and D4/14 (fasted, 6 h).

<sup>1</sup>Safety visit conducted 4±1 days following last dose.

D, day; h, hour; PK, pharmacokinetic; TID, 3 times/day.

Figure 3. Study 2: Randomized, Placebo-controlled, Parallel-arm Study in Healthy Older Adults Comparing Deupirfenidone 550 mg TID Titrated to Deupirfenidone 824 mg TID vs Placebo



# Registration-enabling Program in IPF Guided by Leading Experts

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



## **BILL BRADFORD, MD, PhD**

Former SVP InterMune;  
developed pirfenidone for the  
treatment of IPF



## **VINCENT COTTIN, MD**

Professor at Université Claude  
Bernard Lyon; Coordinator of  
Center for Rare Pulmonary  
Diseases at Louis Pradel Hospital;  
Section Editor of the *European  
Respiratory Journal*



## **KEVIN FLAHERTY, MD**

Professor at University of  
Michigan; PhIII trial of  
nintedanib in pfILD (*NEJM*)



## **TOBY MAHER, MD, PhD**

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



## **PAUL NOBLE, MD**

Chair, Department of Medicine,  
Cedars-Sinai; results of two late-  
stage 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

# LYT-100: Multiple Ways to Win

Current SOC has significant tolerability issues, with GI side effects being the most problematic

## BASE CASE: BETTER SAFETY

- ✓ LYT-100 **550 mg** demonstrates better safety



- ✓ Patients **can stay on the drug longer**



- ✓ Patients may achieve **more durable efficacy** compared to pirfenidone

## UPSIDE: BETTER EFFICACY

- ✓ LYT-100 **825 mg** demonstrates better efficacy



- ✓ Patients **retain more lung function**



- ✓ Patients may achieve **superior efficacy**

# LYT-100: Phase 2b Trial

1st of two potentially registration-enabling studies in patients with IPF

## PRIMARY AIM:

To evaluate activity of LYT-100 in patients with IPF

## PRIMARY ENDPOINT:

Slope of decline in FVC for LYT-100 compared to placebo over 6 months

## TRIAL DESIGN

**N= ~240 IPF patients**

- Placebo
- Pirfenidone 801 mg TID
- LYT-100 550 mg TID
- LYT-100 825 mg TID

**6-month treatment duration**



Phase 2b topline data expected in Q4 2024

# LYT-100: Potential to Address Multiple Underserved Diseases

## CURRENT INDICATION: IPF



Pirfenidone has been shown to improve survival by approximately 3 years compared to supportive care alone<sup>1</sup>

Pirfenidone reduces decline in lung function<sup>2</sup>

**Topline results from registration-enabling trial expected in 4Q 2024**

## NEXT INDICATION: PF-ILD



~650K non-IPF PF-ILD patients in the 16 major markets<sup>3</sup> are affected with few treatment options worldwide

Pirfenidone derisked due to similar pathophysiology of IPF and PF-ILD & clear development path

Pirfenidone showed initial efficacy signals in Ph2 RELIEF study

## MEDICAL COUNTERMEASURES



LYT-100 as medical countermeasure

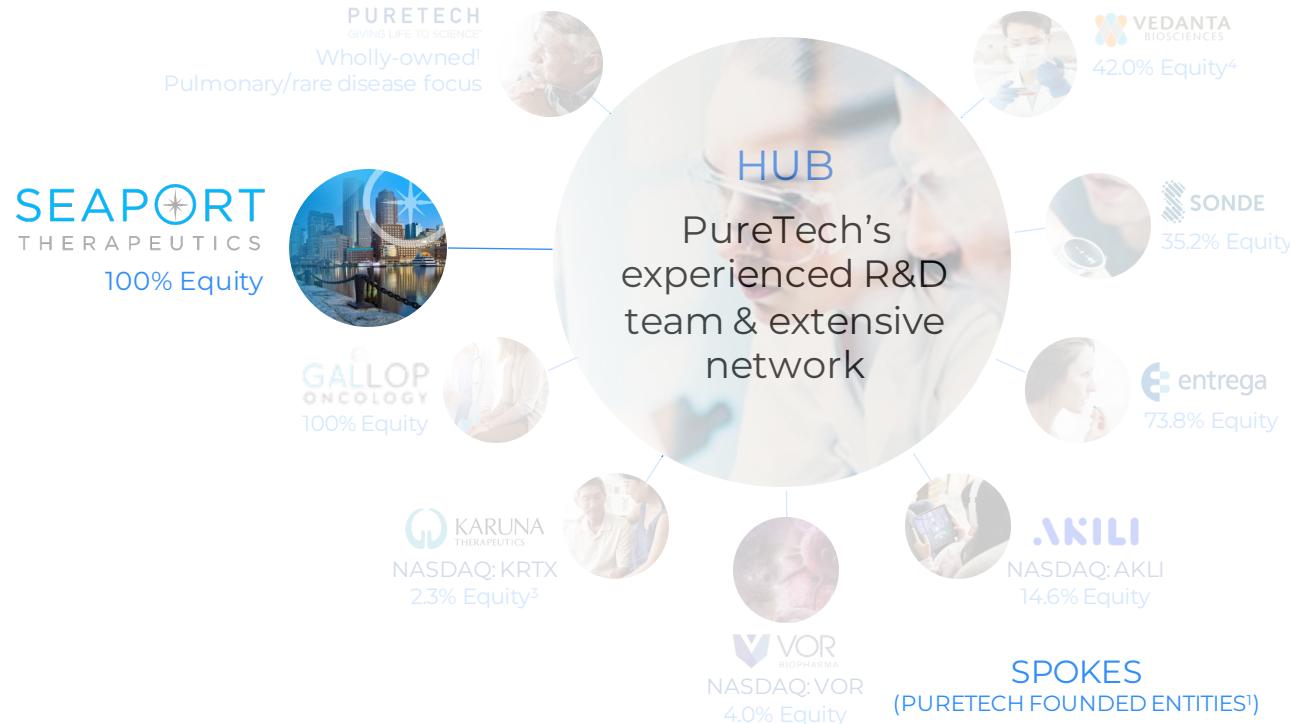
Pirfenidone mitigates radiation-induced lung fibrosis in preclinical study<sup>4</sup>

Subject to Animal Rule; allows for approval based on animal models when human efficacy studies are not feasible

Additional opportunities where pirfenidone has shown human efficacy signals (e.g. HFpEF, FSGS)

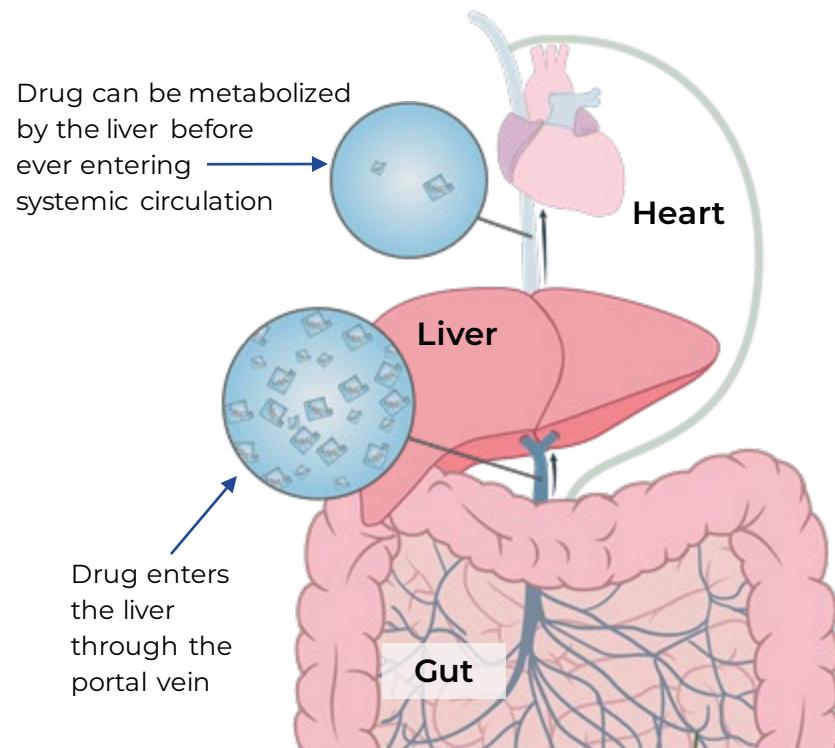
# The PureTech-Pioneered Hub-and-Spoke Model

Robust pipeline of new medicines poised for tremendous growth

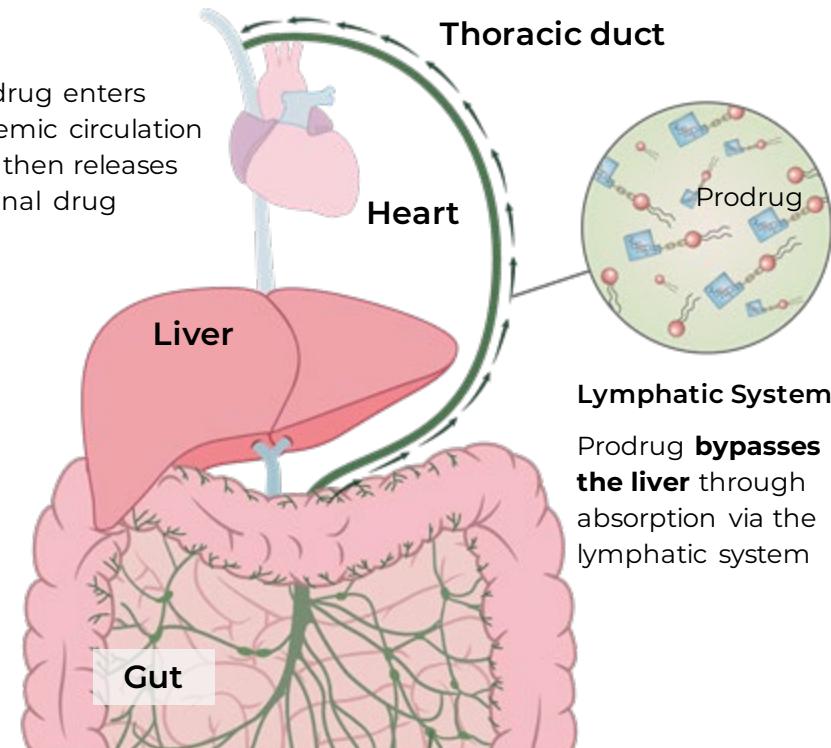


# Glyph™: PureTech's Proprietary Oral Prodrug Platform

## Conventional oral drug transport



## Glyph oral drug transport via the **lymphatic system**



# Seaport Therapeutics: First & Best-in-Class CNS Medicines

## OUR PROGRAMS<sup>1</sup>

### DISCOVERY

### PRECLINICAL

### PHASE 1

### PHASE 2

### PHASE 3

**LYT-300**  
Glyph Allo pregnanolone

Neuropsychiatric & rare CNS conditions

**LYT-310**  
Glyph Cannabidiol

Epilepsies & other neurological  
indications

**LYT-320**  
Glyph Agomelatine

Anxiety & mood  
disorders

Undisclosed

Undisclosed

Undisclosed

Undisclosed

# LYT-300 (Glyph Allopregnanolone)

For neuropsychiatric & rare CNS conditions



- ✓ 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
- ✓ **LYT-300 retains the activity & potency of endogenous allopregnanolone in an oral form**

# LYT-300: Human Data Summary

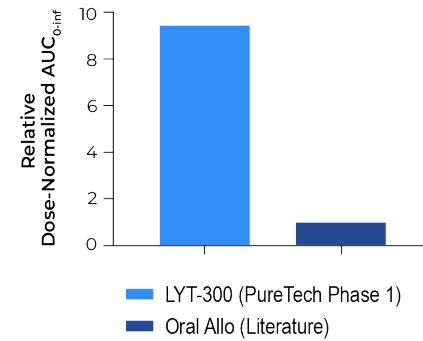
Multi-part Phase 1 program in healthy volunteers completed in 2022 (N=~90)

## PHASE 1 DEMONSTRATED

- **Oral bioavailability in healthy adults**, with blood levels of allopregnanolone **at or above those associated with therapeutic effect** and **9x greater** than orally administered allopregnanolone, based on third-party published data<sup>1</sup>
- **Target engagement with GABA<sub>A</sub> receptors via  $\beta$ -EEG\***, known to regulate mood and other neurological conditions
- **Generally well-tolerated** with no treatment-related severe or serious AEs, including no sudden loss of consciousness, observed



