Filed by AVROBIO, Inc.
Pursuant to Rule 425 under the Securities Act of 1933
Deemed filed pursuant to Rule 14a-12 under the Securities Exchange Act of 1934

Subject Company: AVROBIO, Inc.
Commission File No.: 001-38537
Date: April 4, 2024

This filing relates to the proposed transaction pursuant to the terms of that certain Agreement and Plan of Merger and Reorganization, dated as of January 30, 2024, among AVROBIO, Inc., a Delaware corporation ("AVROBIO"), Alpine Merger Subsidiary, Inc., a Delaware corporation and a wholly-owned subsidiary of AVROBIO ("Merger Sub"), and Tectonic Therapeutic, Inc., a Delaware corporation ("Tectonic"), (the "Merger Agreement"), pursuant to which, and subject to the satisfaction or waiver of the conditions set forth in the Merger Agreement, Merger Sub will be merged with and into Tectonic (the "Merger"), with Tectonic continuing after the Merger as the surviving corporation and a wholly-owned subsidiary of AVROBIO. The following is Tectonic's updated corporate deck made available on Tectonic's website at https://tectonictx.com on April 4, 2024.

# Transforming the Discovery of Novel GPCR-Targeted Therapies

April 2024

TECTONIC Therapeutic

AVROBIO

# DISCLAIMER

This communication contains "forward-looking statements" within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995, including but not limited to, express or implied statements regarding the structure, timing and completion of the proposed merger; the combined company's listing on Nasdaq after closing of the proposed merger (the "Merger") with AVROBIO, Inc. ("AVROBIO") and Tectonic Therapeutic, Inc. ("Tectonic"); expectations regarding the ownership structure of the combined company; the anticipated timing of closing of the proposed Merger; the expected executive officers and directors of the combined company; expectations regarding the structure, amount, timing and completion of the private placement financings, including investment amounts from investors, timing of closing of the proposed Merger, expected proceeds and impact on ownership structure; each company's and the combined company's expected cash position at the closing of the proposed Merger and cash runway of the combined company following the Merger and private financing; the future operations of the combined company, including commercialization activities, timing of launch, buildout of commercial infrastructure; the nature, strategy and focus of the combined company; the development and commercial potential and potential benefits of any product candidates of the combined company; the location of the combined company's corporate headquarters; anticipated preclinical and clinical drug development activities and related timelines, including the expected timing for data and other clinical results; the competitive landscape of the combined company; and other statements that are not historical fact. All statements other than statements of historical fact contained in this communication are forward-looking statements. These forward-looking statements are made as of the date they were first issued, and were based on the then-current expectations, estimates, forecasts, and projections, as well as the beliefs and assumptions of management. Forward-looking statements are subject to a number of risks and uncertainties, many of which involve factors or circumstances that are beyond AVROBIO's, Tectonic's or the combined company's control. Actual results could differ materially from those stated or implied in forward-looking statements due to a number of factors, including but not limited to (i) the risk that the conditions to the closing of the proposed Merger are not satisfied, including the failure to timely obtain shareholder approval for the transaction, if at all; (ii) uncertainties as to the timing of the consummation of the proposed Merger and the ability of each of AVROBIO and Tectonic to consummate the proposed Merger; (iii) risks related to AVROBIO's ability to manage its operating expenses and its expenses associated with the proposed Merger pending closing of the proposed Merger; (iv) risks related to the failure or delay in obtaining required approvals from any governmental or quasi-governmental entity necessary to consummate the proposed Merger; (v) the risk that as a result of adjustments to the exchange ratio, AVROBIO shareholders and Tectonic stockholders could own more or less of the combined company than is currently anticipated; (vi) risks related to the market price of AVROBIO's common stock relative to the value suggested by the exchange ratio; (vii) unexpected costs, charges or expenses resulting from the transaction; (viii) potential adverse reactions or changes to business relationships resulting from the announcement or completion of the proposed Merger; (ix) the uncertainties associated with Tectonic's platform technologies, as well as risks associated with the clinical development and regulatory approval of product candidates, including potential delays in the commencement, enrollment and completion of clinical trials; (x) risks related to the inability of the combined company to obtain sufficient additional capital to continue to advance these product candidates and its preclinical programs; (xi) uncertainties in obtaining successful clinical results for product candidates and unexpected costs that may result therefrom; (xii) risks related to the failure to realize any value from product candidates and preclinical programs being developed and anticipated to be developed in light of inherent risks and difficulties involved in successfully bringing product candidates to market; (xiii) risks associated with the possible failure to realize certain anticipated benefits of the proposed Merger, including with respect to future financial and operating results; (xiv) risks associated with AVROBIO's financial close process; (xv) the risk that the private financing is not consummated, among others. These and other risks and uncertainties are more fully described in filings that AVROBIO makes and will make with the Securities and Exchange Commission ("SEC") in connection with the proposed Merger, including the factors described in the section titled "Risk Factors" in AVROBIO's Annual Report on Form 10-K for the year ended December 31, 2023, which was filed with the SEC on March 14, 2024, and in other filings that AVROBIO makes and will make with the SEC in connection with the proposed Merger, including the Proxy Statement described below under "Additional Information and Where to Find It." You should not place undue reliance on these forward-looking statements, which are made only as of the date hereof or as of the dates indicated in the forward-looking statements. AVROBIO, Tectonic and the combined company expressly disclaims any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in their expectations with regard thereto or any change in events, conditions or circumstances on which any such statements are based.

Tectonic obtained the industry, market and competitive position data used throughout this presentation from its own internal estimates and research, as well as from industry and general publications, and research, surveys and studies conducted by third parties. Internal estimates are derived from publicly available information released by industry analysts and third-party sources, Tectonic's internal research and its industry experience, and are based on assumptions made by Tectonic based on such data and its knowledge of the industry and market, which it believes to be reasonable. In addition, while Tectonic believes the industry, market and competitive position data included in this presentation is reliable and based on reasonable assumptions, Tectonic has not independently verified any third-party information, and all such data involve risks and uncertainties and are subject to change based on various factors.



