

**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION**  
Washington, D.C. 20549

**FORM 8-K**

**CURRENT REPORT**  
Pursuant to Section 13 OR 15(d)  
of The Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): July 30, 2024

**TECTONIC THERAPEUTIC, INC.**  
(Exact name of registrant as specified in its charter)

**Delaware**  
(State or other jurisdiction  
of incorporation)  
  
**490 Arsenal Way, Suite 210**  
**Watertown, MA**  
(Address of principal executive offices)

**001-38537**  
(Commission  
File Number)

**81-0710585**  
(IRS Employer  
Identification No.)

**02472**  
(Zip Code)

**(339) 666-3320**  
(Registrant's telephone number, including area code)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2.):

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol	Name of each exchange on which registered
Common Stock, par value \$0.0001 per share	TECX	Nasdaq Global Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

**Item 7.01. Regulation FD Disclosure.**

On July 30, 2024, Tectonic Therapeutic, Inc. (the “Company”) issued a press release titled “Tectonic Therapeutic Announces U.S. FDA Clearance of IND Application of TX45 for Subjects with Group 2 PH Due to Heart Failure with Preserved Ejection Fraction.” A copy of the press release is furnished as Exhibit 99.1 to this Current Report on Form 8-K.

The Company has updated its corporate presentation for use in meetings with investors, analysts and others. A copy of the updated corporate presentation is furnished as Exhibit 99.2 to this Current Report on Form 8-K. Investors may access the presentation by visiting the “Events & Presentations” section of the Company’s investor website at <https://investors.tectonictx.com>.

The information furnished under this Item 7.01, including Exhibits 99.1 and 99.2, shall not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934 (the “Exchange Act”) or subject to the liabilities of that section, nor shall it be deemed to be incorporated by reference into any of the Company’s filings with the Securities and Exchange Commission, regardless of any general incorporation language in such a filing.

**Item 8.01. Other Events.**

The Company announced today that the U.S. Food and Drug Administration (the “FDA”) has cleared its Investigational New Drug (“IND”) application for TX45, an Fc-relaxin fusion protein being evaluated for the treatment of patients with Group 2 Pulmonary Hypertension (“PH”) due to Heart Failure with Preserved Ejection Fraction (“HFpEF”).

The Company is also updating its guidance in regard to the TX45 program as follows:

- Topline trial results of the Phase 1a clinical trial of TX45 in healthy volunteers is expected to be released in September 2024.
- Phase 1b hemodynamic trial evaluating single doses of TX45 in subjects with Group 2 PH due to HFpEF continues to enroll as planned, with topline trial results expected in mid-2025.
- The Company expects to initiate a global, 24-week Phase 2 clinical trial to evaluate TX45 administered subcutaneously in subjects with Group 2 PH due to HFpEF in the third quarter of 2024.

**Forward-Looking Statements**

Statements contained in this Current Report on Form 8-K regarding matters that are not historical facts are “forward looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995. The Company may, in some cases, use terms such as “aims”, “anticipates”, “believes”, “could”, “estimates”, “expects”, “forecasts”, “goal”, “intends”, “may”, “plans”, “possible”, “potential”, “seeks”, “will” and variations of these words or similar expressions that are intended to identify forward-looking statements, although not all forward-looking statements contain these words. Forward-looking statements include, but are not limited to, statements regarding: the design, objectives, initiation, timing, progress and results of current and future clinical trials of the Company’s product candidate, TX45, including the ongoing Phase 1a and Phase 1b clinical trials of TX45 and initiation of the Phase 2 clinical trial of TX45. These forward-looking statements are based on the Company’s expectations and assumptions as of the date of this filing. Each of these forward-looking statements involves risks and uncertainties that could cause the Company’s clinical development programs, future results or performance to differ materially from those expressed or implied by the forward-looking statements. Many factors may cause differences between current expectations and actual results, including: the potential that success in preclinical testing and earlier clinical trials does not ensure that later clinical trials will generate the same results or otherwise provide adequate data to demonstrate the efficacy and safety of a product candidate; the impacts of macroeconomic conditions, including the conflict in Ukraine and the conflict between Israel and Hamas, heightened inflation and uncertain credit and financial markets, on the Company’s business, clinical trials and financial position; unexpected safety or efficacy data observed during preclinical studies or clinical trials; clinical trial site activation or enrollment rates that are lower than expected; the Company’s ability to realize the benefits of its collaborations and license agreements; changes in expected or existing competition; changes in the regulatory environment; the uncertainties and timing of the regulatory approval process; and unexpected litigation or other disputes. Other factors that may cause the Company’s actual results to differ from those expressed or implied in the forward-looking statements are identified in the section titled “Risk Factors” in the final prospectus on Form 424(b)(3) filed by AVROBIO with the Securities and Exchange Commission on May 3, 2024, and in other filings that the Company makes and will make with the Securities and Exchange Commission in the future. The Company expressly disclaims any obligation to update any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise, except as otherwise required by law.

**Item 9.01. Financial Statements and Exhibits.**

(d) Exhibits

Exhibit No.	Description
99.1	<a href="#">Press release dated July 30, 2024.</a>
99.2	<a href="#">Corporate Presentation dated July 2024.</a>
104	Cover Page Interactive Data File (formatted as Inline XBRL).