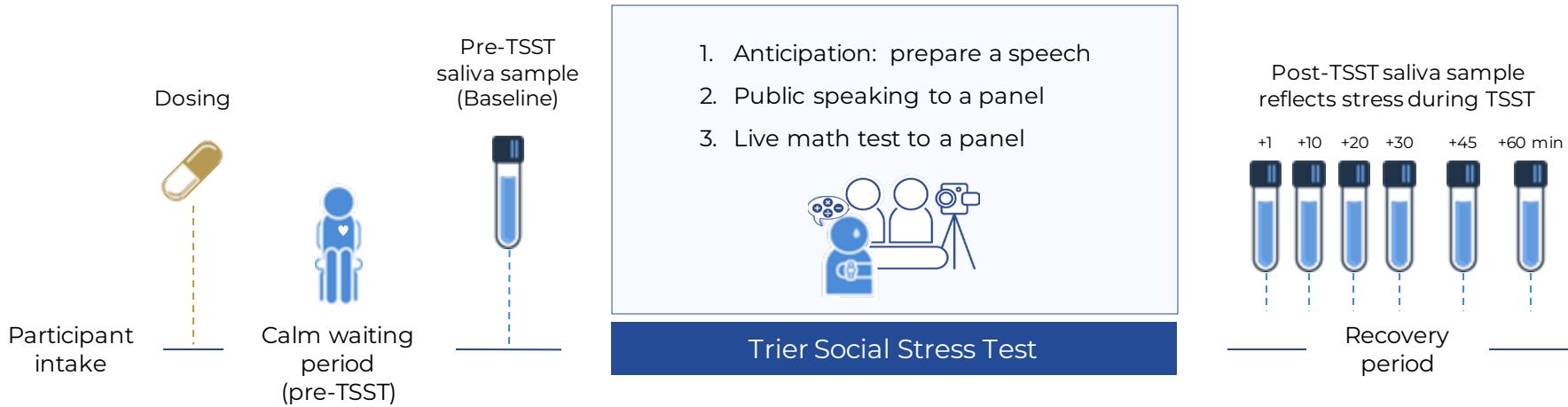
## LYT-300 Oral Systemic Exposure (Human) LYT-300 Phase 1 vs. Literature Data<sup>2,1</sup>



\* $\beta$ -EEG (electroencephalogram  $\beta$ -frequency) power at 13-30 Hz frequency range, is a real-time, quantitative measurement of electrical activity in the brain which changes in response to GABA<sub>A</sub> receptor activation<sup>1</sup>

# Phase 2a Trial Design in Acute Anxiety

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



## PRIMARY AIM:

To characterize pharmacology of LYT-300 for potential anxiety indications

## PRIMARY ENDPOINT:

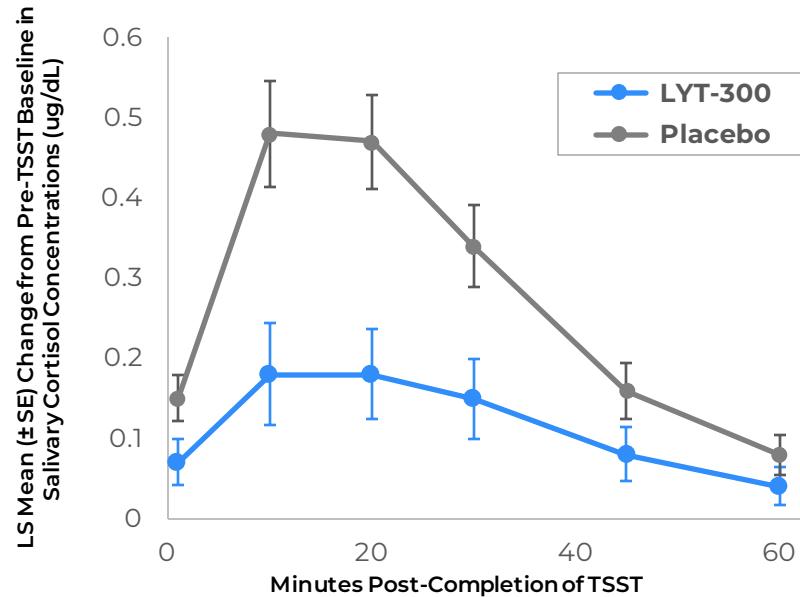
Reduction in salivary cortisol, a stress hormone

## TRIAL DESIGN:

N=80 randomized to LYT-300 or placebo

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

LYT-300 achieved primary endpoint ( $p=0.0001$ ) in stress hormone response<sup>1</sup>



## POSITIVE DATA

- ✓ LYT-300 had a similar effect size of 0.72 to previously observed results for alprazolam in the TSST<sup>2</sup>
- ✓ Generally well tolerated: All treatment-related adverse effects were transient, mild or moderate

## VALIDATION

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

# LYT-300: Potential First-in-Disease Therapy for FXTAS

PureTech awarded ~\$11.4M grant in competitive process



## LATE ONSET & DEVASTATING RARE DISEASE

### Fragile X-associated Tremor/Ataxia Syndrome

- Closely related to, but distinct from, fragile X syndrome (FXS); both conditions are the result of repeated elements in the *FMR1* gene
- Clinical signs, including tremor, balance problems and cognitive decline

## UNMET MEDICAL NEED

- Currently, there are **no primary treatments** for FXTAS
- Only **one treatment has shown clinical benefit**: intravenous allopregnanolone significantly ( $p=0.009$ ) improves executive cognitive / motor function (BDS-2), N=6, open label

Phase 2 trial initiation in 2024

<sup>1</sup> National Fragile X Foundation: Prevalence of FXTAS; *FMR1* = Fragile X Messenger Ribonucleoprotein Gene 1.

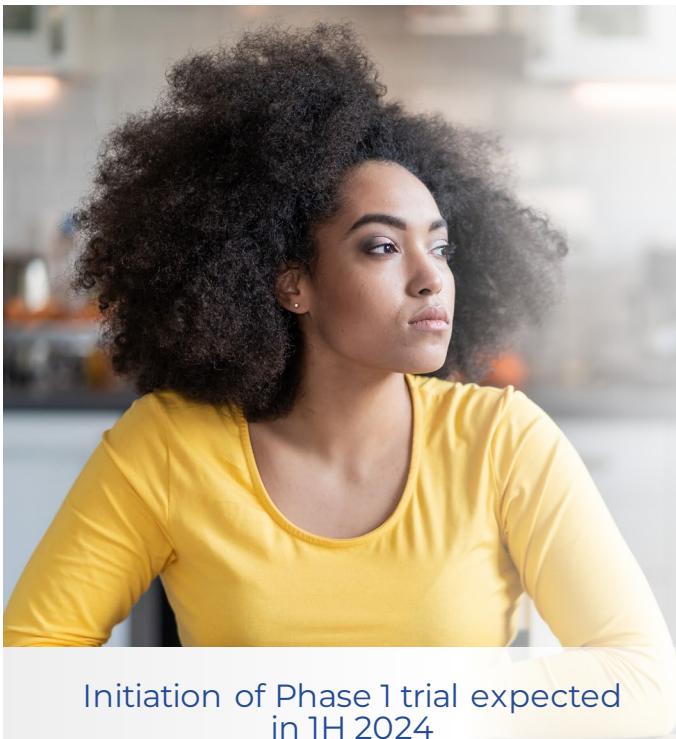
# LYT-310 (Glyph Cannabidiol)

For epilepsies & other neurological indications



- ✓ A CBD-based product is approved in the U.S. and the EU to treat seizures resulting from certain rare conditions
- ✗ ...BUT its dosing (large volume of oily solution via syringe) limits its use in broader indications and age groups
- ✓ LYT-310 has the potential to enable oral administration, improve safety, and reduce GI side effects
- ✓ LYT-310 may allow for a readily scalable, consistent product in a cost-effective manner
- ✓ **LYT-310 could expand the therapeutic application of CBD to a wider range of age groups and indications**

# LYT-310: Potential to Be Highly Differentiated in Epilepsies & Other Neurological Indications



Initiation of Phase 1 trial expected in 1H 2024

## Epilepsies

- **~3 million** adults and 470,000 children are affected by epilepsy in the U.S.<sup>1</sup>
- 20-33% of patients with epilepsy have drug-resistant epilepsy<sup>2</sup>

## UNMET MEDICAL NEED

Despite the many approved antiseizure medications, patients are often refractory to treatments or discontinue effective treatments.

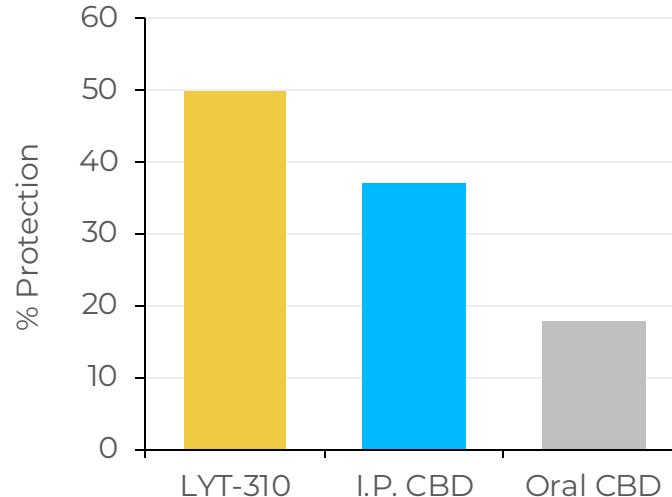
There is a need for treatment options with better safety, tolerability, efficacy, and convenience.

<sup>1</sup> Zack MM, Kobau R. National and state estimates of the numbers of adults and children with active epilepsy — United States, 2015. MMWR. 2017;66:821–825. DOI: 10.15585/mmwr.mm6631a1; <sup>2</sup>Source: Epilepsy Foundation.

# LYT-310: Positive Data in Gold Standard MES Seizure Model

- LYT-310 was more effective at preventing seizures at a dose 3x lower than an oral CBD formulation<sup>1</sup>
- ED<sub>50</sub> for LYT-310 corresponds to an ED<sub>18</sub> for synthetic oral CBD
- Over 85% (18 of 21) of the approved anti-seizure medications for focal seizures were active in MES<sup>2</sup>

LYT-310 ED50 DOSE DEMONSTRATED GREATER SEIZURE PROTECTION AT EQUIVALENT CBD DOSE (N=12/GROUP)



Initiation of Phase 1 trial expected in 1H 2024

# LYT-320 (Glyph Agomelatine)

For anxiety & mood disorders



- ✓ Agomelatine is clinically validated and approved for MDD in the EU and MDD & GAD in Australia
- ✓ Agomelatine has a differentiated mechanism of action and superior tolerability compared to standard-of-care
- ✗ ...BUT it has low oral bioavailability and is associated with hepatotoxicity necessitating liver function monitoring
- ✓ LYT-320 has shown >10x improved oral bioavailability in non-human primates
- ✓ **LYT-320 has the potential to greatly reduce the risk of clinically significant liver enzyme elevations<sup>1</sup>**

# LYT-320: First-in-Class Therapy for Anxiety & Mood Disorders



Initiation of FIH enabling studies & clinical studies expected in 2024 & 1H 2025, respectively

## Anxiety Disorders

- **30% of adults** in the U.S. suffers from any anxiety disorder in a lifetime<sup>1</sup>

## Mood Disorders

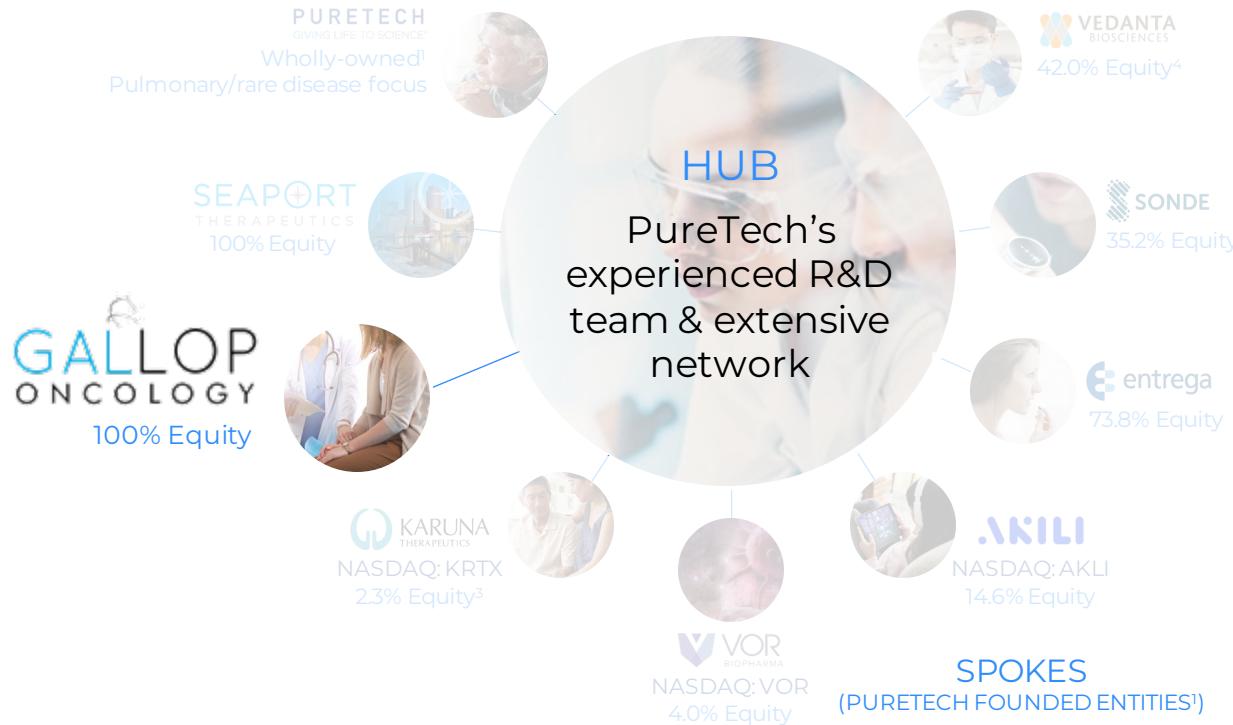
- **~9.7% of adults** in the U.S. had any mood disorder in the past year<sup>2</sup>

