



United Therapeutics: Enabling Inspiration

J.P. MORGAN HEALTHCARE CONFERENCE
JANUARY 8, 2024

INTRODUCTION

Safe Harbor Statement

All statements in this presentation are made as of **January 8, 2024**. We undertake no obligation to publicly update or revise these statements, whether as a result of new information, future events, or otherwise.

Statements included in this presentation that are not historical in nature are “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements include, among others, statements related to our revenue growth expectations, the timing and success of our pipeline programs, our planned manufacturing and field force expansions, our organ manufacturing efforts, and similar statements concerning anticipated future events and expectations.

We caution you that these statements are not guarantees of future performance and are subject to numerous evolving risks and uncertainties that we may not be able to accurately predict or assess, including the risk factors that we describe in our Securities and Exchange Commission filings, including our most recent Annual Report on Form 10-K or Quarterly Report on Form 10-Q. Any of these factors could cause actual results to differ materially from the expectations we express or imply in this presentation.

This presentation and any related discussions or statements are intended to educate investors about our company. Sometimes that process includes reporting on the progress and results of clinical trials or other developments with respect to our products. This presentation and any related discussions or statements are not intended to promote our products, to suggest that our products are safe and effective for any use other than what is consistent with their FDA-approved labeling, or to provide all available information regarding the products, their risks, or related clinical trial results. Anyone seeking information regarding the use of one of our products should consult the full prescribing information for the product available on our website at www.unither.com.



HOW WE OPERATE

Our Focus

Rare Diseases

- **Pulmonary Hypertension**
- **Pulmonary Fibrosis**
- **Neuroblastoma**

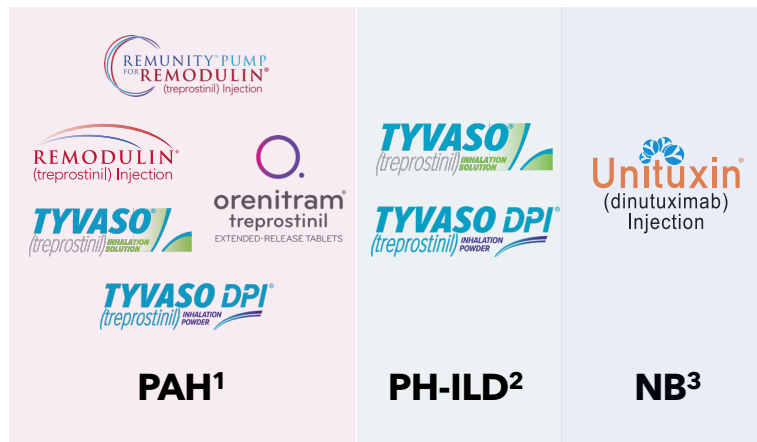
Organ Manufacturing

- **Ex-Vivo Lung Perfusion**
- **Xenotransplantation**
- **Regenerative Medicine**
- **3-D Organ Printing**