TECTONIC Therapeutic

# DISCLAIMER (continued)

**Participants in the Solicitation**

AVROBIO, Tectonic and their respective directors and executive officers may be deemed to be participants in the solicitation of proxies from stockholders in connection with the proposed Merger. Information about the directors and executive officers of AVROBIO is set forth in its Annual Report on Form 10-K for the year ended December 31, 2023, which was filed with the SEC on March 14, 2024, and other documents that may be filed from time to time with the SEC. Additional information regarding the persons who may be deemed participants in the proxy solicitations and a description of their direct and indirect interests, by security holdings or otherwise, have been included in the registration statement on Form S-4 (as amended, the "Form S-4"), which includes a preliminary proxy statement/prospectus and other relevant materials filed, or to be filed, with the SEC. You may obtain free copies of this document as described below.

**Additional Information and Where to Find It**

In connection with the proposed Merger, AVROBIO has filed relevant materials with the SEC, including the Form S-4, which has not yet been declared effective by the SEC and is subject to change. This communication is not a substitute for the Form S-4, the proxy statement/prospectus or for any other document that AVROBIO may file with the SEC and/or send to AVROBIO's stockholders in connection with the proposed Merger. BEFORE MAKING ANY VOTING DECISION, INVESTORS AND SECURITY HOLDERS OF AVROBIO ARE URGED TO READ THE FORM S-4, THE PROXY STATEMENT/PROSPECTUS AND OTHER DOCUMENTS FILED WITH THE SEC CAREFULLY AND IN THEIR ENTIRETY WHEN THEY BECOME AVAILABLE BECAUSE THEY WILL CONTAIN IMPORTANT INFORMATION ABOUT AVROBIO, THE PROPOSED MERGER AND RELATED MATTERS. Investors and security holders may obtain free copies of the Form S-4, the proxy Statement/prospectus and other documents filed by AVROBIO with the SEC through the website maintained by the SEC at http://www.sec.gov. Copies of the documents filed by AVROBIO with the SEC are also available free of charge on AVROBIO's website at www.avrobio.com.

**No Offer or Solicitation**

This communication does not constitute an offer to sell or the solicitation of an offer to buy any securities nor a solicitation of any vote or approval with respect to the proposed transaction or otherwise. No offering of securities shall be made except by means of a prospectus meeting the requirements of Section 10 of the U S. Securities Act of 1933, as amended, and otherwise in accordance with applicable law.

# Transforming the Discovery of Novel GPCR-Targeted Therapies

April 2024

TECTONIC Therapeutic

# Merger of Tectonic Therapeutic and AVROBIO

**OVERVIEW**

- Tectonic Therapeutic, a privately-held biotechnology company focused on discovering and developing GPCR-targeted therapies, intends to merge with AVROBIO, Inc. (Nasdaq: AVRO)
- Supported by the Board of Directors of both companies and subject to stockholder approval and other customary closing conditions

**TRANSACTION SUMMARY**

- Planned $130.7 million private financing from new and existing leading life sciences investors, together with existing cash from both companies at closing, expected to be approximately $165 million and provide cash runway into mid-2027
- Expected pro forma ownership is approximately 40% pre-merger Tectonic shareholders, 22% pre-merger AVROBIO shareholders, and 38% purchasers in the private financing
- Merger and financing expected to close in Q2 2024

**MANAGEMENT**

- Existing Tectonic management to lead the combined company
- Board of Directors of combined company will include one director from the AVROBIO BOD

TECTONIC Therapeutic

# Tectonic Therapeutic – Transforming the Discovery of Novel GPCR-Targeted Therapies, Innovating in Their Development

- Validated platform to discover and optimize biologics that target GPCRs
- Prioritizing high value GPCR targets, where small molecules are not the right modality
- First two assets address indications with no approved therapy
  1. RXFP1 agonist - potential therapy for Group 2 PH[1] in HFpEF[2]
     - >600,000 Patients in US alone (>20 times PAH)
     - Initial Phase 1A PK/PD data demonstrated activity and favorable PK with potential for monthly dosing; full data set from this study expected by mid 2024
     - Phase 1B hemodynamic proof of concept expected in 2025, randomized Phase 2 data expected in 2026
  2. GPCR antagonist antibody addressing hereditary hemorrhagic telangiectasia (HHT)
- Team with extensive track record of drug discovery and development success, resulting in 20 first approvals across multiple therapeutic areas
- Well capitalized by a syndicate of leading institutional funds
- **Transaction expected to provide runway into mid-2027**

1. Pulmonary Hypertension
2. Heart Failure with Preserved Ejection Fraction

TECTONIC Therapeutic

# This Team Has Delivered for Patients and Investors

**Alise Reicin, M.D.**
CEO, Director

Celgene · MERCK · Columbia University · KEYTRUDA (pembrolizumab)

**Christian Cortis, Ph.D.**
COO, CFO

agenus · SYNTA · GEMINX · ATV · Booz | Allen | Hamilton · Columbia University

**Peter McNamara, Ph.D.**
CSO

NOVARTIS · GNF · Penn · BRAFTOVI (encorafenib)

**Anthony Muslin, M.D.**
CDO

NOVARTIS · SANOFI · Washington University in St. Louis School of Medicine · Entresto (sacubitril/valsartan) tablets