## UNMET MEDICAL NEED

- Massive need for novel therapies with new mechanisms

# The PureTech-Pioneered Hub-and-Spoke Model

Robust pipeline of new medicines poised for tremendous growth



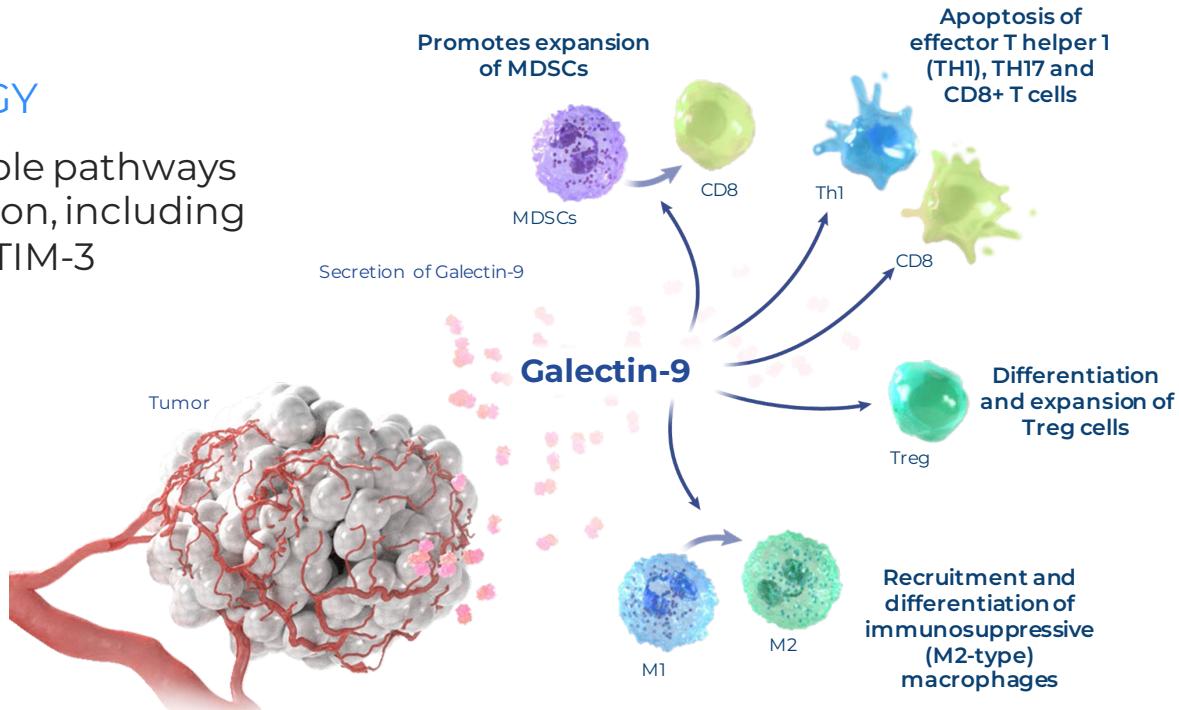
<sup>1</sup> Founded Entities represent companies founded by PureTech in which PureTech maintains ownership of an equity interest and, in certain cases, is eligible to receive sublicense income and royalties on product sales. As of the date of this release, PureTech maintained control over Entrega, Inc. by virtue of majority voting control and the right to elect representation to the entity's Board of Directors. PureTech also controls Seaport Therapeutics, Inc. and Gallop Oncology, Inc. As of the date of this release, PureTech did not have a controlling interest in Karuna Therapeutics, Inc., Akili, Inc., Sonde Health, Inc., Vedanta Biosciences, Inc. and Vor Biopharma, Inc.

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

## Driving immunosuppression through multiple pathways

### FOUNDATIONAL BIOLOGY

Galectin-9 modulates multiple pathways of cancer immunosuppression, including those modulated by PD-1 & TIM-3



# Gallop Oncology:

## LYT-200 (Anti-Galectin-9 mAb) for metastatic solid tumors and hematological malignancies



### LIFE ALTERING & PROGRESSIVE

#### Solid Tumors

- **~ 82,000 new cases of bladder cancer** diagnosed each year<sup>1</sup>;  
~90% are urothelial carcinoma<sup>2</sup>
- **~66,000 new cases of head and neck cancers** diagnosed each year<sup>3</sup>; ~10% metastatic disease at diagnosis & additional 20-30% will develop metastases<sup>4</sup>

#### Hematological Malignancies

**~60,000 new cases of leukemia** diagnosed each year,<sup>5</sup> including  
~20,000 in acute myeloid leukemia (AML)<sup>6</sup>

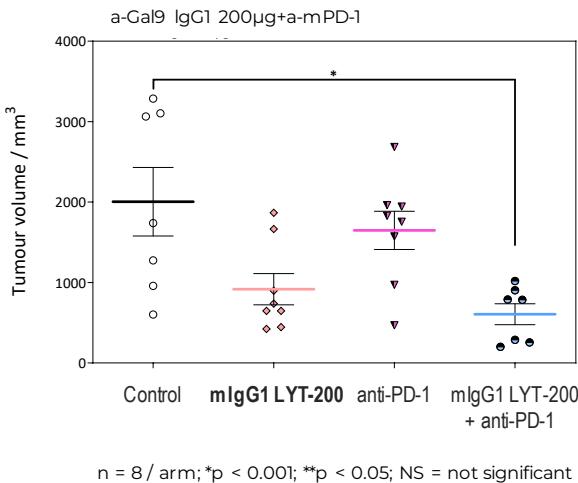
### UNMET MEDICAL NEED

**Over 50%** of AML patients either don't respond to initial treatment or experience relapse or death,<sup>7</sup> with ~12.6% five-year survival rate<sup>8</sup>

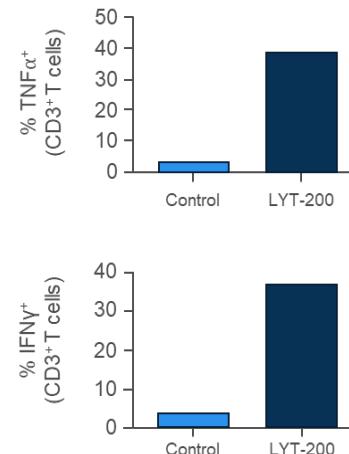
# LYT-200

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



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

High affinity & specificity for galectin-9

Robust activity in preclinical studies:

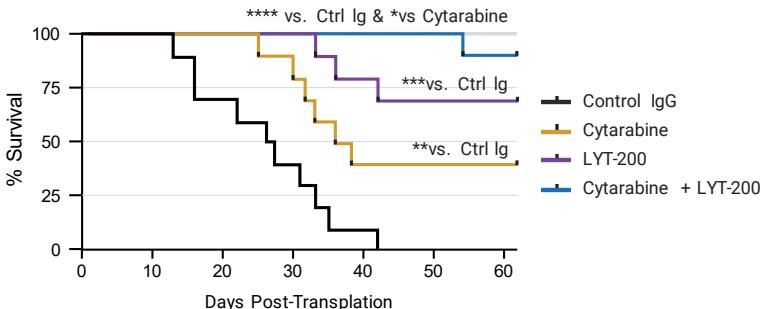
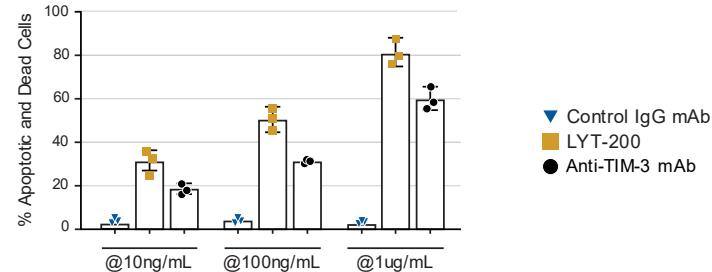
- Single agent causes tumor reduction in pancreatic models where anti-PD-1s don't work
- ~50% tumor reduction with LYT-200 vs. ~22% tumor reduction with anti-PD-1 in melanoma model
- Increase in intra-tumoral CD8 T cells in combination with anti-PD-1
- Activation of intra-tumoral immunity in patient-derived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

# LYT-200

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

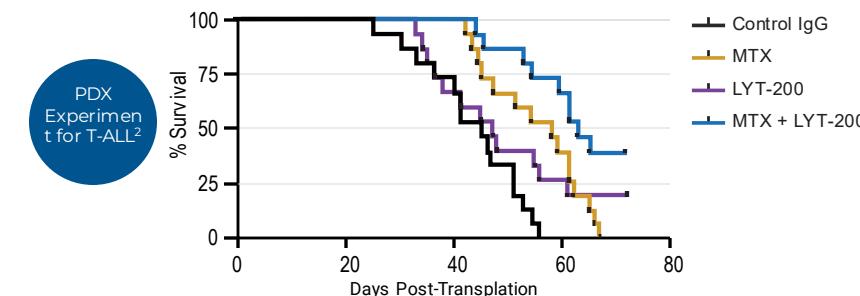
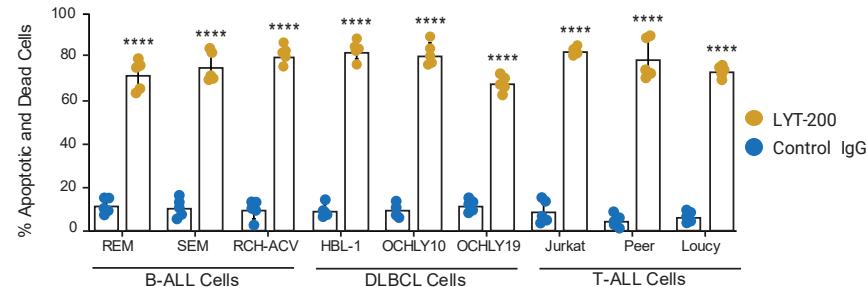
## AML MODEL<sup>1</sup>

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



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

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



# Phase 1b Clinical Trial in Solid Tumors Ongoing

## SOLID TUMOR DOSE ESCALATION & DOSE EXPANSION TRIAL

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

Up to 26 patients

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

Combination cohorts with tislelizumab (anti-PD-1 mAb) initiated in Q1 2023

## CLINICAL INVESTIGATORS



Daniel Fein



Siqing Fu



Eric Sherman

Other sites: Mayo, START, Sarah Cannon

Topline results expected in 2024

# 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)

In a heavily pre-treated patient population, early data demonstrated a favorable safety and tolerability profile of LYT-200 with no dose limiting toxicities;

Additional data from the study to be presented in a scientific forum in 2024

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

## SOLID TUMOR COMBINATION COHORTS<sup>1</sup>

- Combination cohorts of LYT-200 + tislelizumab (PD-1) ongoing in head and neck cancer (HNSCC) and urothelial carcinoma (UC)
- HNSCC: 8 patients dosed to date including 4 evaluable
- UC: 3 patients dosed to date including 2 evaluable

- Of the 4 evaluable HNSCC patients, 3 patients achieved disease control including 1CR, 1 PR, and 1 SD and 1 PD**
- Of the 2 evaluable patients with UC, both achieved SD** including one with near complete resolution of ascites and pleural effusion

## AML/MDS DOSE ESCALATION COHORTS<sup>2</sup>

- Single agent LYT-200 in patients with relapse/refractory AML or high-risk MDS ongoing
- 16 patients dosed to date including 13 evaluable

- Majority of patients have achieved stable disease<sup>3</sup>** per ELN guidelines
- At 7.5 mg/kg cohort (dose escalation continuing) a median duration of treatment was 77 days with **blast reduction observed**

Presented at ESMO IO '23

# PureTech Is a Respected Leader in The Boston Biotech Community: The World's #1 Biotech Hub

**>1000**

biotech companies, with a critical mass of talent

**\$3.3B**

funding from National Institute of Health (NIH) in 2022; **top** NIH-funded state nationwide

**>100**

academic institutions; MA is home to many leading universities and research institutes

**25**

hospitals with many **ranked among the best** in the U.S.