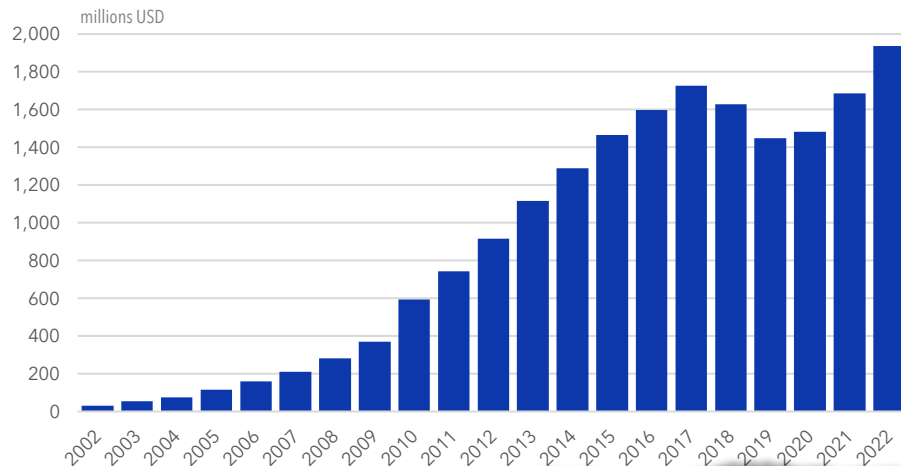
HOW WE OPERATE

Decades of Innovation and Revenue Growth

Six Approved Products Covering Three Indications



>20% Annual Revenue CAGR⁴ Since First Commercial Product Launch



1. PAH = pulmonary arterial hypertension.

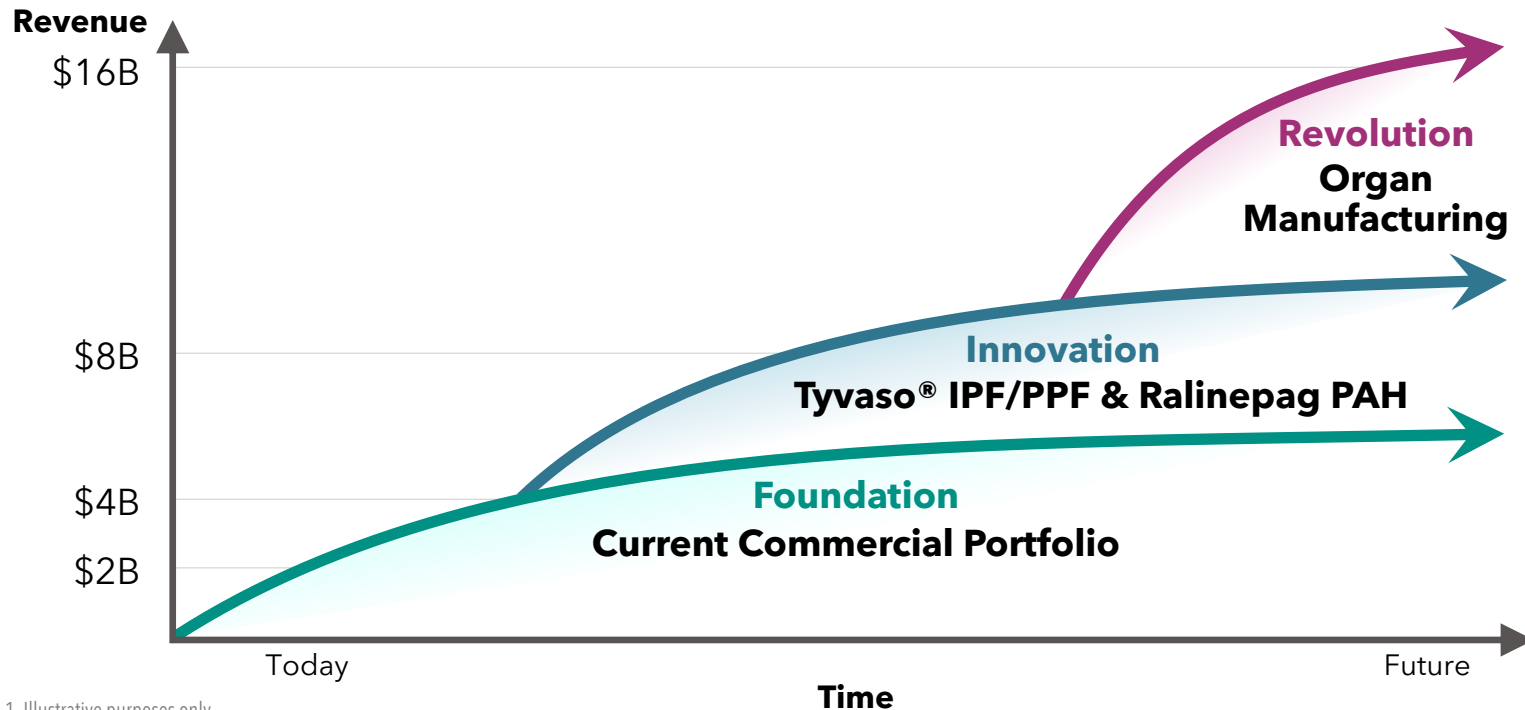
2. PH-ILD = pulmonary hypertension associated with interstitial lung disease.

3. NB = neuroblastoma.

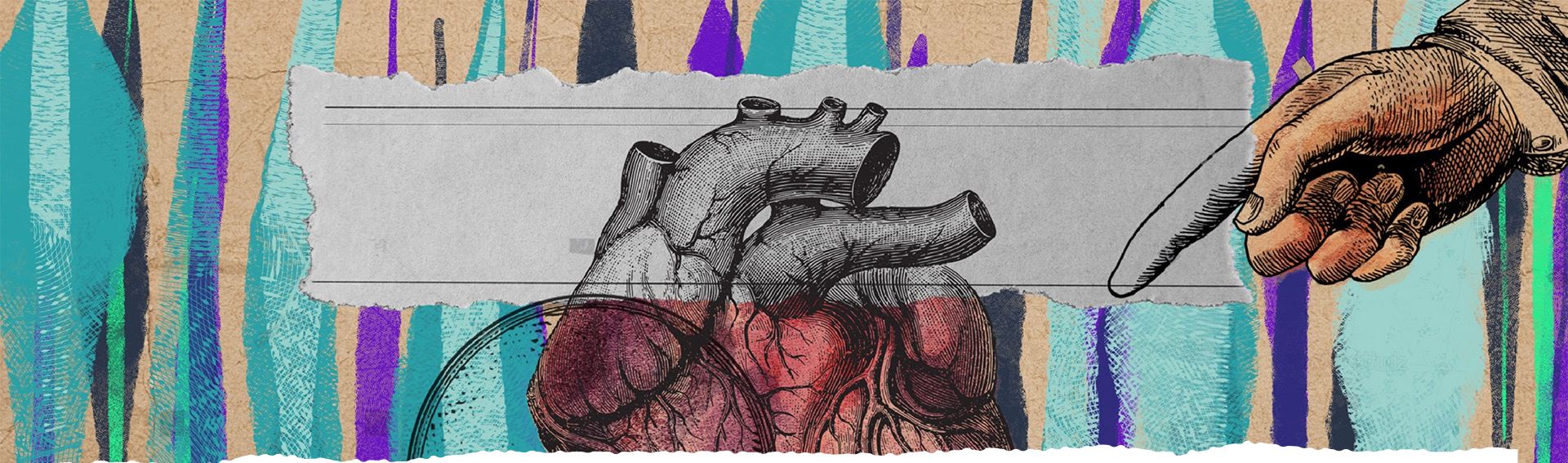
4. CAGR = compound annual growth rate.

HOW WE OPERATE

Positioned for Multiple Waves of Growth¹



1. Illustrative purposes only.



Foundation: Our Commercial Portfolio

FOUNDATION

Solid Foundation Addressing Rare Disease



REMODULIN[®]
(treprostinil) Injection

The **most prescribed** parenteral prostacyclin in the U.S.



Unituxin[®]
(dinutuximab)
Injection

The **most prescribed** antibody therapy for high-risk neuroblastoma in the U.S.