**Marcella Ruddy, M.D.**
CMO

REGENERON · MERCK · Alnylam · MGH 1811 · DUPIXENT (dupilumab) injection

**Marc Schwabish, Ph.D.**
CBO

Fusion · BAYER · Eisai · LEERINK SWANN · RBS

**Timothy Springer, Ph.D.**
Co-Founder

**FOUNDED MULTIPLE SUCCESSFUL COMPANIES**

LeukoSite · moderna · MORPHIC · SEISMIC · Scholar Rock

**2022 Lasker Award**

**Andrew Kruse, Ph.D.**
Co-Founder

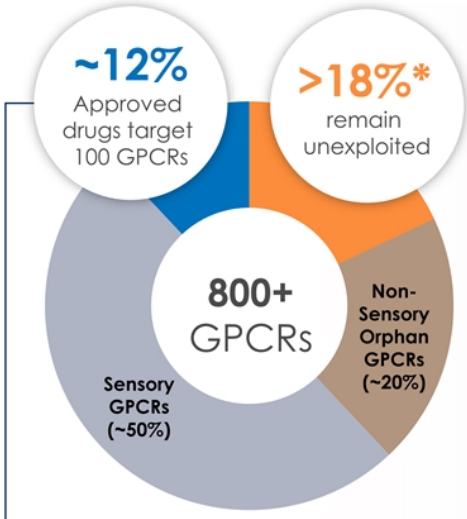
**GPCR EXPERT, FORBES "30 under 30"**

HARVARD MEDICAL SCHOOL · SEISMIC

**Multiple Awards and Fellowships**
(Biomedical Research, NIH, Amgen, Sloan Research)

TECTONIC Therapeutic

# Biologics Offer Advantages Over Small Molecules in Targeting GPCRs in Multiple Settings




- >470 Approved drugs (~33% of all)
- >$180B in annual sales
- Predominantly small molecules
- Address broad range of therapeutic areas
- Only 3 are antibodies

→ **When difficult to drug with small molecules**
Biologic captures complexity of ligand / receptor engagement

→ **If target site similar to domains of different proteins**
Biologic minimizes off target binding to improve safety / tolerability

→ **If use case requires tissue /compartment targeting**
Engineer biologic to target or exclude compartment as needed

→ **When multi-modal action needed**
Bispecific approach enables dual target engagement

(*) Hauser, A.S. et al., Cell. 2018 Jan 11; 172(1-2): 41–54.e19.

* 18% = 100% - 12% (approved drug targets) – 50% (sensory) – 20% (non-sensory, orphan)

TECTONiC Therapeutic

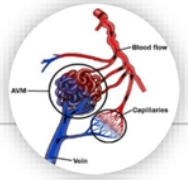
# Our Unique Pipeline Opportunities are Enabled by Biologic Targeting of GPCRs

**GROUP 2 PULMONARY HYPERTENSION (Group 2 PH)**

**Potential Best-in-Class**

**RXFP1 Agonist[1]**

Supporting clinical data

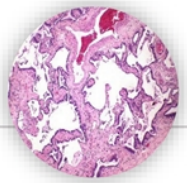



**HEREDITARY HEMORRHAGIC TELANGIECTASIA (HHT)**

**First in Class & Indication**

**GPCR Antagonist[2] (anti-angiogenic)**

Target pathway linked to disease genetics



**FIBROSIS**

**Bi-specific Approach**

**GPCR Antagonist[2] (anti-fibrotic)**

Supporting clinical data for one component of bispecific

**Scale of POC studies: ~50-200 patients per indication**
**3-6 months treatment**

1. Fusion protein – lead molecule in-licensed from Harvard U., optimized using GEODe platform
2. GPCR targeted mAbs discovered internally using GEODe platform

TECTONIC Therapeutic

# Post Close Cash to Support Pipeline Progression Into Mid-2027 and Several Key Inflection Points

## Tectonic Pipeline and Expected Readouts

| | | |
|---|---|---|
| **RXFP1 Agonist** (TX45 – Fc-relaxin) | Phase 1a | • Complete PK/PD Data: mid 2024<br>• Ph 1b hemodynamic proof of concept data: 2025<br>• Randomized Ph 2 data: 2026 |
| **GPCR Antagonist** (HHT Program) | Development Candidate Selection | • Start of Ph 1: Q4 2025 / Q1 2026<br>• Start of randomized studies: late 2026/early 2027 |
| **GPCR Antagonist** (Fibrosis Program) | Discovery | • Develop internally or partner |
| **GPCR Modulators** (Undisclosed) | Discovery | • Develop internally or partner |

[1]Includes in vivo HHT validation

# GEODe Designed to Solve Key Challenges in GPCR Targeted Biologics Discovery

## Challenges

**RETAIN**
endogenous GPCR structure to enable screening against relevant form of receptor

**PURIFY**
target in sufficient quantities to power screening campaign

**INDUCE**
immune response to human GPCR in animals if immunization strategy is pursued

**STABILIZE**
receptor in active conformation to enable agonist discovery

## GEODe™ Platform Features Designed for Success

**1.**
**Receptor Engineering, and Purification Technology**
*delivers abundant receptor reagent in native conformation*

**2.**
**In-vitro Yeast Display Libraries**
*provide high-diversity, without immune editing*

**3.**
**Protein Engineering**
*Optimize protein pharmacology*
*Engineer antigen formats to enable screening for agonists or antagonists as needed*


# TX45: Fc-RELAXIN FUSION PROTEIN

RXFP1 agonist with differentiated profile

# Hemodynamic and Anti-fibrotic Properties of Relaxin Demonstrated by its Role in Pregnancy

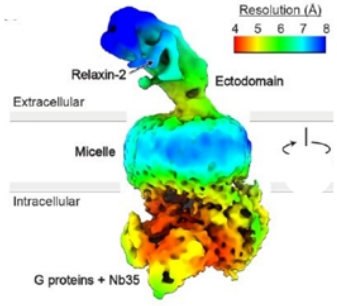
## Pharmacology

### AGONIST

Natural Ligand of RXPF1 Receptor

No RXFP1 internalization from relaxin agonism → no desensitization with chronic therapy

Relaxin upregulated in pregnancy




Local resolution cryo-EM map of full-length RXFP1–Gs complex
BioRxiv: https://doi.org/10.1101/2022.01.22.477343

## Facilitates Gestation

### PULMONARY AND SYSTEMIC VASODILATOR

Increases cardiac output to accommodate the increased demand from developing fetus

### ANTIFIBROTIC

Prepares musculoskeletal tissues for pregnancy and childbirth

**Pharmacologic properties of relaxin hold promise as a potential treatment for cardio-pulmonary and renal disease, but its short half-life has impeded its development**