Massachusetts  
Institute of  
Technology



**HARVARD**  
MEDICAL SCHOOL



MASSACHUSETTS  
GENERAL HOSPITAL



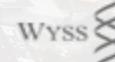
**Boston**  
Children's



**BROAD**  
INSTITUTE



Whitehead  
Institute



WYSS  
INSTITUTE

*“Massachusetts is known as the **most innovative square mile on the planet** and that’s because we have such a rich density of ecosystem, for example, with over a thousand biotech companies, **18 of the top 20 biopharma**, world-class hospital system, and of course the best in class academic institutions.”*

*- Kendalle Burlin O’Connell, Esq., CEO & President of MassBio at the NYSE*

# Why Invest in Biotech?

Source: Stifel 2023 Healthcare Report

1. HISTORY: Returns in biotech have beat the market with **biotech stocks up 20x** over past 30 years. Following past downturns, **biotech indexes tripled**

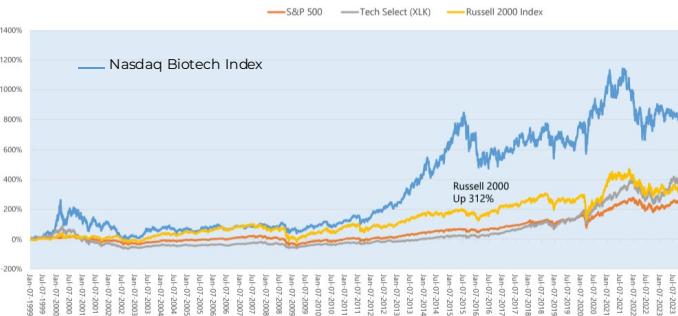
2. VALUATIONS: Valuations are highly attractive now with **70% discount** on the entire biotech sector since 2021 highs

3. MACRO: Macro picture shifting to favor biotech. In past, NBI has weathered the Fed Funds rate tightening well, **up 75%** of years with rate hikes since 1994

4. PHARMA: Pharma needs to acquire biotechs due to **~\$182B revenue at risk** with pharma patent expiration; there is **>\$500B of M&A firepower** at top 18 pharmas

5. DEMAND: Medical spend will accelerate in the future; e.g., **>90M Americans in Medicare by 2060**

NBI, S&P 500, Tech Select (XLK) and Russell 2000 Returns, Jan 1999 to Nov 3, 2023



## Key Drugs Losing Patent Exclusivity by 2028

2023	2024	2025	2026	2027	2028
Company	Product ('22 Sales)	Company	Product ('23 Sales)	Company	Product ('24 Sales)
abbvie	Humira (\$28B)	REGENERON	Eylea (\$10B)	AstraZeneca	Imolti (\$2.7B)
johnson-johnson	Stelara (\$10B)	AstraZeneca	Brilinta (\$1.4B)	NOVARTIS	Entresto (\$7B)
AMERISERUM	Xyrem (\$1B)	Xarelto (\$3B)	Bristol Myers Squibb	Pfizer	Cabometyx (\$1B)
Biogen	Tysabri (\$1.9B)	Victoza (\$1.3B)	Pfizer	Pfizer	abivive (\$1B)
sunovion	Latuda (\$2B)	AMGEN	Xeljaca (\$2B)	Merck	Ibrance (\$9B)
NOVARTIS	Gilenya (\$1.4B)	AMGEN	Prolia / Kevra (\$6B)	Lilly	Obinutuzumab (\$1B)
Takeda	Vyosine (\$3.4B)	Roche	Perjeta (\$5.5B)	Pfizer	Trulicity (\$8B)
Total At-Risk Revenue:					
\$41B					
\$16B					
\$14B					
\$17B					
\$44B					
\$50B					

# Key Value Drivers

Multiple clinical milestones expected across Wholly Owned Programs, Seaport & Gallop

## THERAPEUTIC CANDIDATE<sup>1</sup>

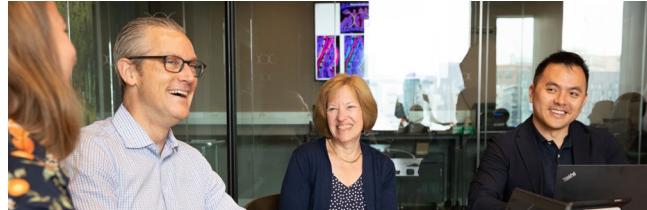
## MILESTONES

LYT-100	Deupirfenidone	<ul style="list-style-type: none"><li><b>Results from registration-enabling trial in IPF</b></li></ul>	4Q 2024
LYT-200	Anti-Galectin-9 Mab	<ul style="list-style-type: none"><li>Additional results from Phase 1b in combination w/ tislelizumab in solid tumors</li></ul>	2024
LYT-300	Glyph Allopregnanolone	<ul style="list-style-type: none"><li>Initiation of Phase 2 clinical trial in FXTAS</li></ul>	2024
LYT-310	Glyph Cannabidiol	<ul style="list-style-type: none"><li>Initiation of clinical trial</li></ul>	1H 2024
		<ul style="list-style-type: none"><li>Initiation of first-in-human enabling studies</li></ul>	2024
LYT-320	Glyph Agomelatine	<ul style="list-style-type: none"><li>Initiation of clinical studies</li></ul>	1H 2025

Key anticipated milestones are **bolded**

Multiple additional catalysts across Founded Entities

# PureTech Team - Bringing Our Vision to Life





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

**271,841,570** outstanding  
shares as of January 2024

Market capitalization \$676M  
(£533M) as of December 29, 2023;  
1.27 USD:GBP

**\$320M** estimated Consolidated  
Cash, Cash Equivalents & Short-  
Term Investments at year end 2023<sup>1</sup>

## ANALYST COVERAGE

### Peel Hunt LLP

Miles Dixon

### Leerink Partners LLC

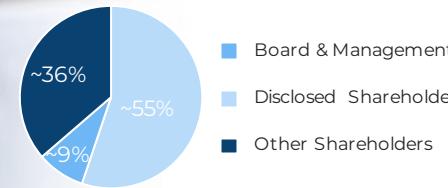
Thomas J. Smith

### Liberum

Edward Thomason

### Jefferies International Limited

Peter Welford



Disclosed Shareholders as of December 31, 2023, include Invesco Asset Management, Lansdowne Partners LLP, Baillie Gifford & Co., M&G Investment Management, LTD., Vanguard Group, Patient Capital Management, Recordati S.p.A. Pharmaceutical Company.

Headquartered in  
Seaport, Boston

<sup>1</sup>The preliminary selected financial results reported by the Company are unaudited, subject to adjustment, and provided as an approximation in advance of the Company's announcement of complete financial results in April 2024.

# Appendix Contents

- **Appendix A: Wholly Owned Pipeline**

- LYT-100 Preclinical Data
- LYT-100 Market Research
- LYT-100 Payor Research
- LYT-100 In the Face of Generics
- Pirfenidone Safety Data
- Lung Disease Prevalence
- Glyph Technology Platform
- LYT-200 Supplemental Data

- **Appendix B: Founded Entities**

- Seaport
- Vedanta
- Akili
- Vor
- Sonde
- Entrega
- Founded Entities Upcoming Catalysts

- **Appendix C: Supplemental Materials**

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

# Appendix A: Wholly Owned Pipeline

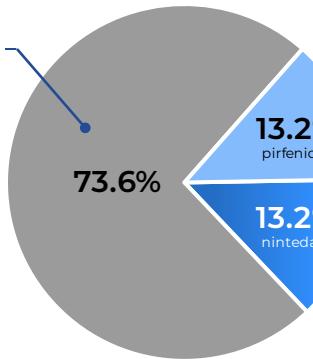
# IPF Treatment Rates are Low Due to Side Effects

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)

Nearly 75% of  
patients in U.S. never  
receive antifibrotic  
therapy



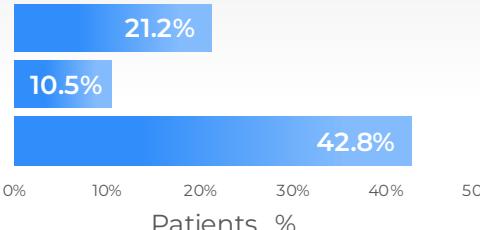
Initiated pirfenidone  
or nintedanib since  
FDA approval in 2014

Experienced nausea,  
diarrhea, or myalgias

Switched to the  
other antifibrotic

Discontinued therapy

Over 40% of patients eventually  
discontinue antifibrotic therapy



# LYT-100 Clinical Trials<sup>1</sup>

## 1. Initial PK studies

### FOUNDATIONAL PK DATA

Multiple-dose safety, tolerability, and PK

MAD 1.0



Tolerable up to 1000mg BID, linear PK

Determine dose with same exposure as pirfenidone

PK



800 – 850 mg BID matches pirfenidone AUC

## 2. Head-to-head tolerability

### TOLERABILITY ADVANTAGE VS. PIRFENIDONE

**550 mg TID LYT-100 vs. pirfenidone: Comparable AUC, reduced  $C_{max}$**

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



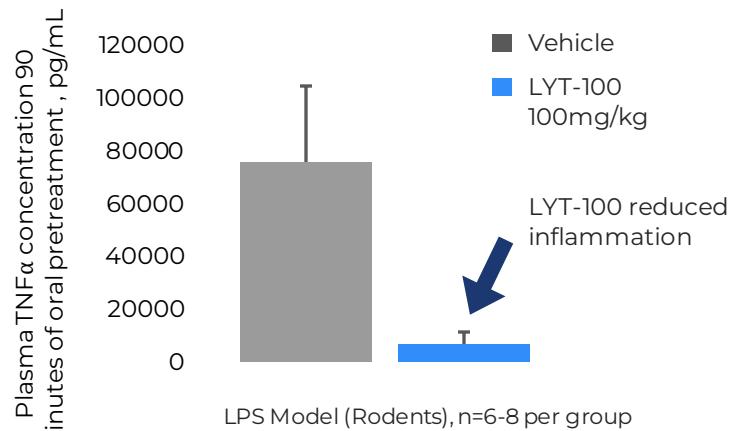
Tolerable up to 2000mg BID with no dose limiting toxicity



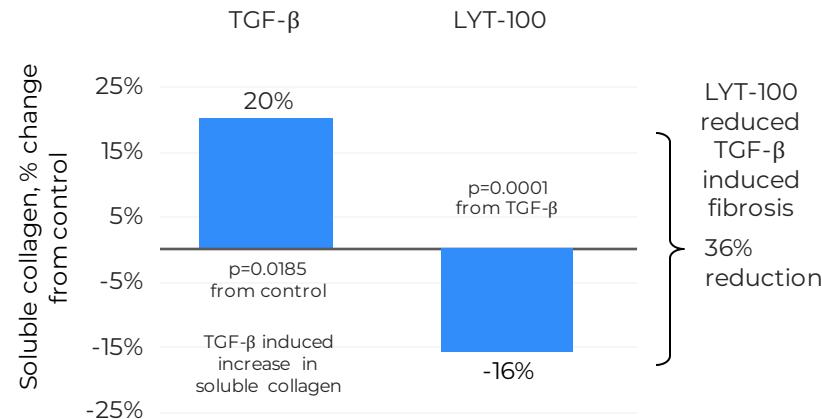
# LYT-100:

Preclinical POC demonstrates anti-inflammatory & anti-fibrotic pharmacology

## PRECLINICAL PLASMA CONCENTRATIONS OF TNF $\alpha$ WITH LYT-100 VERSUS CONTROL

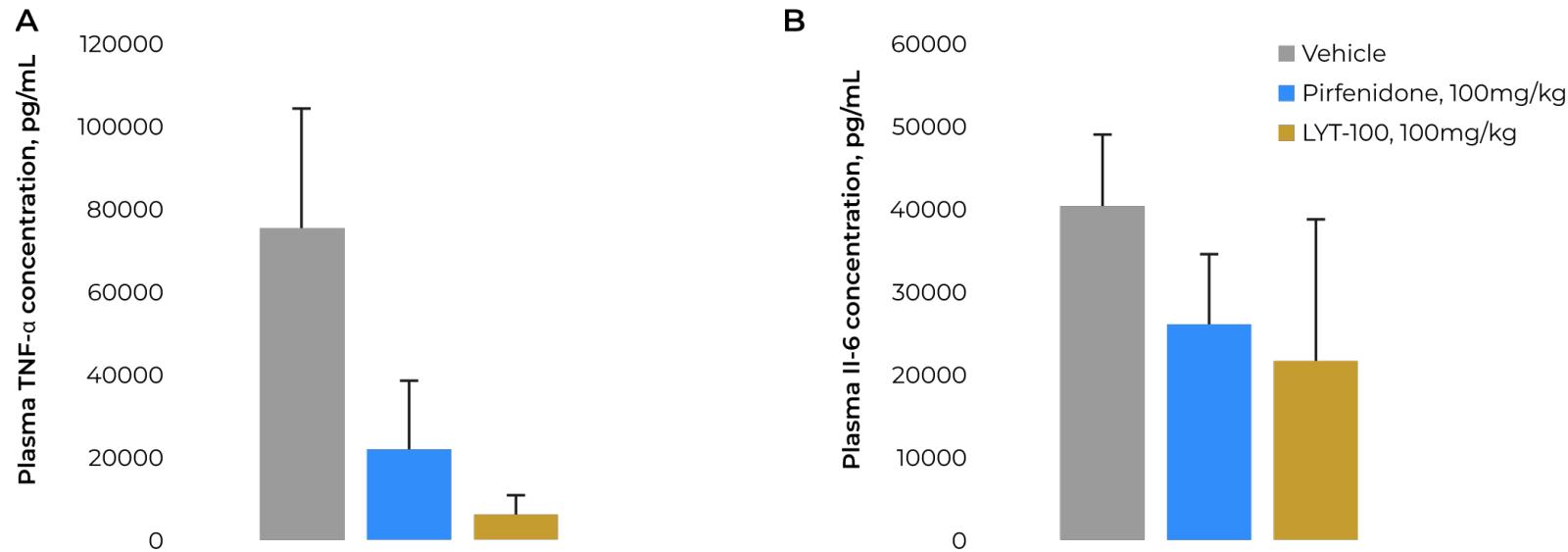


## IN VITRO REDUCTION OF TGF- $\beta$ INDUCED SOLUBLE COLLAGEN PRODUCTION (MOUSE FIBROBLASTS)



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

# LYT-100 Could Address Several Segments of IPF Patients

Independent research shows profile attractive to surveyed pulmonologists<sup>1</sup>



1

## Newly diagnosed patients

Pulmonologists would prescribe LYT-100 to **~44% of newly diagnosed** patients with IPF

2

## Patients currently on SOC treatment

Pulmonologists would **switch** some patients currently treated with SOC, particularly ESBRIET (pirfenidone), to LYT-100

3

## Currently untreated patients

Potentially address currently untreated patients who:

- (1) have never started treatment, AND
- (2) who started treatment but discontinued

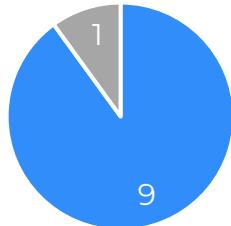
<sup>1</sup> Market research survey of 100 pulmonologists conducted by Day & Associates. No pricing information/assumptions was shared. Research completed in April 2022 based on the latest target product profile and findings were consistent with our prior market research.<sup>2</sup> ESBRIET® and OFEV® are trademarks of Genentech and Boehringer Ingelheim Pharmaceuticals, respectively, and are not owned by or affiliated with PureTech Health. LYT-100 is an investigational drug not approved by any regulatory authority. <sup>3</sup>Based on 2021 ESbRIET® and OFEV® total WW sales. Ofev sales are inclusive of SSc-ILD, PF-ILD and IPF indications. SOC = Standard of care (Esbriet or Ofev).

# LYT-100 Payor Market Research

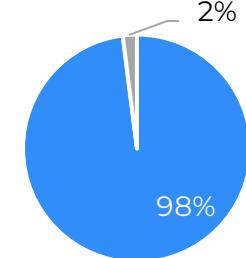
Independent research indicates payors in favor of profile<sup>1</sup>

## LYT-100 COVERAGE EXPECTATIONS<sup>2</sup>

By Payor  
(N=10)



By Total Payor  
Covered Patients  
(N=~279M)



- Payors are aware of unmet needs in IPF and recognize the clinical value of a product designed to provide improved safety/tolerability vs. pirfenidone, while maintaining efficacy
- **Nine out of ten payors understood the LYT-100 clinical story and would consider putting it on formulary** if successfully developed and approved, with a profile that shows superior safety/tolerability to pirfenidone<sup>3</sup>
- Payors indicated that coverage of LYT-100 could be similar to other branded IPF therapies (PA to label, Tier 3/Specialty Tier)

“...50% [tolerability improvement] would be really significant...30% would also be significant.”<sup>4</sup> – Regional Payor

Select quote from survey

# LYT-100 in The Face of Generics & Novel MOAs

## LYT-100 VS. GENERICS

- ✓ The **safety/tolerability advantage of LYT-100 remains attractive and meaningful to pulmonologists and payers even in the face of generic competition**<sup>1</sup>.
- ✓ Only ~25% of patients in the U.S. are currently on SOC primarily due to poor tolerability. 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 LYT-100** due to the significant tolerability challenges with current standard of care.

## LYT-100 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 LYT-100 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 all ongoing programs, it remains to be seen if **early Ph2 data can be replicated in Ph3 studies**

# LYT-100 in The Face of Generics & Novel MOAs (Cont'd)

Base Case: LYT-100 at equivalent dose to pirfenidone with improved safety/tolerability

COMPETITOR	OVERVIEW	POSITIONING OF LYT-100
Generic pirfenidone and nintedanib	<ul style="list-style-type: none"><li>Both generic pirfenidone and generic nintedanib are expected to be on the market at time of LYT-100 launch<sup>1</sup></li><li>Assume all payers add generics to generic Tier<sup>2</sup>; some payers require step edits<sup>3</sup> of generics before allowing treatment with branded agents</li></ul>	<ul style="list-style-type: none"><li>Safety/tolerability advantage will enable <b>LYT-100 to complete for new patient starts in plans without step edits</b></li><li>In plans with step edits, LYT-100 will be used as second line of treatment for <b>patients who fail on generic antifibrotics</b></li><li>Even if all payers require step edits, <b>~50% of patients will be eligible for LYT-100</b></li></ul>
Reformulated pirfenidone and nintedanib	<ul style="list-style-type: none"><li>A few reformulated pirfenidone and nintedanib approaches, including inhaled and sustained release, are in early development</li></ul>	<ul style="list-style-type: none"><li>LYT-100 will offer oral systemic delivery of the medication, <b>without the AEs associated with inhaled (e.g., cough) and other reformulations of the currently approved drugs</b></li><li>None of the localized delivery candidates have demonstrated the same evidence of efficacy as systemic therapies</li></ul>
Novel Mechanisms	<ul style="list-style-type: none"><li>Nearly all new mechanisms are being studied on top of/or after the standard of care (currently pirfenidone &amp; nintedanib)</li></ul>	<ul style="list-style-type: none"><li><b>Potential for LYT-100 to be the backbone standard of care for future combination regimens</b></li><li>Pirfenidone and nintedanib remain key competitors for LYT-100</li></ul>

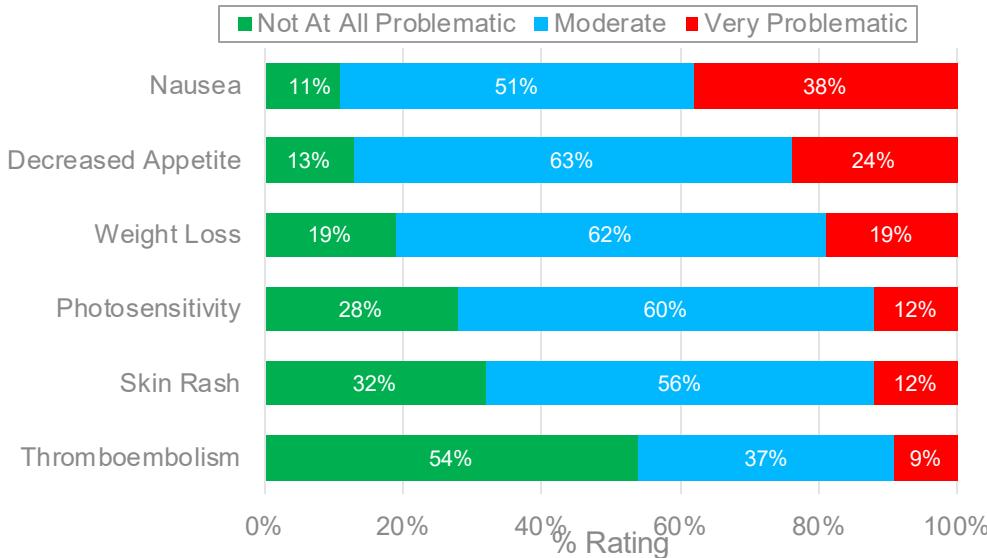
<sup>1</sup> Generic pirfenidone is currently available in the U.S. and most of EU; generic nintedanib is expected to be available within the next five years; <sup>2</sup> Tiering = List of prescription drugs that are covered under a healthcare plan drugs are usually divided into tiers or levels based on cost, type of medication, clinical effectiveness; <sup>3</sup> Step edit = When payers require patients to try a certain medication before allowing access to another.

# ESBRIET (pirfenidone) and OFEV (nintedanib):

Both have significant tolerability issues, with GI side effects being the most problematic

- In a market research survey of 100 pulmonologists, respondents reported that, aside from efficacy, **safety/tolerability is the most important consideration** when treating patients with IPF
- However, **>70% of pulmonologists expressed they are “not at all satisfied” or only “moderately satisfied” with the safety/tolerability profile of SOC today**
- In particular, **GI side effects were noted as the most concerning/problematic** adverse events

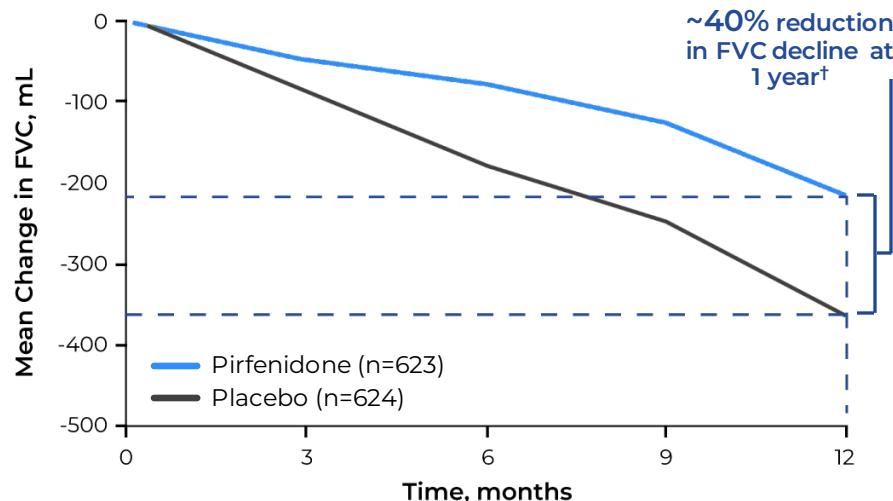
## HOW PROBLEMATIC ARE AEs ASSOCIATED WITH IPF SOC? (N=100)



# Pirfenidone:

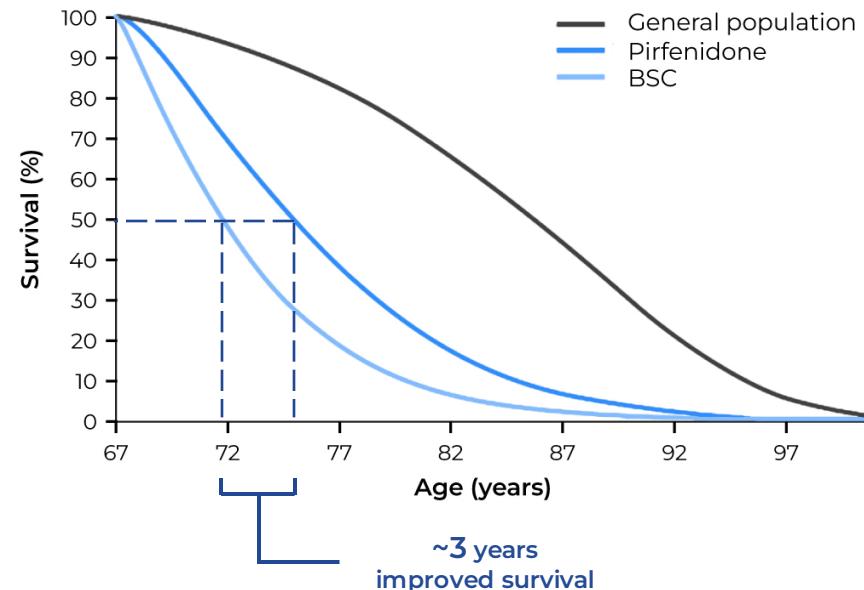
A clinically validated treatment for IPF with beneficial effects on FVC and survival