FOUNDATION

Solid Foundation Addressing Rare Disease



The **only prostacyclin** with the ability to transition from infused therapies and maintain **infused therapy dose exposure**



The **most prescribed** prostacyclin in the U.S.

FOUNDATION

Tyvaso DPI®: Early, Easy, Effective



TYVASO DPI®
(treprostinil) INHALATION
POWDER

FOUNDATION

Tyvaso DPI®: Early, Easy, Effective



An option for appropriate patients identified **early**^{1,3,5}



Easy-to-use prostacyclin delivery^{1,2}



Proven **efficacy** and **safety** across multiple clinical trials^{1,2,3,4}

1. TYVASO DPI [package insert]. Research Triangle Park, NC: United Therapeutics Corporation; 2022. 2. Spikes LA, Bajwa AA, Burger CD, et al. BREEZE: open-label clinical study to evaluate the safety and tolerability of treprostinil inhalation powder as Tyvaso DPI™ in patients with pulmonary arterial hypertension. *Pulm Circ.* 2022;12(2):e12063. doi:10.1002/pul2.12063. 3. McLaughlin VV, Benza RL, Rubin LJ, et al. Addition of inhaled treprostinil to oral therapy for pulmonary arterial hypertension: a randomized controlled clinical trial. *J Am Coll Cardiol.* 2010;55(18):1915-1922. 4. Benza RL, Seeger W, McLaughlin VV, et al. Long-term effects of inhaled treprostinil in patients with pulmonary arterial hypertension: the Treprostinil Sodium Inhalation Used in the Management of Pulmonary Arterial Hypertension (TRIUMPH) study open-label extension. *J Heart Lung Transplant.* 2011;30(12):1327-1333. 5. Cascino TM, McLaughlin VV. Upfront combination therapy for pulmonary arterial hypertension: time to be more ambitious than AMBITION. *Am J Respir Crit Care Med.* 2021;204(7):756-759.

FOUNDATION

Recent Manuscript¹ Ties Low Flow to Deep Lung Deposition



VOLUME 81, AUGUST 2023 ISSN 1094-5539

PULMONARY
PHARMACOLOGY
& THERAPEUTICS

Tyvaso DPI: Drug-device characteristics and patient clinical considerations

Colleen McEvoy^a, Rahul Argula^b, Sandeep Sahay^c, Shelley Shapiro^d, Christina Eagan^e, Anthony J. Hickey^f, Chad Smutney^g, Chris Dillon^h, Thomas Winkler^h, Brittany N. Davis^h, Meredith Broderick^h, Charles Burger^{i,*}

1. Colleen McEvoy, et al. Tyvaso DPI: Drug-device characteristics and patient clinical considerations, *Pulmonary Pharmacology & Therapeutics*, Volume 83, 2023, 102266, ISSN 1094-5539, <https://doi.org/10.1016/j.pupt.2023.102266>.

FOUNDATION

Recent Manuscript¹ Ties Low Flow to Deep Lung Deposition



While many have **incorrect beliefs** about high-resistance devices, research and real-world clinical evidence have shown that patients with pulmonary disease, including PH, **can generate the inspiratory force needed to properly use these devices.**^{2,3,4}

2. L.A. Spikes, A.A. Bajwa, C.D. Burger, et al., *BREEZE*: open-label clinical study to evaluate the safety and tolerability of treprostinil inhalation powder as Tyvaso DPI™ in patients with pulmonary arterial hypertension, *Pulm. Circ.* 12 (2) (2022), <https://doi.org/10.1002/pul2.12063>.
3. S. Sahay, R. Holy, S. Lyons, E. Parsley, M. Maurer, J. Weers, Impact of human behavior on inspiratory flow profiles in patients with pulmonary arterial hypertension using AOS dry powder inhaler device, *Pulm. Circ.* 11 (1) (Jan-Mar 2021), 2045894020985345, <https://doi.org/10.1177/2045894020985345>.
4. Malmberg. Inspiratory flows through dry powder inhaler in chronic obstructive pulmonary disease: age and gender rather than severity matters, *Int. J. Chronic Obstr. Pulm. Dis.* (2010) 257, <https://doi.org/10.2147/copd.s11474>.

FOUNDATION

Recent Manuscript¹ Ties Low Flow to Deep Lung Deposition



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PULMONARY
PHARMACOLOGY
& THERAPEUTICS

The minimum [peak inspiratory pressure] needed to create adequate powder dispersion to empty the Tyvaso DPI cartridge is 2 kPa for ≥ 2 seconds, resulting in **complete dose delivery from the device**.^{5,6,7}