# Evidence of Serelaxin's Safety and Benefit in Acute Heart Failure (AHF)

- A meta-analysis of 6 studies and >11,000 patients demonstrated that **a 2-day infusion of serelaxin was safe and resulted in a 23% decrease in 5-day worsening heart failure**
- One of two pivotal studies include in meta-analysis, RELAX-AHF-2, failed to achieve the co-primary endpoints, and we believe that two factors contributed to this outcome
  - It was ambitious to expect that a two-day infusion of serelaxin, with its short half-life and mechanism of action, would demonstrate clinical benefit at day 5 and, more puzzlingly at 6 months
  - Operational challenges with patient enrollment may also have had an impact
- Limitations of serelaxin's PK inhibited further development, but **its clinical performance supports advancement of TX45 whose PK profile permits chronic dosing for chronic diseases** such as pulmonary hypertension and heart failure

*Teerlink J.R. et al. Eur. J. Heart Fail. 2019; 22: 315-329; patients from RELAX-AHF-JP (N=30 total) not listed in table

# TX45 is Engineered to Solve a Critical PK Problem Observed with Other Relaxin Molecules

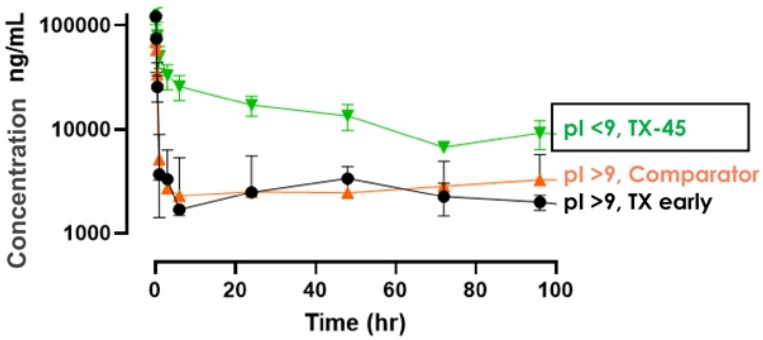
Relaxin has **very short *in vivo* half-life** Fc-fusion needed to improve PK

Relaxin Fc-fusions **have steep decline in exposure after dosing** (>90%) because of glycocalyx binding due to high pI[1]

Engineering TX45 to **reduce net positive charge (and lower pI) prevents rapid clearance**

## TX45 EXHIBITS SUPERIOR PROFILE vs. PARENT COMPOUND AND COMPARATOR[2] MOLECULE[3]

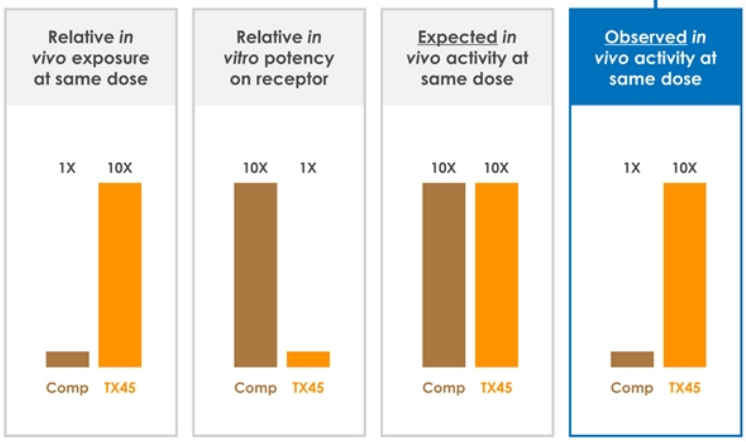
Preclinical Rat Pharmacokinetic Data

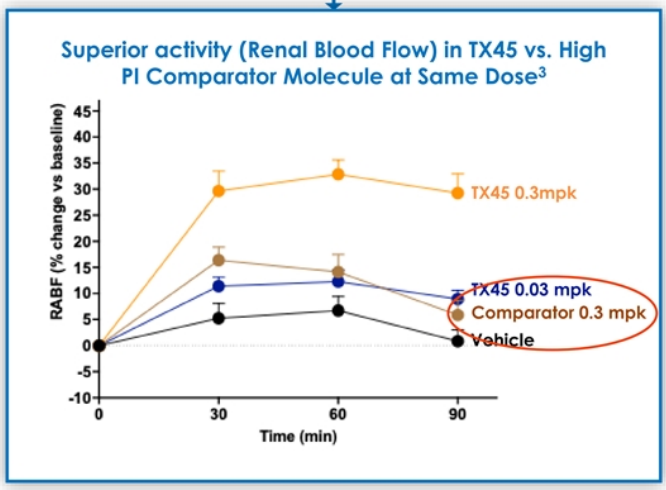



1. Isoelectric Point
2. High pI Fc-relaxin fusion protein described in literature
3. Source: Tectonic internal data

# TX45 Reflects Significant Protein Engineering to Optimize Its Pharmacology

**TX45 results in ~10x greater *in vivo* potency by dose over comparator[1] molecule than predicted based on PK and *in vitro* activity[2] – potentially from reduced trapping of drug in glycocalyx, resulting in increased free drug available to activate RXFP1 in tissues**




1. High pI Fc-relaxin fusion protein described in literature

2. ~0.03 mpk of TX45 has similar activity as 0.3 mpk of Comparator

3. Source: Tectonic internal data

TECTONIC Therapeutic

# TX45 – Optimized RXFP1Agonist for Group 2 PH in HFpEF

| | |
|---|---|
| ✓ **Potential Best-in-Class Relaxin Agonist with Optimized PK** | • Protein engineering has extended pharmacologic half-life to support monthly dosing |
| ✓ **High Unmet Need in Group 2 PH with HFpEF[1]** | • No approved therapy<br>• >600,000 patients in US<br>• High 5-year high mortality |
| ✓ **Mechanism may be Ideal to Address Group 2 PH** | • Pulmonary + systemic vasodilation, cardiac relaxation<br>• Reversal of fibrosis in pulmonary vasculature and heart<br>• Anti-inflammatory |
| ✓ **Supporting Clinical and Pre-clinical Data** | • Hemodynamic benefit in studies of serelaxin in AHF<br>• Clear benefit observed with TX45 in rodent PH and CHF models |
| ✓ **Streamlined Development Strategy** | • No outcome study needed<br>• Enrichment strategy for CpcPH where there is greatest unmet need<br>• Enables potential early launch relative to congestive heart failure |
| ✓ **Potential to Expand Indications** | • Other PH Groups, Heart failure, renal disease |