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



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

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



# Design & Tolerability Findings of Pirfenidone Studies

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

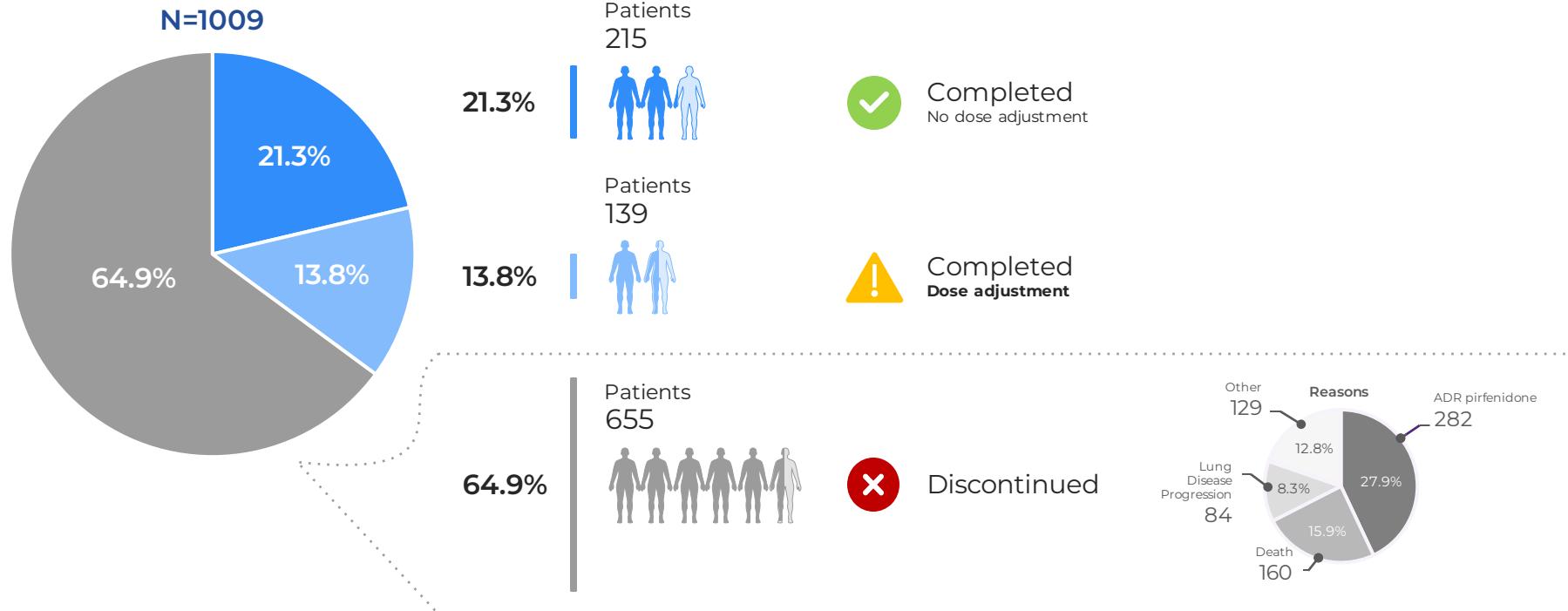
Pirfenidone GI AEs:

- 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-dose in healthy older adults, 44% women			801mg single-dose in healthy adults, 36% women																																																					
Most common AEs	<table><thead><tr><th>Most common AEs</th><th>Pirfenidone N=16</th></tr></thead><tbody><tr><td>Nausea</td><td>43.8%</td></tr><tr><td>Dizziness</td><td>37.5%</td></tr></tbody></table>		Most common AEs	Pirfenidone N=16	Nausea	43.8%	Dizziness	37.5%	<table><thead><tr><th>Most common AEs</th><th>Pirfenidone N=44</th></tr></thead><tbody><tr><td>Nausea</td><td>29.5%</td></tr><tr><td>Dizziness</td><td>18.2%</td></tr><tr><td>Headache</td><td>9.1%</td></tr><tr><td>Constipation</td><td>9.1%</td></tr><tr><td>Vomiting</td><td>4.5%</td></tr><tr><td>Dyspepsia</td><td>4.5%</td></tr></tbody></table>		Most common AEs	Pirfenidone N=44	Nausea	29.5%	Dizziness	18.2%	Headache	9.1%	Constipation	9.1%	Vomiting	4.5%	Dyspepsia	4.5%	<table><thead><tr><th>Most common GI AEs<sup>1</sup></th><th>Pirfenidone N=623</th><th>Placebo N=624</th></tr></thead><tbody><tr><td>Nausea</td><td>36%</td><td>16%</td></tr><tr><td>Rash</td><td>30%</td><td>10%</td></tr><tr><td>Ab. pain</td><td>24%</td><td>15%</td></tr><tr><td>Diarrhea</td><td>26%</td><td>20%</td></tr><tr><td>Headache</td><td>22%</td><td>19%</td></tr><tr><td>Dyspepsia</td><td>19%</td><td>7%</td></tr><tr><td>Dizziness</td><td>18%</td><td>11%</td></tr><tr><td>Vomiting</td><td>13%</td><td>6%</td></tr><tr><td>Anorexia</td><td>13%</td><td>5%</td></tr></tbody></table>			Most common GI AEs <sup>1</sup>	Pirfenidone N=623	Placebo N=624	Nausea	36%	16%	Rash	30%	10%	Ab. pain	24%	15%	Diarrhea	26%	20%	Headache	22%	19%	Dyspepsia	19%	7%	Dizziness	18%	11%	Vomiting	13%	6%	Anorexia	13%	5%
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<sup>1</sup>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%), arthralgia (10% vs. 7%)

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



# Enduring High Unmet Need in Interstitial Lung Diseases Including IPF

Progressive Fibrosing ILDs (PF-ILDs) are estimated to affect >1.3M patients in the 16 Major markets<sup>1,2</sup>

IPF (>720K)

Non-IPF PF-ILDs (>650K)

PF-CTD-ILDs

PF-sarcoidosis

PF-uILD

PF-chronic fibrotic HP

PF-iNSIP

Other

Major potential to improve care in IPF & address other interstitial lung diseases

# Proprietary Technology Platforms

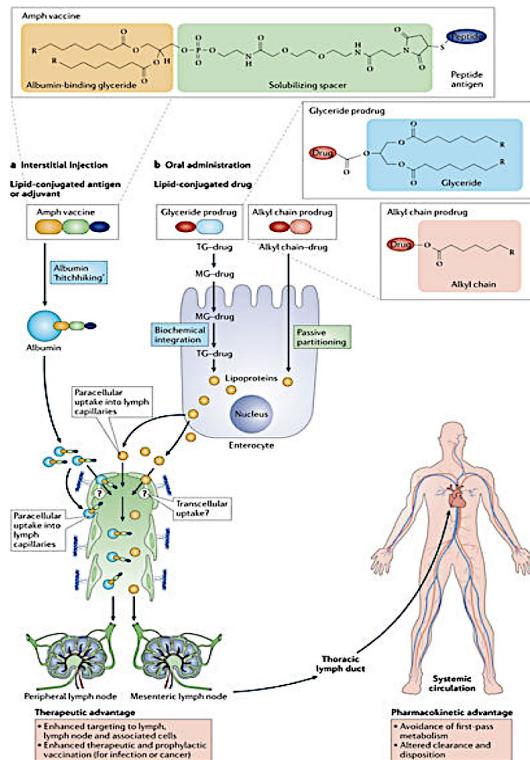
Designed to harness the lymphatic system & administer therapeutics to immune, lymphatic and inflamed tissue



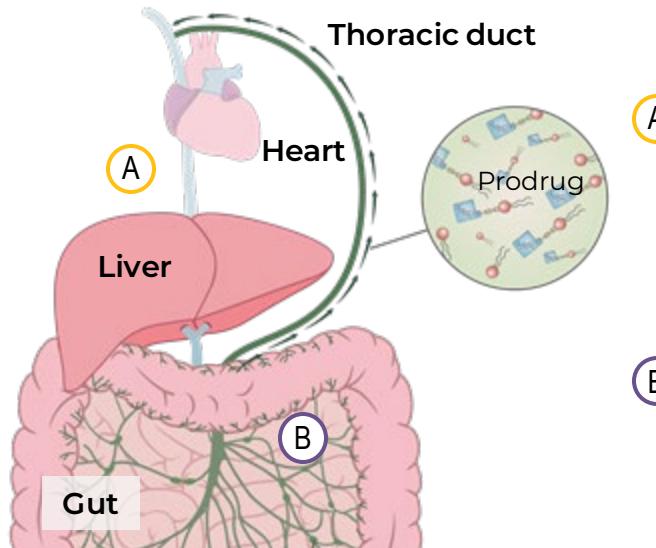
TECHNOLOGY PLATFORM	APPLICATION/FOCUS
<b>Glyph™</b>	Employs the body's natural lipid absorption & transport process to <b>orally administer drugs</b> via the lymphatic system by <b>bypassing first-pass metabolism</b>
<b>Other oral drug delivery technologies and capabilities</b>	Enable <b>oral administration</b> of therapeutic payloads, such as <b>mRNA, biologics, vaccines and other drugs</b> , that are otherwise not efficiently absorbed when taken orally or are otherwise administered exclusively by injection

# Glyph™ Technology Platform:

Designed to utilize natural lipid transport system to enable lymphatic targeting



## LIPID PRODRUGS PROVIDE MULTIPLE OPPORTUNITIES TO ENHANCE SMALL MOLECULE DRUGS



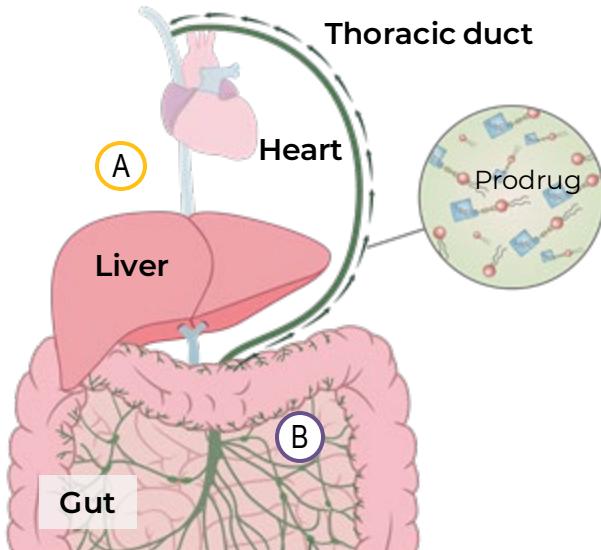
Enable oral route via first-pass bypass

Transport to mesenteric lymph nodes

# Glyph™ Technology Platform:

Exploring therapeutic approaches enabled by transporting via the lymphatic system

## LIPID PRODRUGS PROVIDE MULTIPLE OPPORTUNITIES TO ENHANCE SMALL MOLECULE DRUG DISTRIBUTION

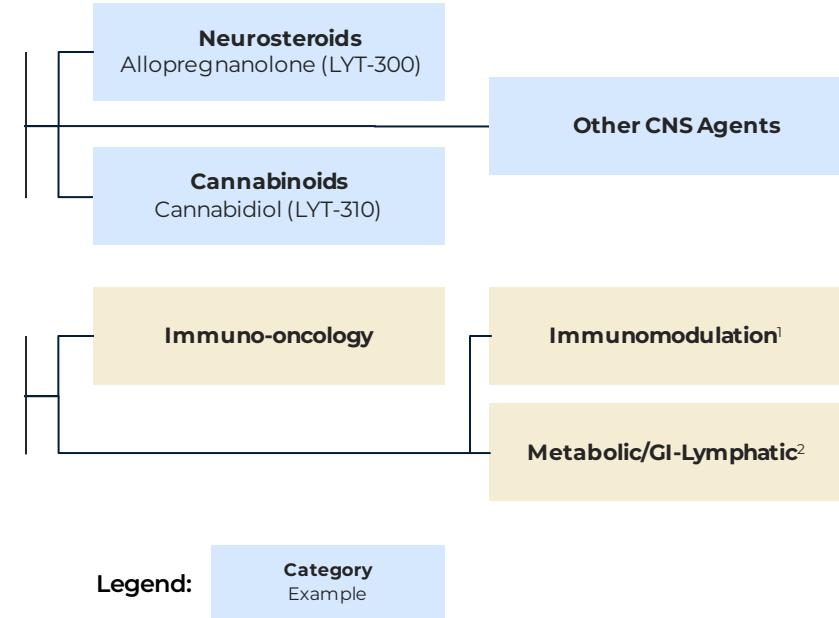


A

Enable oral route via first-pass bypass

B

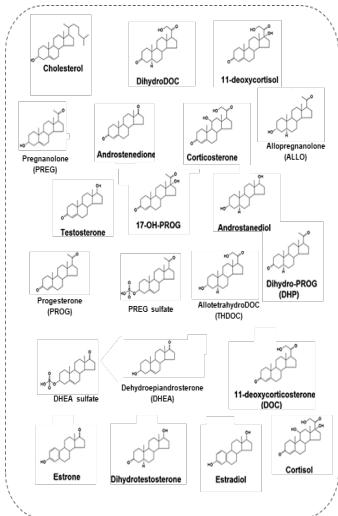
Transport to mesenteric lymph nodes



# Glyph™ Technology

Technology enables oral administration of natural neurosteroids

## NATURALLY-OCCURRING NEUROSTEROIDS



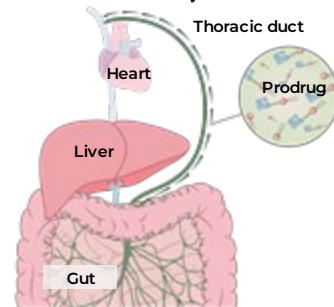
## UNTAPPED OPPORTUNITIES DUE TO CLINICAL TRANSLATION HURDLES

- a) Not orally bioavailable
- b) Properties not drug-like
- c) No composition-of-matter IP