FOUNDATION

Recent Manuscript¹ Ties Low Flow to Deep Lung Deposition

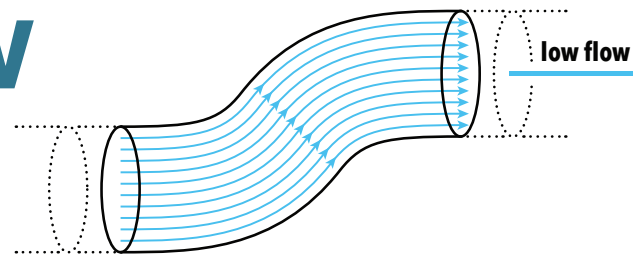


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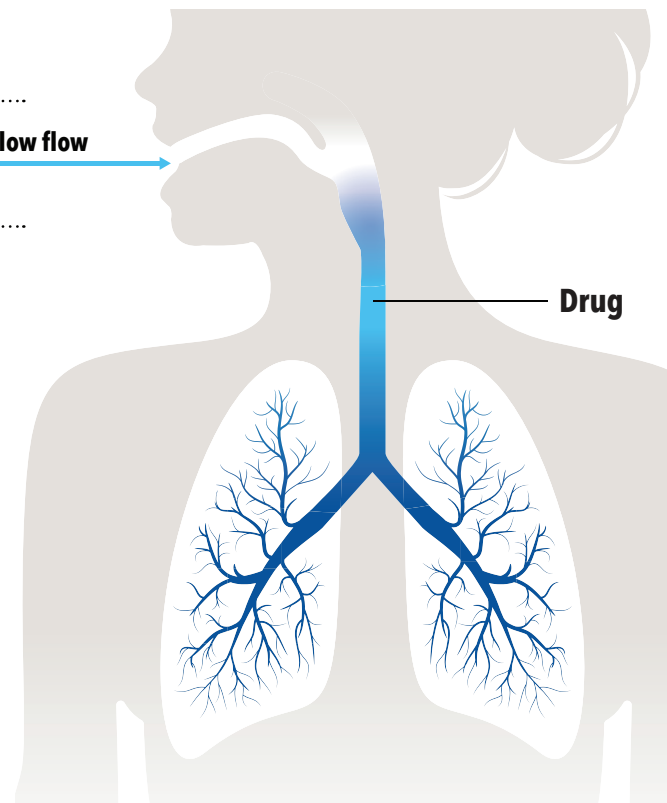
PULMONARY
PHARMACOLOGY
& THERAPEUTICS

Low inhalation pressures generated by the user ... are efficient to induce low-flow rates ... through the DPI.⁸

Tyvaso DPI® is LOW FLOW



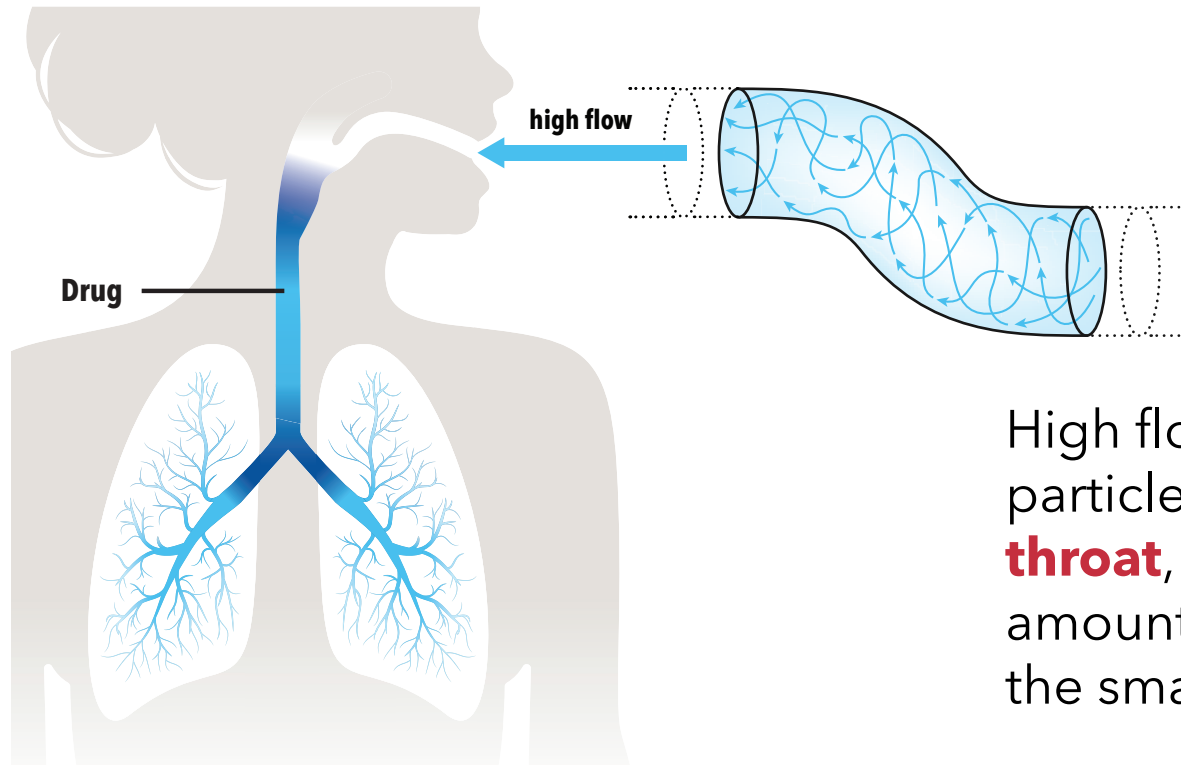
Low flow, coupled with the FDKP carrier molecule, allows more drug deposition in the **smaller airways of the lungs** rather than the throat