1. Heart Failure with preserved Ejection Fraction

# Pulmonary Hypertension Consists of 5 Distinct Diseases

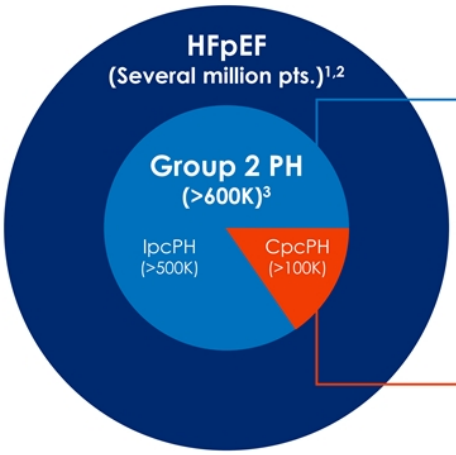
## Group 2 PH is of Greatest Interest for TX45's Initial Indication

| Group 1 ("PAH") (~25,000[1]) | Group 2 (>600,000[1]) | Group 3 | Group 4 ("CTEPH") | Group 5 (Misc.) |
|---|---|---|---|---|
| • Idiopathic<br>• Hereditary<br>• Connective tissue disease-associated<br>• Congenital heart disease-associated<br>• Drug-induced | • **Due to left heart disease (HFpEF, HFrEF) or valvular heart disease**<br>• **CAD, HTN, T2DM[2], high cholesterol are risk factors**<br>• **Two Subtypes: CpcPH / IpcPH** | • Due to lung disease or hypoxia<br>• May be due to COPD, interstitial lung disease (i.e., IPF) or obstructive sleep apnea | • Chronic thrombo-embolic pulmonary hypertension –i.e., as a consequence of blood clots | • Miscellaneous group with causes unclear or multiple underlying factors |

1. US Prevalence
2. CAD: Coronary Artery Disease, HTN: Hypertension, T2DM: Type 2 Diabetes Mellitus
Nat. Pul. Hypertension Unit, Ireland

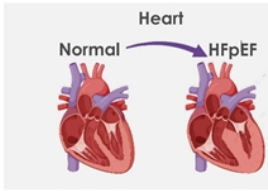
# Our Focus is on the Group 2 PH Subset of Heart Failure with Preserved EF (HFpEF)

## Clinical Program Designed to Enable Evaluation of Efficacy in Each Subgroup



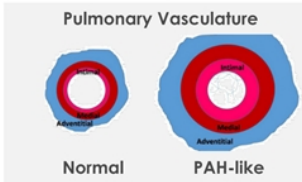

**IpcPH** (**I**solated, **p**ost **c**apillary **PH**)

Increased Left Ventricle Filling Pressures
↓
Increased Pulmonary Venous Pressures
↓
Passive Pressure Backflow
↓
Pulmonary Hypertension




**CpcPH** (**C**ombined, **p**re- and post **c**apillary **PH**)

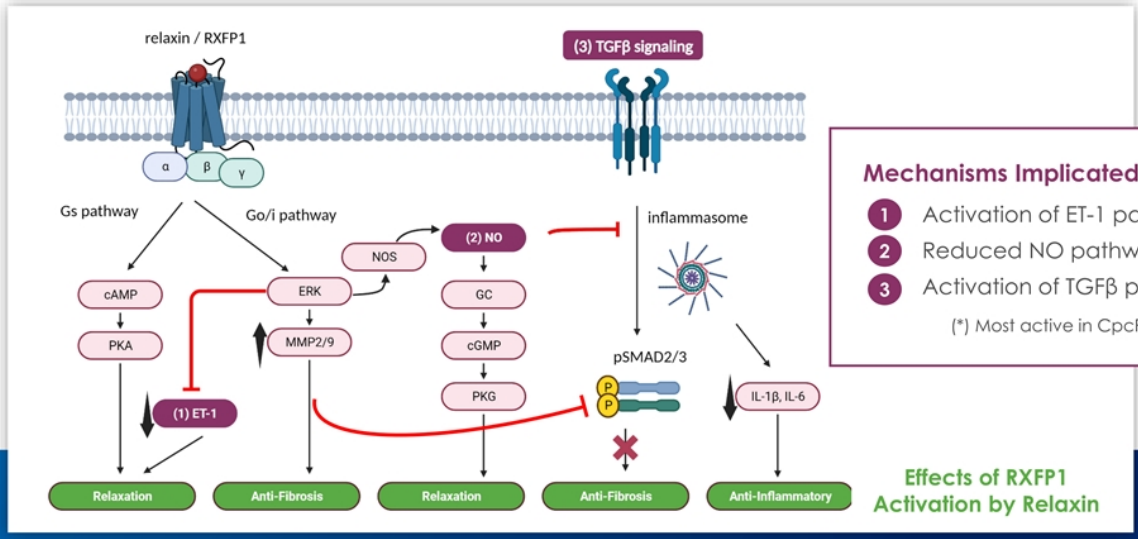
Chronic PH and/or Other Drivers
↓
Permanent Vascular Changes, e.g. Pulmonary Artery Remodeling
↓
Increased Vascular Resistance
↓
Right Heart Failure




1. US prevalence numbers. Estimates based on data from
2. Kapelios, C. et al., Cardiac Failure Review 2023;9:e14
3. Sera F. et al. Heart 2023;109:626–633