***Chemical modifications may alter target engagement***

## UNLOCKING THERAPEUTIC POTENTIAL/VALUE

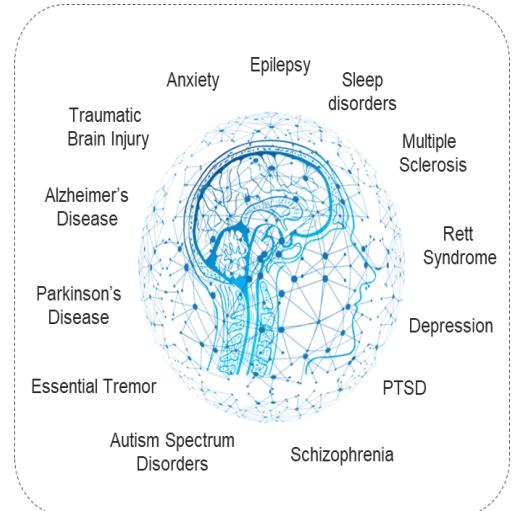
Overcoming first-pass metabolism by the liver



Chemical composition of matter protection for a range neurosteroid lipid prodrugs

Harnesses natural mechanisms (validated efficacy)

## POTENTIALLY APPLICABLE TO A RANGE OF CNS CONDITIONS



# Appendix B: Founded Entities

# LYT-310: Oral CBD A Highly Differentiated Profile for Broad Application

## APPROVED CBD ORAL SOLUTION

1yr+, Primarily Children



Target Population

Approved in US for 3 Rare Epilepsies

Approved in US and EU for Lennox-Gastaut syndrome, Dravet syndrome, or tuberous sclerosis complex

Large Volume of Oily Solution

Administered via syringe twice per day



Target Indications

Diarrhea, Elevated Liver Enzymes



Side Effects

Complex, Nonstandard Manufacturing



Manufacturing

Processed from extraction of cannabis plant

## PURETECH'S LYT-310

1yr+, Primarily Teens/Adults



Pediatric form planned with target down to 1 year old

Epilepsies & Other CNS Indications

Exploring range of rare and more common forms of epilepsy as well as other CNS disorders



Capsules & Other Flexible Routes

Capsule dosage form plus water-based emulsion planned for pediatric patients



Potential for Reduced Side Effects

...due to lower dose to GI & liver, a result of bypassing first-pass metabolism in liver



Standard Manufacturing

Standard pharmaceutical manufacturing techniques

### INNOVATION

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

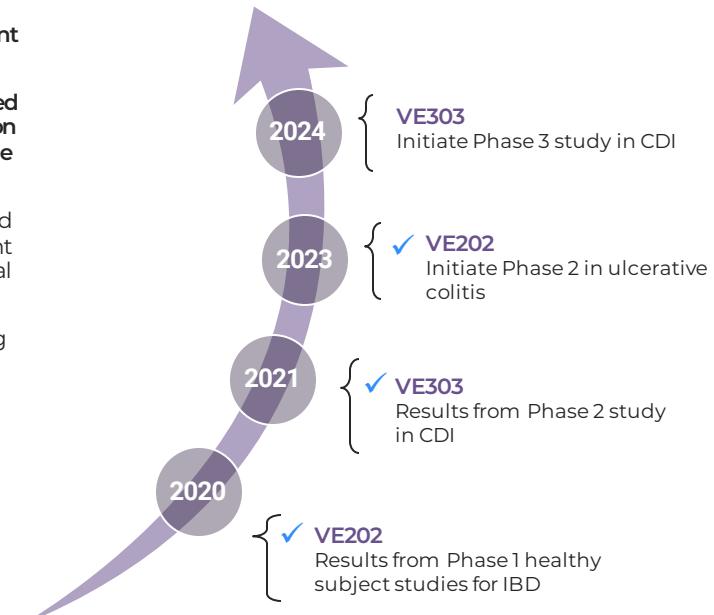


### VALIDATION

- Four clinical-stage programs in development
- VE303 (*C. difficile*) demonstrated **accelerated gut microbiota restoration** after antibiotics in a **Phase 1a/1b 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: 41.0%<sup>1</sup>)

### UPCOMING MILESTONES<sup>2</sup> & VALUE REALIZATION



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

### First game-based digital therapeutic cleared by the FDA for ADHD

#### INNOVATION

~6.4M pediatric ADHD patients in the US

Treatment of many neuropsychiatric disorders is only partially served, or not served at all, by current medications or in-person behavioral therapy

Engaged with leading experts who had been studying the effects of video games on cognition



- ✓ In-licensed from University of California, San Francisco the intellectual property invented by Adam Gazzaley, MD, PhD
- ✓ Oversaw initial product development & design

#### VALIDATION

Helped build top development & commercial team & raise funds

- ✓ Planned & completed initial pilot & POC studies



#### VALUE REALIZATION

##### FDA Clearance & European CE Mark

- ✓ FDA cleared & granted European marketing authorization for pediatric patients age 8-12 years old with primarily inattentive or combined-type ADHD
- ✓ EndeavorRx<sup>®2</sup> (AKL-T01) showed statistically significant improvement compared to active control ( $p=0.006$ ) on T.O.V.A.® in pivotal study; recently showed statistically significant improvement in ADHD when used with & without stimulants
- ✓ Achieved primary endpoint, improving cognitive impairments in MDD
- ✓ Development & commercialization partnership with Shionogi in Japan & Taiwan (\$20M up front; milestones up to \$105M plus royalties)

#### UPCOMING MILESTONES

- Plans to pursue regulatory approval for OTC labeling of its treatment products
- Data submission to the FDA to convert EndeavorRx to OTC in 2024
- Shionogi pivotal trial data in 6-17 year old children with ADHD in Japan expected in 2024

EndeavorOTC for adults 18 y.o. and older with ADHD now available without a prescription nationwide

<sup>1</sup>As of August 3, 2023. PureTech's percentage ownership of Akili is approximately 14.6 percent. <sup>2</sup> Endeavor Rx is the first and only FDA-authorized treatment delivered through a video game to treat children ages 8 to 12 years old with primarily inattentive or combined-type ADHD. Endeavor Rx is indicated to improve attention function as measured by computer-based testing in children ages 8 to 12 years old with primarily inattentive or combined-type ADHD. Endeavor Rx is not a digital game, but a prescription medication and a digital health device. Endeavor Rx is a prescription digital therapeutic indicated to improve attention function in children ages 8-12. Endeavor OTC is available under the U.S. Food and Drug Administration's current Emergency Policy for Digital Health Devices for Treating Psychiatric Disorders During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency. Endeavor Rx has not been cleared or authorized by the U.S. Food and Drug Administration for its indications. It is recommended that patients speak to their health care provider before restarting Endeavor-OTC treatment. No serious adverse events have been reported in any of our clinical studies. To learn more visit Endeavor-OTC.com.

## INNOVATION

**~42.5K** new diagnoses of AML patients each year in the US, Europe & Japan

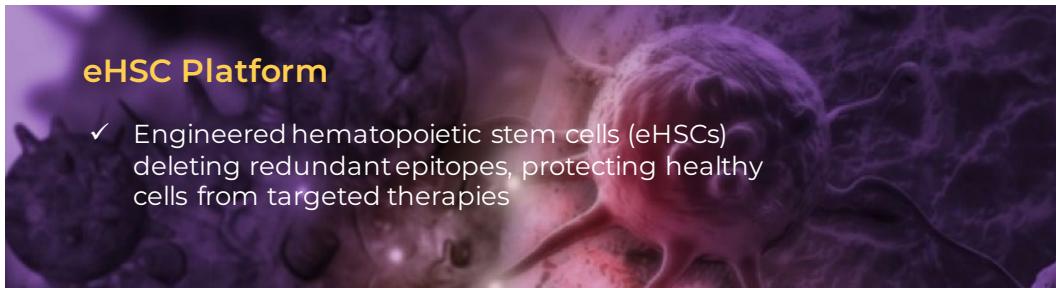
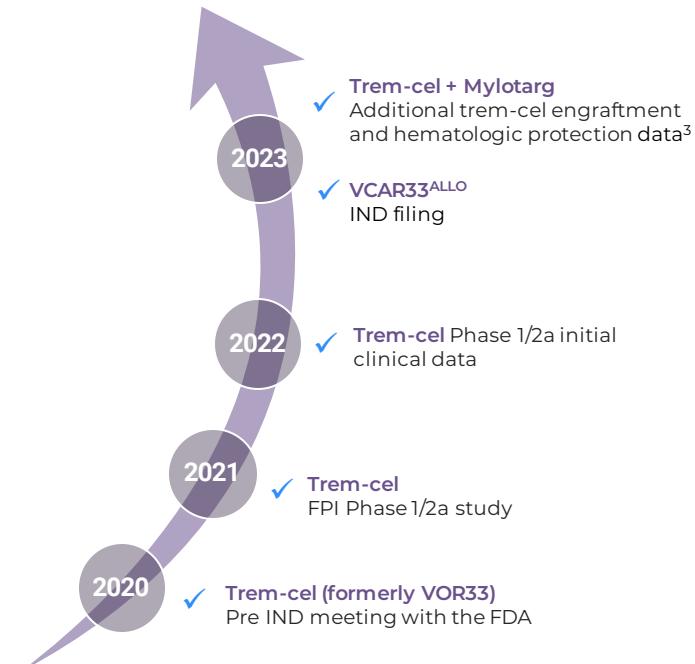
Prognosis for relapsed & refractory blood-borne malignancies is very poor

Median 5 year survival rate for patients with AML is <30%, but there are significant differences in prognosis depending on several factors, including the age of the patient at diagnosis

## VALIDATION

- Ex vivo & mouse **proof-of-concept studies** led by Siddhartha Mukherjee, MD, PhD; Also published in *PNAS*
- Optimize targeted therapies including ADCs, T cell engager/ bispecific antibodies, conventional mAbs & CAR-T cells
- May lead to **limited on-target toxicity & durable antitumor activity**

- Conducting ongoing discovery efforts for non-myeloid malignancies
- Announced \$110M Series B financing in July 2020**
- Completed \$176.9M IPO in February 2021
- Completed \$115.8M follow-on offering in December 2022

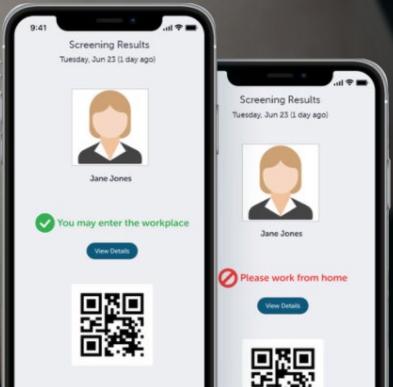
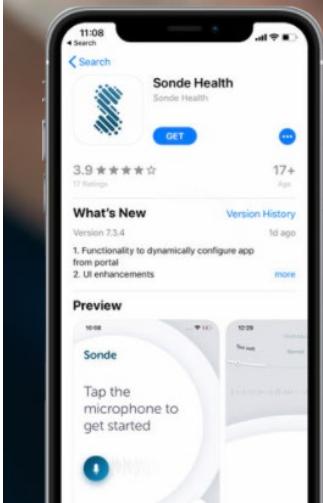
UPCOMING MILESTONES<sup>2</sup> & VALUE REALIZATION

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

~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

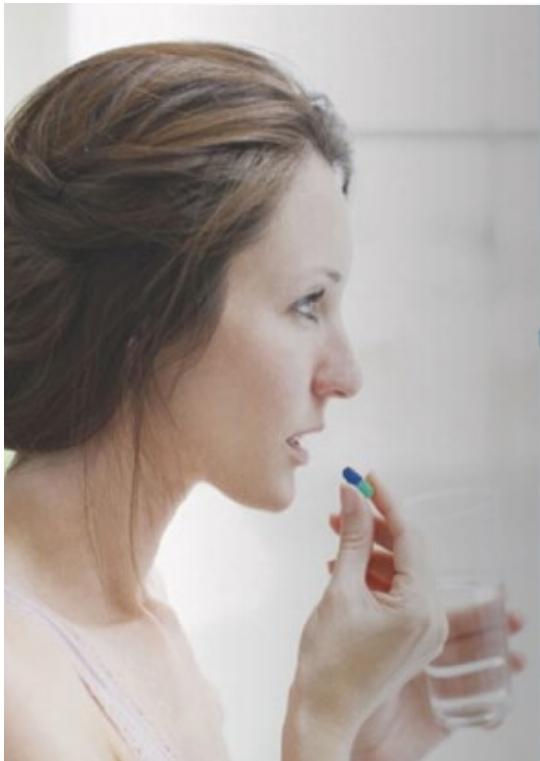
## KEY HIGHLIGHTS

- 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**

# Entrega

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

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

A photograph of a woman in profile, facing right, taking a blue and white capsule with a glass of water. The background is a plain, light-colored wall.