Drug concentration

low

high

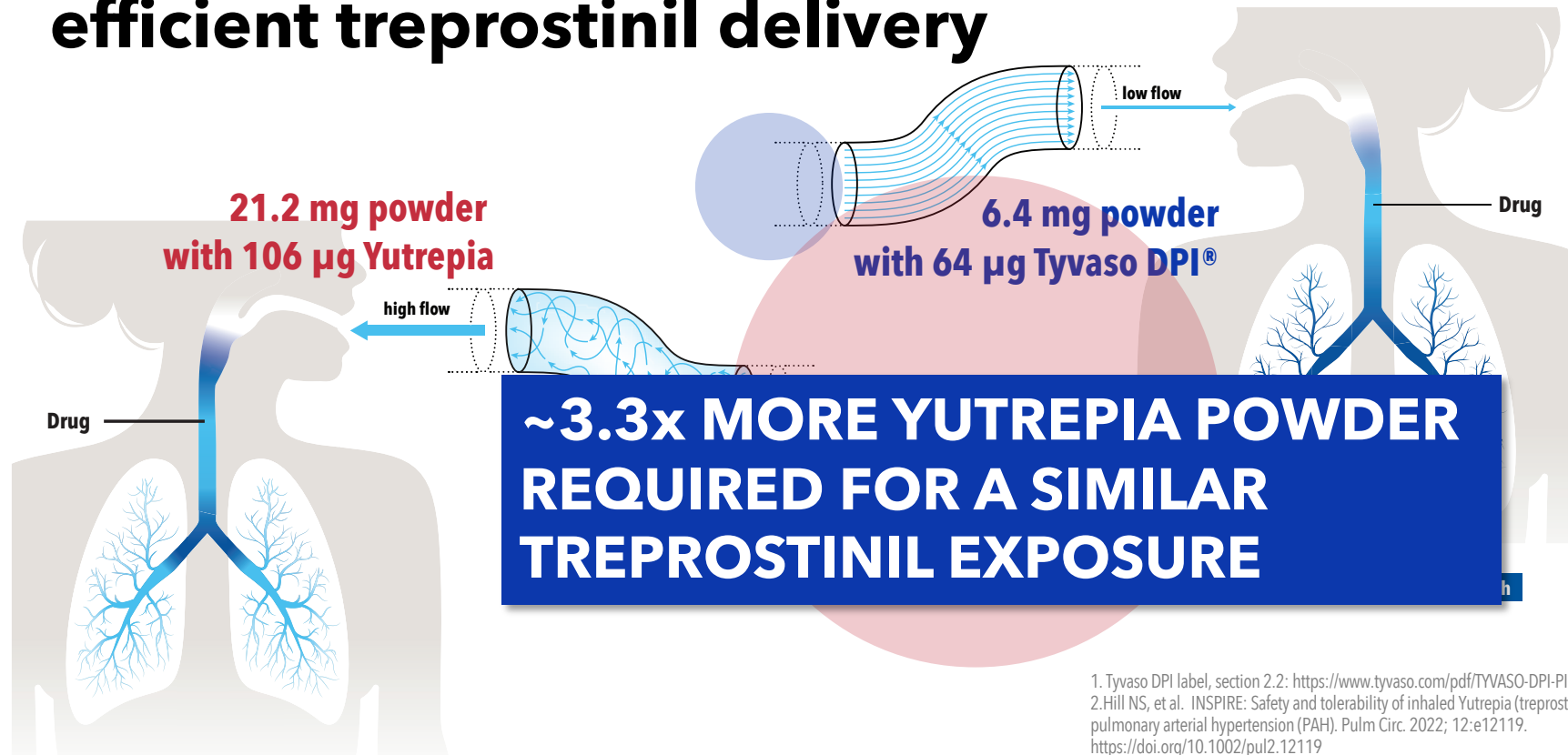


Other DPI devices are **HIGH FLOW**

High flow devices cause more particles to **deposit in the throat**, decreasing the amount of drug distributed to the smallest airways

Colleen McEvoy, et al. Tyvaso DPI: Drug-device characteristics and patient clinical considerations, *Pulmonary Pharmacology & Therapeutics*, Volume 83, 2023, 102266, ISSN 1094-5539, <https://doi.org/10.1016/j.pupt.2023.102266>.

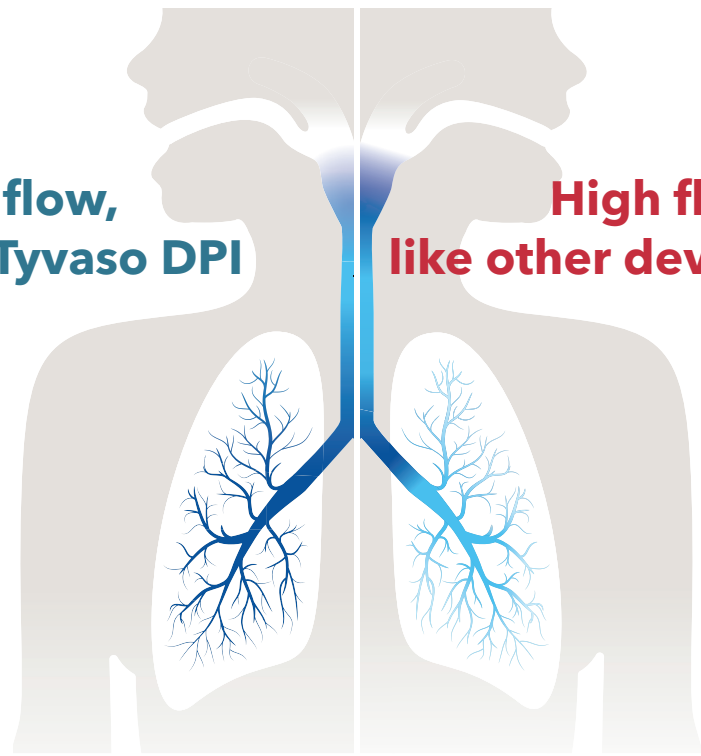
LOW FLOW of Tyvaso DPI® leads to efficient treprostinil delivery



Tyvaso DPI®: The **first and only** DPI tailored for drug delivery to the distal lungs for PH

Low flow,
like Tyvaso DPI

High flow,
like other devices



Drug concentration

low

high

Tyvaso DPI®: The **first and only** DPI tailored for drug delivery to the distal lungs for PH¹