TECTONIC Therapeutic

# Relaxin Multimodal MOA Addresses Pathways Implicated in Group 2 PH Pathophysiology




**Mechanisms Implicated in Group 2 PH**

1. Activation of ET-1 pathway(*)
2. Reduced NO pathway activity(*)
3. Activation of TGFβ pathway

(*) Most active in CpcPH subset

**Effects of RXFP1 Activation by Relaxin**

- ✓ Pulmonary and systemic arterial vasodilation
- ✓ Favorable remodeling: anti-fibrotic effect in heart and pulmonary vasculature
- ✓ Anti-inflammatory

TECTONIC Therapeutic

# Relaxation and Anti-Fibrotic Effects of Relaxin Have Potential for Disease Modification in Group 2 PH

- Heart, and vascular dysfunction contribute to disease pathology
- Renal dysfunction also present in many of these patients

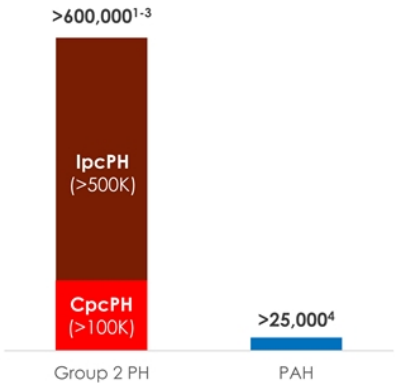
| CHARACTERISTICS OF GROUP 2 PH | IpcPH | CpcPH | ANTICIPATED RELAXIN EFFECTS |
|---|---|---|---|
| Pulmonary artery narrowing, thickening, stiffening, fibrotic remodeling | | ✓ | Pulmonary Vasodilation<br>Anti-inflammatory, anti-fibrotic |
| Right Ventricular Dysfunction | ✓ | ✓ | Right ventricular remodeling |
| Thickening and stiffening of Left Ventricle | ✓ | ✓ | Peripheral vasodilation, cardiac relaxation, left ventricular remodeling |
| Compromised kidney function | ✓ | ✓ | Improvement in kidney function |

**Balanced vasodilation in pulmonary and peripheral vasculature needed for safety and efficacy**

# Group 2 PH vs. PAH

- Significant opportunity for a first-in-indication therapy
- Highly motivated physicians and patients

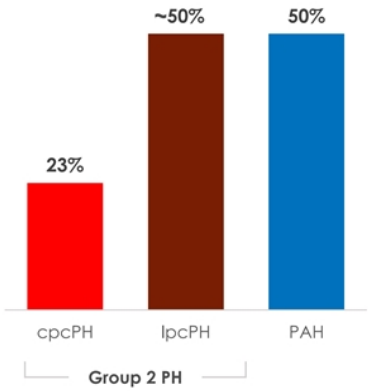
## US PREVALENCE >> PAH




**Multi-$ Billion Market Opportunity**

**>$4 Billion Market in US Today[5]**

## 5 YEAR SURVIVAL ≤ PAH[6]




## NO THERAPEUTIC OPTIONS

| Group 2 PH | PAH |
|---|---|
| **No approved therapies** … Limited pipeline *PAH Drugs have not demonstrated convincing benefits in Group 2 PH with the exception of PDE5i in CpcPH* | **Multiple drugs/ mechanisms approved** ET1R antagonists PDE5 inhibitors GC stimulators ACTRII-Trap |

1. US prevalence numbers. Estimates based on data from
2. Kapelios, C. et al., Cardiac Failure Review 2023;9:e14
3. Sera F. et al. Heart 2023;109:626–633
4. www.pahinitiative.com
5. GlobalData
6. Caravita S. et al. https://doi.org/10.1371/journal.pone.0199164; Gall H. et al The Journal of Heart and Lung Transplantation, Vol 36, No 9, September 2017; estimates from synthesis of different studies

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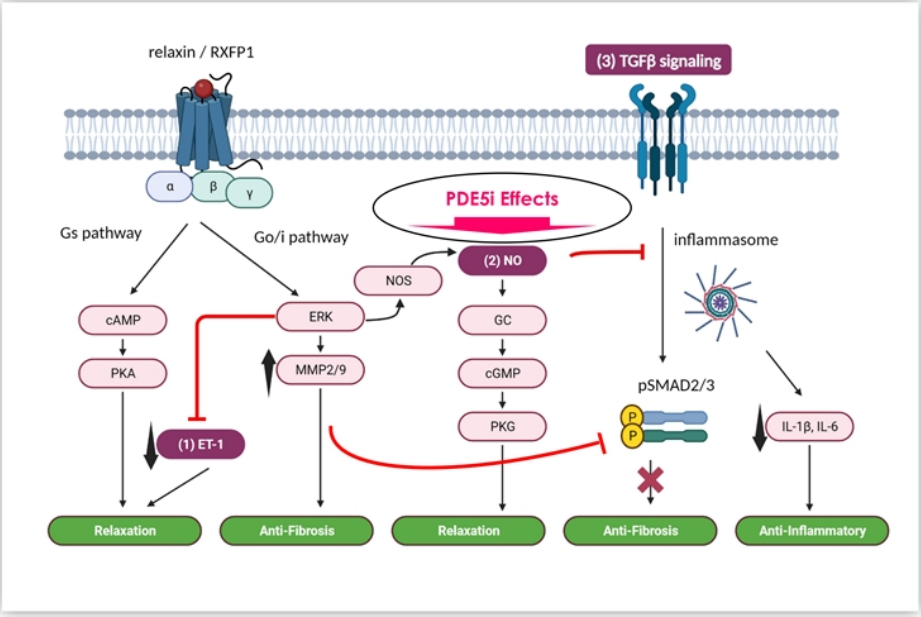
# PDE5 Inhibitors Affect Only One of Several Pathways Addressed by Relaxin




PDE5 inhibitors demonstrated benefits across 3 studies [1-3] including:

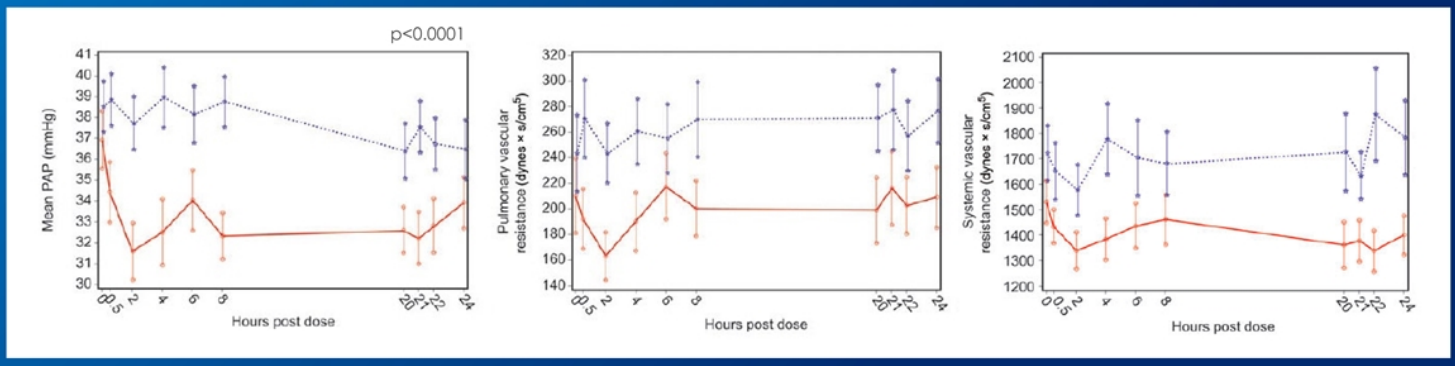
- ✓Reduction in PVR
- ✓Improvement in exercise capacity
- ✓Decrease in heart failure hospitalizations

TX45 anticipated to be beneficial in both Cpc-PH and Ipc-PH because it targets additional anti-fibrotic and anti-inflammatory mechanisms on top of activation of the NO pathway

1. Guazzi et al. 2011
2. Belyavskiy et al. 2020
3. Kramer et al. 2019

# Relaxin Improves Hemodynamics in Heart Failure

## Balanced pulmonary and peripheral vasodilation, and increased cardiac output relevant to Group 2 PH




- Above: serelaxin infusion for 20hrs in Acute Heart Failure patients with elevated pulmonary artery pressure (PAP) **rapidly lowered mPAP, pulmonary vascular resistance (PVR), systemic vascular resistance (SVR) and improved renal function***
- Not shown: serelaxin also improved additional hemodynamic parameters including **pulmonary capillary wedge pressure (PCWP), right atrial pressures (RAP)**
- In a similar study in patients with chronic CHF, **a reduction in PCWP and an increase in cardiac output** was demonstrated**

*Ponikowski P. et al. Eur. Heart J. 2014, **Dschietzig T. et al. Ann NY Acad Sci 2009

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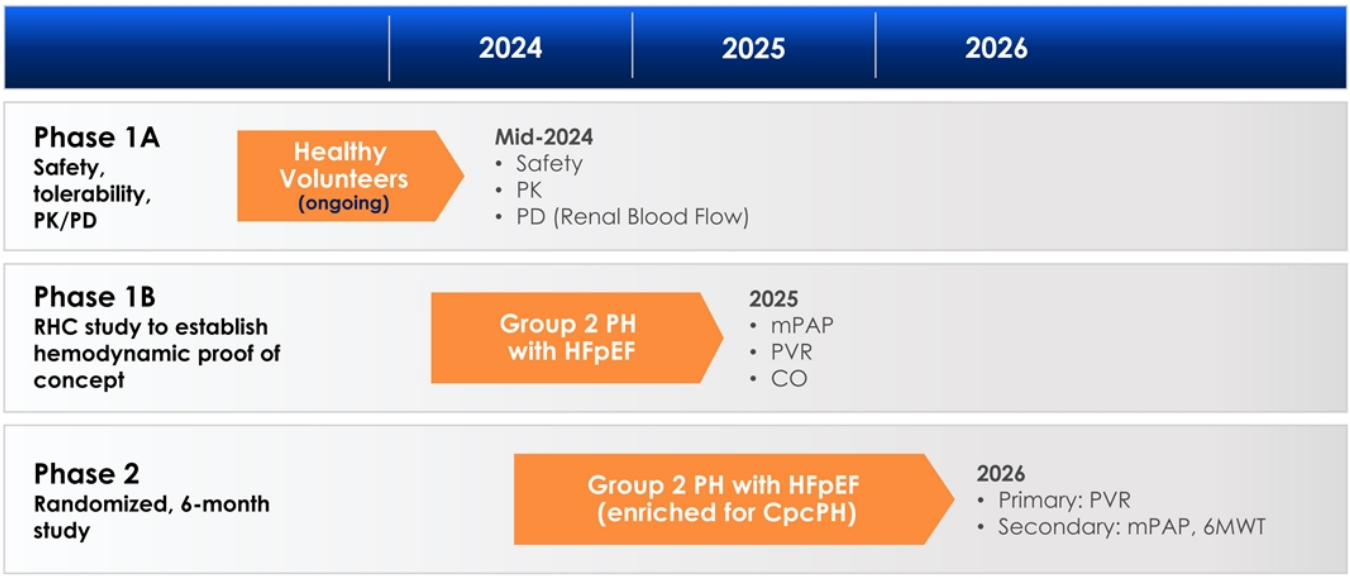
# TX45 Development Program Overview

## Planned readouts in mid-2024, 2H 2025, 2026




**RHC:** Right Heart Catheter
**mPAP:** Mean Pulmonary Arterial Pressure
**PVR:** Pulmonary Vascular Resistance
**CO:** Cardiac Output
**6MTW:** 6-Minute Walk Test

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# Preliminary PK/PD Analysis After TX45 Administration in Healthy Volunteers