Entrega is focused on the oral administration of biologics, vaccines and other drugs that are otherwise not efficiently absorbed when taken orally. The vast majority of biologic drugs, including peptides, proteins and other macromolecules are currently administered by injection, which can present challenges for healthcare administration and compliance with treatment regimes.

## MILESTONES ACHIEVED

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

# Upcoming Value Drivers: Founded Entities

Potential launch momentum & source of capital to further fund advancement of Wholly Owned Programs

ENTITY	PURETECH OWNERSHIP <sup>1</sup>	THERAPEUTIC CANDIDATE	EXPECTED MILESTONES
Karuna (NASDAQ: KRTX)	2.3%	KarXT <sup>3</sup>	<ul style="list-style-type: none"> <li><input checked="" type="checkbox"/> <b>NDA submission for KarXT in schizophrenia</b> 3Q 2023</li> <li><input type="radio"/> <b>Results from Phase 3 EMERGENT-4 &amp; EMERGENT-5 trials for schizophrenia</b> 2H 2024</li> <li><input type="radio"/> <b>Results from Phase 3 ARISE trial for schizophrenia</b> 2H 2025</li> <li><input type="radio"/> <b>Results from Phase 3 ADEPT-1 &amp; ADEPT-2 trials</b> 2026</li> <li><input type="radio"/> Initiation of Phase 1b trial for MDD 2024</li> </ul>
Akili (NASDAQ: AKLI)	14.6%	KAR-2618	<ul style="list-style-type: none"> <li><input checked="" type="checkbox"/> <b>Secure label expansion for 13-17 y/o children with ADHD</b> 2023</li> <li><input type="radio"/> Data submission to FDA to market EndeavorOTC as OTC treatment for adults with ADHD 2024</li> </ul>
Vor (NASDAQ: VOR)	4.0%	AKL-T01 <sup>4</sup> EndeavorOTC <sup>4</sup>	<ul style="list-style-type: none"> <li><input checked="" type="checkbox"/> Additional trem-cel engraftment and hematological protection data updates 2023</li> <li><input checked="" type="checkbox"/> <b>IND application to support Phase 1/2 clinical trial</b> 1H 2023</li> </ul>
Vedanta	41.0% <sup>2</sup>	VE303 <sup>3</sup>	<ul style="list-style-type: none"> <li><input type="radio"/> Initiation of Phase 3 in <i>C. difficile</i> 1H 2024</li> </ul>
Sonde	35.2%	Sonde App	<ul style="list-style-type: none"> <li><input type="radio"/> Launch of key pilot programs 2023</li> </ul>

 Indicates completed milestone

 Key anticipated milestones are **bolded**

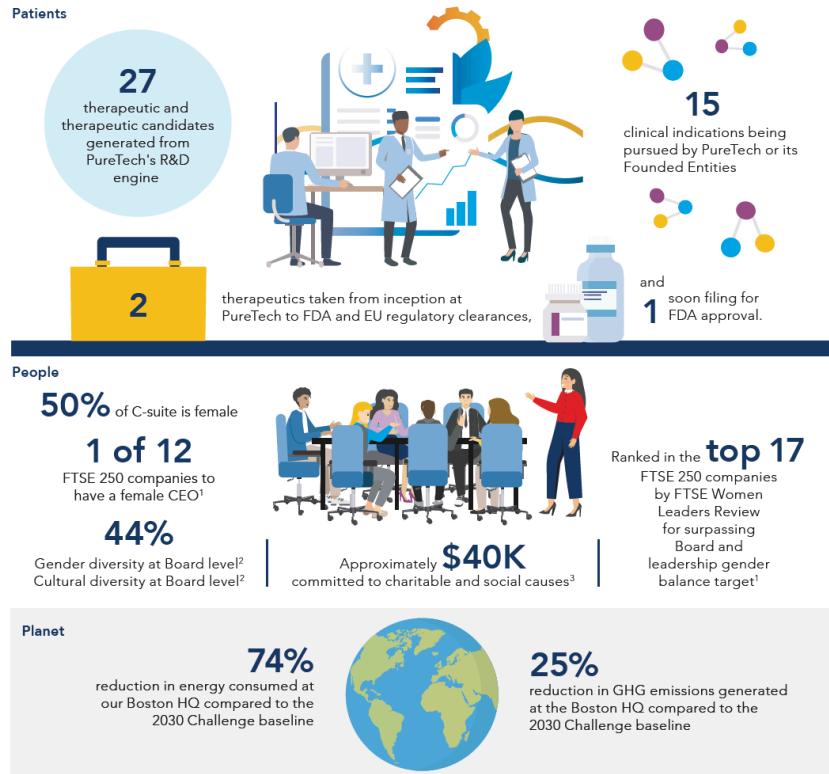
<sup>1</sup>This figure represents the stage of development for each Founded Entity's most advanced therapeutic candidate. Founded Entities represent companies founded by PureTech in which PureTech maintains ownership of an equity interest and, in certain cases, is eligible to receive sublicense income and royalties on product sales. Relevant ownership interests for Vedanta and Sonde were calculated on a partially diluted basis (as opposed to a voting basis) as of July 30, 2023, including outstanding shares, options and warrants but excluding unvested shares authorized to be issued pursuant to equity incentive plans. Karuna, Akili and Vor ownerships were calculated on a beneficial ownership basis in accordance with SEC rules as of February 15, 2024, August 3, 2023, and November 3, 2023, respectively.<sup>2</sup>Vedanta's \$106.5 million financing round was structured as convertible debt. 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.<sup>3</sup>Products are investigational and have not been cleared by the FDA for use in the U.S.<sup>4</sup> Please see footnotes on slide 70 for EndeavorOTC indication and overview, and footnotes on slide 73 for EndeavorOTC.

# Appendix C: Supplemental Materials

# PureTech ESG Program

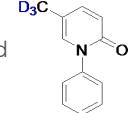
3 areas of focus: patients, people & planet

Named as one of the 2022 top-rated ESG companies by Sustainalytics<sup>3</sup> & ranked in the top 3 percent of pharmaceutical companies



# 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
KarXT, invented by PureTech Team	<b>Karuna's KarXT</b> for schizophrenia & psychosis in Alzheimer's disease	Xanomeline is highly effective in reducing psychosis	Xanomeline has GI tolerability issues	Pairing xanomeline with peripherally-restricted muscarinic antagonist improved AE profile and unlocked 1st new class in 50+ years   
Wholly Owned Pipeline includes multiple clinical programs building on PureTech's expertise & platforms. Certain CNS programs & relevant Glyph intellectual property to be advanced via Seaport Therapeutics	<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/ improved tolerability & potential for improved efficacy 
	<b>LYT-300</b> 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 exposure-dependent target engagement w/ GABA <sub>A</sub> receptors <sup>2</sup> . Approach may have advantages vs. oral chemical analogs 
	<b>LYT-310</b> for epilepsies & other neurological indications	Cannabidiol (CBD) effective in several epilepsies	GI tolerability & liver safety issues as well as undesirable dosing of large amounts of oily liquid via oral syringe	Using proprietary Glyph technology, developed CBD prodrug that enables capsule formulation w/ higher bioavailability, reducing GI/liver exposure & potentially related AEs 

KarXT, LYT-100, LYT-300 & LYT-310 are investigational drugs not approved by any regulatory authority.

<sup>1</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. <https://doi.org/10.18553/jmcp.2017.23.3-b.s72>

<sup>2</sup>Breanolone NDA 211371 Multi-disciplinary Review and Evaluation, FDA CDER, 2018; FXTAS = Fragile X-associated Tremor/Ataxia Syndrome.

# PureTech is Executing & Delivering Results

## REGULATORY

FDA Clearance & **EndeavorRx<sup>®1</sup>** (AKL-T01)  
European CE Mark **Plenify<sup>2</sup>** (Gelesis100)

## R&D & DATA PRESENTATIONS

- ✓ **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**
- ✓ Results for Akili's AKL-T01 in children with ADHD alone or as an adjunct to stimulants
- ✓ Akili's AKL-T03 data on MDD presented at ACNP
- ✓ 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 LYT-100 at **CHEST & ATS & ERS**
- ✓ PureTech's LYT-100 MAD study published in **Clinical Pharmacology in Drug Development**

## PARTNERSHIPS

- ✓ **Akili's partnership with Shionogi**  
Up to **\$20M** in upfront payments with the potential to receive milestone payments for Japan & Taiwan commercialization of up to an additional **\$105M** in addition to royalties on product sales
- ✓ **PureTech's partnership with Imbrum 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
- ✓ **Karuna's strategic collaboration with Zai Lab**  
\$35 million in upfront payment for development, manufacturing, & commercialization of KarXT in Greater China, & up to an additional \$80 million in development and regulatory milestones; Karuna also eligible to receive up to \$72 million in sales milestones & low-double-digit to high-teens tiered royalties based on annual net sales of KarXT in Greater China
- ✓ **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 Karuna's KarXT. After \$2 billion sales threshold, PureTech to retain 67% of royalty payments

## FINANCINGS

- ✓ **Karuna's \$124M Series A+B financings; \$103M IPO**  
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
- ✓ **Akili's Nasdaq debut ('AKLI') via SPAC merger**  
Transaction generated more than \$163M in gross proceeds, which will be used to fund the commercial launch of EndeavorRx<sup>®</sup>, its potential expansion into additional ADHD patient populations, and will also support the advancement of the company's late-stage pipeline
- ✓ **Vedanta's \$106.5M financing**  
Syndicate led by new investors AXA IM Alts and The AMR Action Fund along with existing investors Bill & Melinda Gates Foundation, Skyviews Life Science, and others

# Financial Highlights

Estimated  
December 31, 2023  
\$ millions

## Cash Flow and Liquidity<sup>1</sup>

Consolidated Cash, Cash Equivalents, and Short-Term Investments	320.0
Less: Cash and Cash Equivalents held at non-wholly-owned subsidiaries	(1.2)
PureTech Level Cash, Cash Equivalents, and Short-Term Investments <sup>2</sup>	318.8

# 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 and cash equivalents

**Measure type:** Core performance.

**Definition:** Cash and cash equivalents held at PureTech Health plc and only wholly-owned subsidiaries (PureTech LYT, PureTech LYT-100, Alivio Therapeutics, Inc., PureTech Management, Inc., PureTech Health LLC, PureTech Securities Corp, PureTech Securities II Corp)

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

# Non-IFRS Measures Reconciliation – Karuna ROI

<b>Investments Held at Fair Value @ 12/31/2022 in audited consolidated balance sheet</b>	<b>251.9</b>
(-) Other Investments Held at Fair Value @ 12/31/2022	(44.7)
<b>Karuna Investment Held at Fair Value @ 12/31/2022</b>	<b>207.2</b>
(+/-) Sale of 167,579 shares of Karuna in October through December 2023	(33.3)
(+/-) Karuna Fair Value Gain/ Loss for the period 12/31/2022 to 12/31/2023	118.8
<b>(a) Karuna Investment Held at Fair Value @ 12/31/2023</b>	<b>292.7</b>
 <b>Proceeds From Sale of Investments Held at Fair Value @ 12/31/2020</b>	<b>350.6</b>
(-) Sale of 2,119,696 shares of resTORbio	(3.0)
<b>Proceeds From Sale of Karuna @ 12/31/2020</b>	<b>347.5</b>
(+/-) Sale of 1,000,000 shares of Karuna @ 2/9/2021	118.0
(+/-) Sale of 750,000 shares of Karuna @ 11/10/2021	100.1
(+/-) Sale of 602,100 shares of Karuna during August and September 2022	115.5
(+/-) Sale of 167,579 shares of Karuna in October through December 2023	33.3
<b>(b) Proceeds From Sale of Karuna</b>	<b>714.4</b>
 <b>(a) + (b) Total Karuna Investment Held at Fair Value and Proceeds @ 12/31/2023</b>	<b>1,007.1</b>
 <b>(c) Total PureTech Principal Investment in Karuna</b>	<b>18.5</b>
 <b>[ (a + b - c) / c ] Return on Investment (ROI)</b>	<b>53.5</b>