ONE BREATH per cartridge²

DEEP LUNG delivery¹

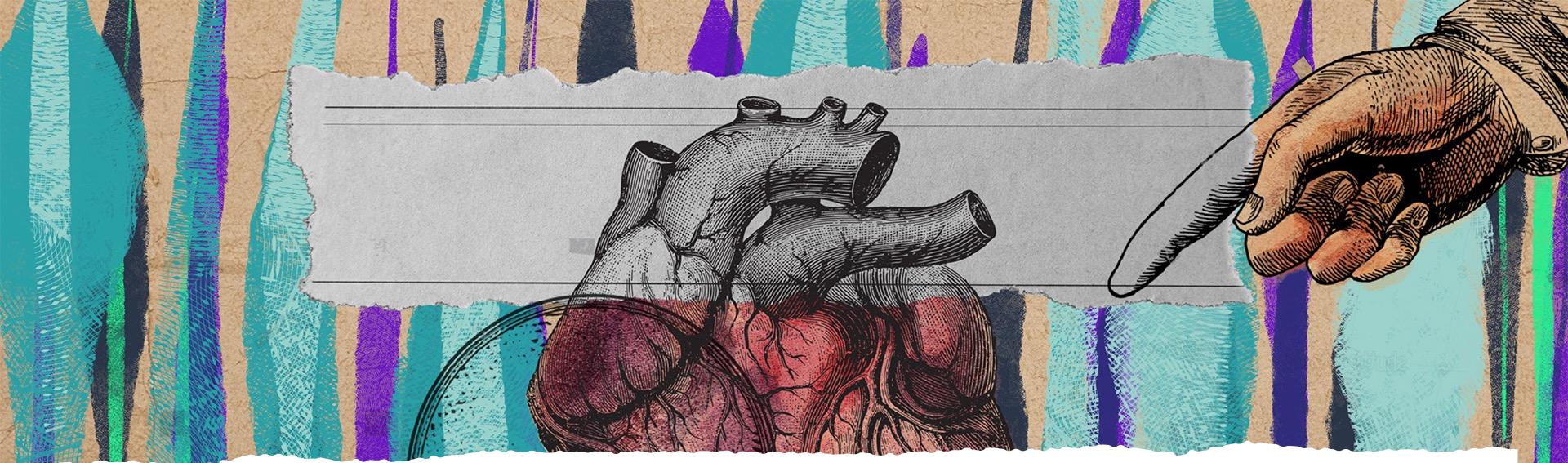
NO CLEANING required³

ROOM TEMP storage⁵

NO MAX labeled dose⁴

HIGH PATIENT satisfaction⁶

1. Colleen McEvoy, et al. Tyvaso DPI: Drug-device characteristics and patient clinical considerations, *Pulmonary Pharmacology & Therapeutics*, Volume 83, 2023, 102266, ISSN 1094-5539, <https://doi.org/10.1016/j.pupt.2023.102266>. 2. Tyvaso DPI label, section 2.1: "Tyvaso DPI is administered using a single inhalation per cartridge." <https://www.tyvaso.com/pdf/TYVASO-DPI-PI.pdf>. 3. Tyvaso DPI label, section 2.1: "Wipe the outside of the inhaler with a clean, dry cloth only, if needed. Do not rinse or wash the Tyvaso DPI Inhaler; always keep the inhaler dry." <https://www.tyvaso.com/pdf/TYVASO-DPI-PI.pdf>. 4. Tyvaso DPI label, section 2.1: "If the prescribed dose is higher than 64 mcg per treatment session, more than 1 cartridge will be needed per session." <https://www.tyvaso.com/pdf/TYVASO-DPI-PI.pdf>. 5. Tyvaso DPI label, section 16: "Room temperature storage 20°C to 25°C (68°F to 77°F), excursions permitted 15°C to 30°C (59°F to 86°F)." <https://www.tyvaso.com/pdf/TYVASO-DPI-PI.pdf>. 6. Spikes LA, Bajwa AA, Burger CD, et al. BREEZE: open-label clinical study to evaluate the safety and tolerability of treprostinil inhalation powder as Tyvaso DPI™ in patients with pulmonary arterial hypertension. *Pulm Circ.* 2022;12(2):e12063. doi:10.1002/pul2.12063.



Innovation: Our Near-Term Pipeline



INNOVATION

Development Engine Addressing Unmet Needs

NON-REGISTRATION

REGISTRATION

APPROVED

Tyvaso®

TETON 1 - Idiopathic Pulmonary Fibrosis - U.S. and Canada

TETON 2 - Idiopathic Pulmonary Fibrosis - ROW¹

TETON PPF - Progressive Pulmonary Fibrosis

Ralinepag

ADVANCE OUTCOMES - PAH²

Organ Manufacturing

EVLP³/CLES⁴ - Lung Transplant

Pre-clinical Organ Programs

UKidney™

UHeart™

MiroliverELAP®

ULung™

Miroidney®

UThymoKidney™

ULobe™

IVIVA Kidney

3DAP Kidney

Miroliver™

1. ROW = rest of world outside the U.S. and Canada. 2. PAH = pulmonary arterial hypertension. 3. EVLP = ex-vivo lung perfusion; 4. CLES = centralized lung evaluation system.