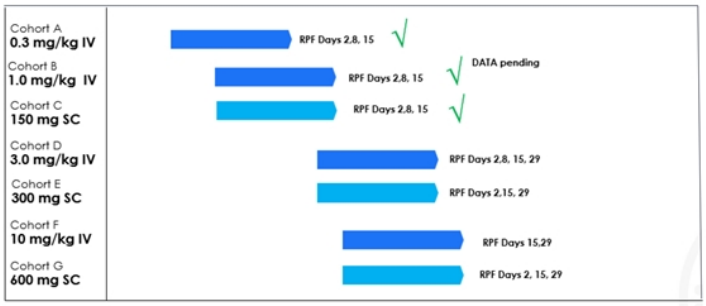
April 2024

# Summary of preliminary data from TX45 SAD study[1]

## Cohort A (0.3 mg/kg IV) and Cohort C (150 mg SC)

- **Well tolerated with minimal adverse events, no drug-related SAEs**
- **Pharmacokinetics**
  - Low intersubject variability in serum concentrations (≤ 20%)
  - No evidence of immune mediated clearance
- **Pharmacodynamics from 0.3 mg/kg cohort (lowest dose)**
  - ~30% increase in renal plasma flow on Day 2 post dose persisting at least until Day 8 post dose
  - Consistent with serelaxin's effect
  - **Meets "go criteria"**

### TX45 SAD Dose Escalation Plan



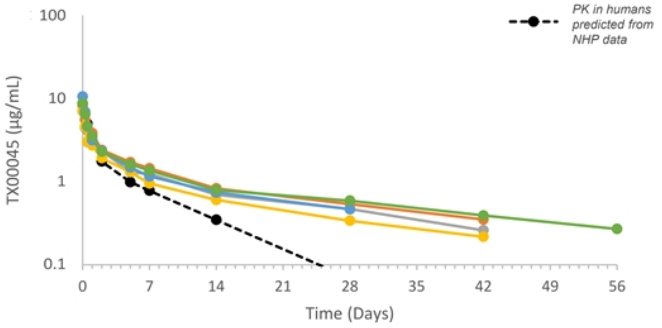

RPF= Renal Plasma Flow
*Cohorts F and G are optional

**Based on preliminary data, we anticipate Q4W dosing at optimal SC dose**

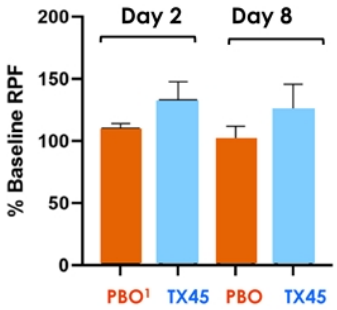
1. As of Jan 18, 2024

# Phase 1A Study
# Preliminary Single Dose TX45 PK/PD Data (0.3 mg/kg)

### TX45 Serum Concentrations from Phase 1A Subjects
Cohort A 0.3 mg/kg IV

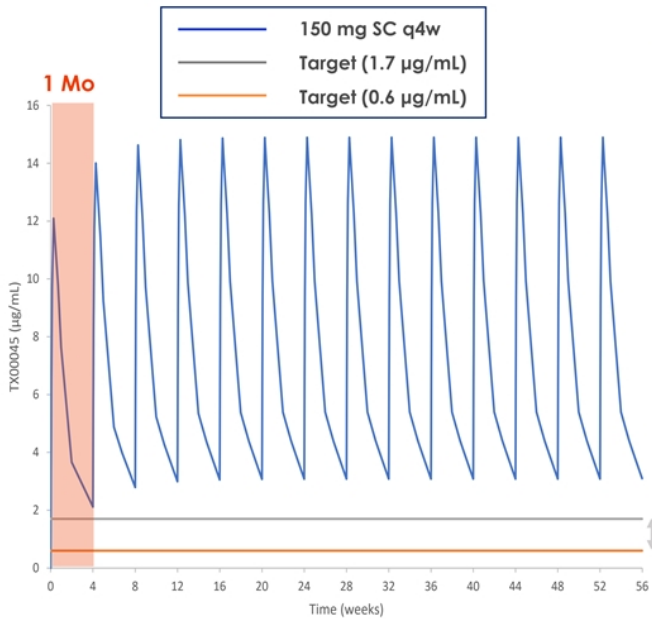



### Renal Plasma Flow in Phase 1A Subjects
**TX45 Dosed on Day 1** - Cohort A 0.3 mg/kg IV




1. Placebo

# PK Modeling based on Preliminary Data Suggests TX45 Can be Given Monthly




- A model was constructed using observed data from both 0.3 mg/kg IV and 150 mg SC cohorts to predict trough concentrations of 150 mg SC Q4W
- Terminal $t_{1/2}$ is based on 0.3 mg/kg IV cohort as data beyond 14 days from 150 mg SC cohort was not available for accurate half life determination

Model assumptions

- Steady state terminal $t_{1/2}$ similar for IV and SC
- **Terminal $t_{1/2}$ of 16.7 days**, observed in 0.3mg/kg IV cohort is maintained in additional cohorts

Target Exposure Range Predicted to Provide Maximal Efficacy based on Preclinical Models

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# Significant Pharma Interest in Relaxin
# Tectonic has Potential Best-in-Class Molecule

| Company | Format | Formulation | Expected Dosing Frequency |
|---|---|---|---|
| TECTONIC Therapeutic | Fc-Fusion<br>*Engineered for optimal PK, biodistribution, high [C] formulation* | SubQ<br>*High [C] achievable* | Q4 Weeks |
| AstraZeneca | Fc-Fusion | SubQ | Q2 Weeks |
| Lilly | h-Albumin-mAb-Fusion | SubQ<br>*Injection site reactions* | Q Weekly |


# Summary

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# Uniquely Positioned to Deliver on Value Creating Milestones

| Pipeline of Uniquely Differentiated Assets | Accomplished Team World-leader Founders | Strong Balance Sheet Anticipated Post Transaction |
|---|---|---|
| **Multiple Inflection Points 2024, 2025, 2026** | **20 1st Approvals**<br>**>$50 Billion in Annual Sales** | **~$165 Million**<br>**>3 Year Runway** |
| Address important clinical problems, underserved patient populations | Leadership with Proven Track Record | Well positioned to execute |

# Transforming the Discovery of Novel GPCR-Targeted Therapies

April 2024

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