INNOVATION

Tyvaso® *TETON* program

	<i>TETON 1</i>	<i>TETON 2</i>	<i>TETON PPF</i>
Indication	Idiopathic pulmonary fibrosis		Progressive Pulmonary Fibrosis
U.S. Addressable Population	100,000 patients		60,000 ^{6,7,8}
Study Size	576	576	698
Study Geography	U.S./Canada	ROW ¹	Worldwide
Primary Endpoint	Change in absolute FVC ² from baseline to week 52		
Enrollment Progress ³	~65%	~60%	PPFV ⁵

Complete Enrollment for *TETON 1* and *2* Targeted for Year-End 2024⁴

1. ROW = rest of world outside the United States and Canada; 2. FVC = forced vital capacity, or the amount of air that can be forcibly exhaled from your lungs after taking the deepest breath possible. 3. As of December 15, 2023. 4. Enrollment target is our current target for full enrollment of the study at the time of this presentation. Our timing expectations may change. 5. PPFV = first patient, first visit. PPFV for *TETON PPF* was in October 2023. 6. Am J. Respir Crit Care Med, vol 150, pp 967-972, 1994. 7. Adv Ther (2021) 38:4100-4114. 8. Cottin V, Teague R, Nicholson L, Langham S and Baldwin M (2022) The Burden of Progressive-Fibrosing Interstitial Lung Diseases. Front. Med. 9:799912. doi: 10.3389/fmed.2022.799912

INNOVATION

Ralinepag

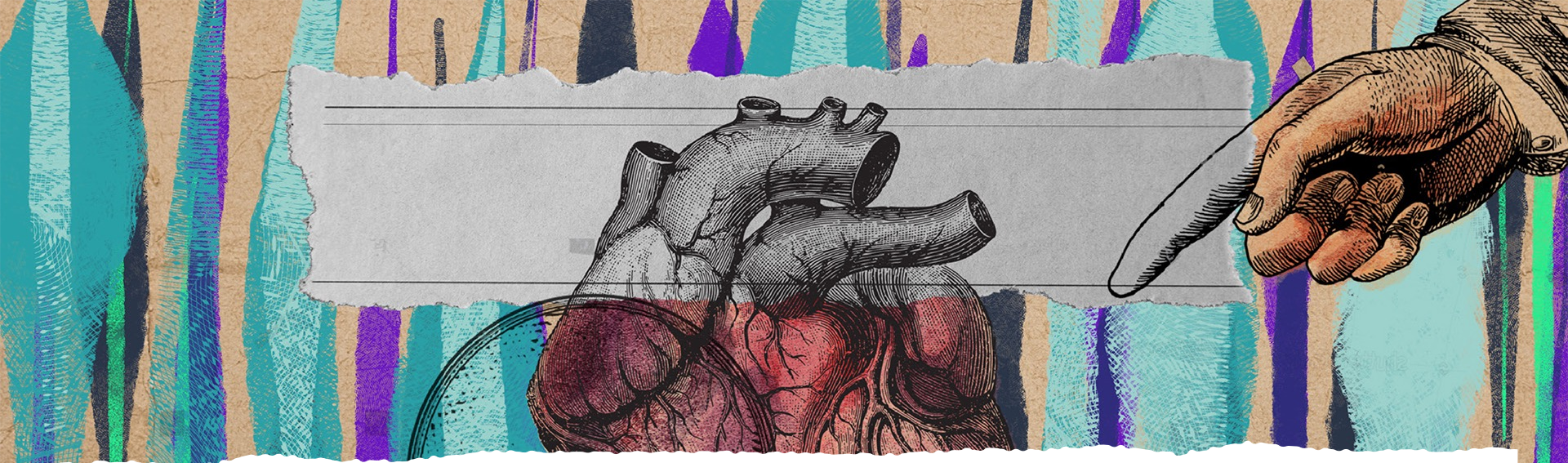
ADVANCE OUTCOMES Study

Indication	Group 1 PAH ¹
U.S. Addressable Population	50,000 patients
Study Size	~700 to 1,000 patients
Study Geography	Global
Primary Endpoint	Time from randomization to the first adjudicated protocol-defined clinical worsening event
Enrollment Progress ²	> 530 patients

**Trial Completion
Targeted in 2025³**

**DSMC⁴ recommended continuation
of both studies after an unblinded
safety review of 510 patients**

1. PAH = pulmonary arterial hypertension. 2. As of December 15, 2023. 3. Completion timing is our current target for total event accrual at the time of this presentation. Our timing expectations may change. 4. DSMC = data safety monitoring committee



Revolution: Our Organ Manufacturing Efforts



REVOLUTION

Four Platforms with Four Organs; Multiple Shots on Goal

1. 3DAP = 3D autologous printed.
2. Bio-Art = Bioartificial

	Xeno	Regen Med	3DAP ¹	Bio-Art ²
Kidney	UKidney™ UTHymoKidney™		3DAP Kidney	IVIVA Kidney Mirokidney®
Heart	UHeart™			
Lung		ULobe™	ULung™	
Liver			3DAP Liver	MiroliverELAP®/ Miroliver®

REVOLUTION

Xenotransplants March Toward the Clinic

Pre-clinical progress

- "Pivotal" pre-clinical studies underway
- Last non-clinical xenokidney transplant expected by mid-2024
- FDA meeting to discuss IND and clinical protocol for 10-gene xeno-organs

Designated Pathogen Free Facility (DPF)

- ~\$75 million investment in Christiansburg, VA
- 125-organ annual capacity from up to 50 animals
- **Construction complete**; animal introduction expected in 1H/24



REVOLUTION

Xenokidneys Represent a Multi-Billion-Dollar Opportunity

90,000 patients

PREVALENCE IN THE U.S.

450,000 patients

U.S. KIDNEY TRANSPLANT WAIT LIST

~90k patients¹

PATIENTS ON DIALYSIS NOT ON THE WAIT LIST

~450k patients²

1. Organ Procurement and Transplantation Network (OPTN) data as of 12/20/2023 (88,941).

2. Extrapolated from OPTN data and National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) data, <https://www.niddk.nih.gov/health-information/health-statistics/kidney-disease> (467,520).

REVOLUTION

Xenokidneys Represent a Multi-Billion-Dollar Opportunity

25,000 patients

INCIDENCE IN THE U.S.

100,000 patients

ANNUAL KIDNEY TRANSPLANTS

~25k patients¹

ANNUAL PATIENTS STARTING DIALYSIS NOT ON WAIT LIST

~100k patients²

1. Organ Procurement and Transplantation Network (OPTN) data for FY 2022 (25,500).

2. Extrapolated from 2018 National Kidney Foundation Data. <https://www.kidney.org/news/newsroom/fsindex> (103,000).

REVOLUTION

Xenokidneys Represent a Multi-Billion-Dollar Opportunity

REVENUE OPPORTUNITY IN THE U.S.

FULLY ADDRESS FUTURE ANNUAL NEED

\$30 billion to \$90 billion

ANNUAL MEDICARE SPEND FOR KIDNEY CARE

\$51 billion in 2020¹

\$30 billion

\$51 billion

1. The United States Renal Data System 2022 Annual Data Report. <https://usrds-adr.niddk.nih.gov/2022/end-stage-renal-disease/9-healthcare-expenditures-for-persons-with-esrd>

REVOLUTION

Xenokidneys Represent a Multi-Billion-Dollar Opportunity

ANNUAL REVENUE PER DPF¹ FACILITY

1,000 organ throughput
\$300 million to \$900 million

2,000 organ throughput
\$600 million to \$1.8 billion

3,000 organ throughput
\$900 million to \$2.7 billion

\$900 million

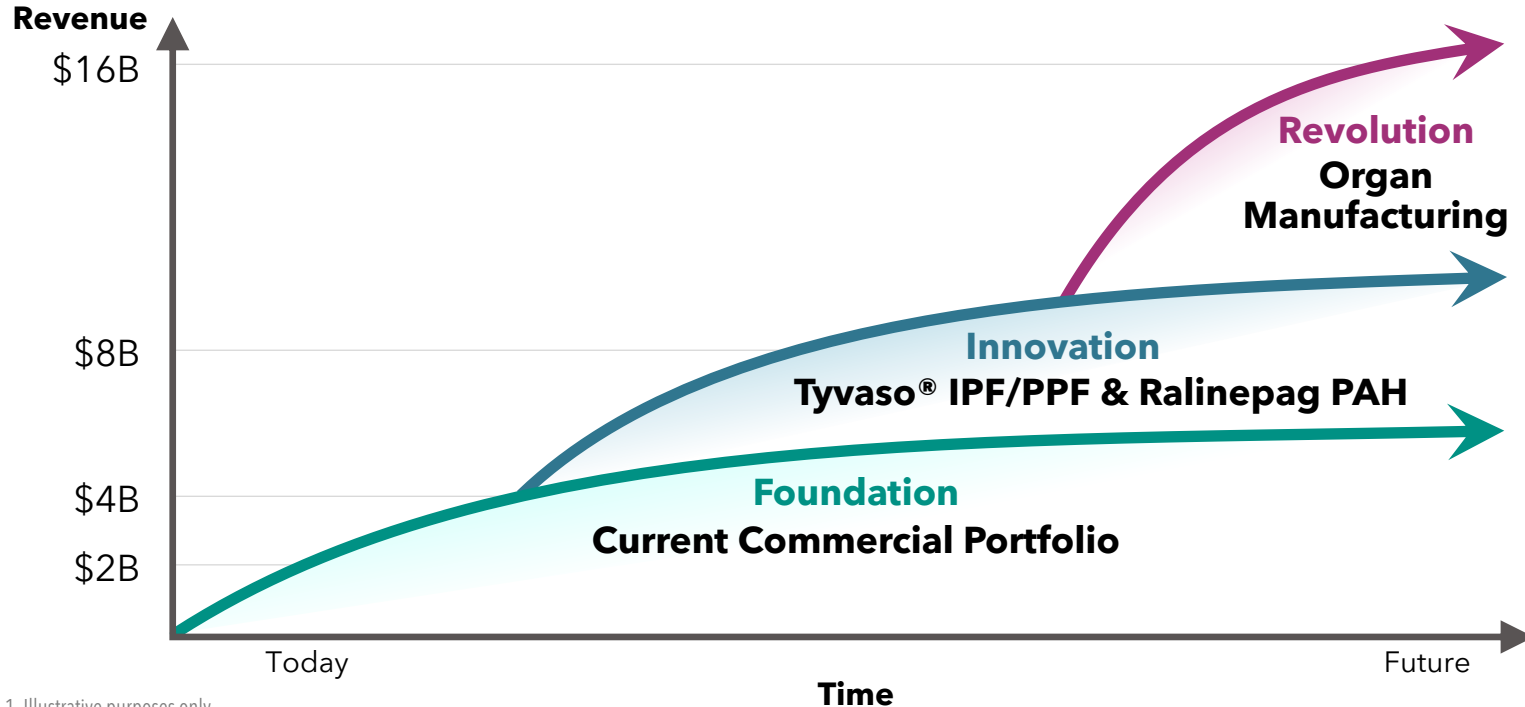
\$1.8 billion

\$2.7 billion

1. DPF = designated pathogen free.

REVOLUTION

UTHR: Positioned for Multiple Waves of Growth¹



1. Illustrative purposes only.

Q&A

Dr. Martine Rothblatt

Chairperson & Chief Executive Officer

Michael Benkowitz

President & Chief Operating Officer

James Edgemon

Chief Financial Officer & Treasurer





**United
Therapeutics**

C O R P O R A T I O N