**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

**TECTONIC THERAPEUTIC, INC.**

Date: July 30, 2024

By: /s/ Daniel Lochner

\_\_\_\_\_  
Daniel Lochner  
Chief Financial Officer

**Tectonic Therapeutic Announces US IND Clearance for Lead Program, TX45**

- *TX45 is an Fc-relaxin fusion protein being evaluated in patients with Group 2 Pulmonary Hypertension (PH) due to Heart Failure with Preserved Ejection Fraction (HFpEF), a serious condition estimated to affect over 600,000 people in the U.S. alone, currently with no approved therapies*
- *Planned initiation of global, 24-week Phase 2 clinical trial to evaluate TX45 administered subcutaneously in subjects with Group 2 PH due to HFpEF (PH-HFpEF) in the third quarter of 2024, with topline trial results expected in 2026*
- *Phase 1a topline trial results of TX45 in healthy volunteers are expected to be released this September, with detailed data to be subsequently presented at a scientific meeting*
- *Phase 1b hemodynamic trial evaluating single doses of TX45 in subjects with Group 2 PH-HFpEF continues to enroll as planned, with topline study results expected in mid-2025*

**WATERTOWN, MA (GLOBENEWSWIRE)** – July 30, 2024 – Tectonic Therapeutic, Inc. (NASDAQ: TECX) (Tectonic), a clinical stage biotechnology company focused on the discovery and development of therapeutic proteins and antibodies that modulate the activity of G-protein coupled receptors (GPCRs), today announced that the U.S. Food and Drug Administration (FDA) has cleared its Investigational New Drug (IND) application for TX45, an Fc-relaxin fusion protein being evaluated for the treatment of patients with Group 2 PH-HFpEF. TX45 aims to address the physiological abnormalities of PH-HFpEF through its effects on both pulmonary and systemic vasodilation, cardiac diastolic dysfunction and potential remodeling in both the pulmonary vessels and cardiac muscle, which could translate into a clinically meaningful improvement in exercise capacity in these patients.

“We believe our novel Fc-relaxin fusion protein has been engineered to optimize the pharmacology of TX45,” commented Alise Reicin, M.D., President and CEO of Tectonic. “The safety, pharmacokinetic and pharmacodynamic data we have received to date supports the initiation of our Phase 2 clinical trial in our target patient population. We expect to report topline results from our Phase 1a single dose healthy volunteer trial this September and topline results from our Phase 1b single dose patient trial in mid-2025. We remain enthusiastic about the potential of TX45 to address the unmet needs of patients living with PH-HFpEF for whom there is no approved therapy.”

Tectonic expects to initiate the global Phase 2 clinical trial of TX45 in PH-HFpEF in the third quarter of 2024, with topline results anticipated in 2026. The trial is designed to evaluate efficacy in the broad PH-HFpEF population and enrich for the subset of Group 2 PH patients with a more severe form of disease known as combined post and precapillary pulmonary hypertension (CpcPH) defined by baseline pulmonary vascular resistance (PVR) of greater than 3 Wood units. The trial plans to enroll up to 180 subjects who will be randomized to one of two dose regimens of TX45 or placebo. TX45 will be administered by subcutaneous (SC) injection for 24-weeks followed by an 8-week follow-up period. The primary and secondary endpoints of the trial include change from baseline in PVR as well as other relevant hemodynamic changes. It will also explore TX45’s effect on change in six-minute walk distance.

#### **About TX45, a long-acting Fc-relaxin fusion protein**

Tectonic's lead program, TX000045 (TX45), is an Fc-relaxin fusion protein with optimized pharmacokinetics and biophysical properties that activates the RXFP1 receptor, the GPCR target of the hormone relaxin. Relaxin is an endogenous protein, expressed at low levels in both men and women. In normal human physiology, relaxin is upregulated during pregnancy where it exerts vasodilative effects, reduces systemic and pulmonary vascular resistance and increases cardiac output to accommodate the increased demand for oxygen and nutrients from the developing fetus. Relaxin also exerts anti-fibrotic effects on pelvic ligaments to facilitate delivery of the baby.

TX45's pharmacological profile, with an extended half-life compared with native relaxin, is a direct result of applying Tectonic's protein engineering capabilities. It has the potential to address patients with Group 2 PH-HFpEF as the initial disease setting. Treatment with TX45 could potentially improve hemodynamics through effects on pulmonary and systemic vasodilation, cardiac diastolic dysfunction and potential remodeling in both the pulmonary vessels and the heart, which could translate into a clinically meaningful improvement in exercise capacity in these patients.

The Phase 1a clinical trial of TX45 in healthy volunteers was designed as a single ascending dose trial evaluating the safety, tolerability, pharmacokinetics and pharmacodynamics (including renal blood flow) of TX45 administered intravenously (IV) (four doses ranging from 0.3 mg/kg to 10 mg/kg) and SC (three doses, 150 mg, 300 mg and 600 mg). Topline results are expected to be reported from this trial this September, followed by more detailed data at a later scientific meeting.

The Phase 1b clinical trial of TX45 in patients with Group 2 PH-HFpEF is a single dose, open-label trial to evaluate safety, tolerability and acute hemodynamic effects of IV administration of TX45, with study results expected in mid-2025. The trial will evaluate the change from baseline in PVR as determined by right heart catheterization, as well as improvement in mean pulmonary artery pressure (mPAP), pulmonary capillary wedge pressure (PCWP), cardiac output, and systemic vascular resistance (SVR).

#### **About Group 2 Pulmonary Hypertension in HFpEF**

The World Health Organization has defined 5 groups of PH. Tectonic is focused on the Group 2 subtype, a condition that develops as a consequence of left-sided heart disease, specifically pulmonary hypertension secondary to left heart failure with preserved ejection fraction (PH-HFpEF). There are an estimated 6 million patients with heart failure in the United States, with HFpEF representing up to ~50% of heart failure cases. Tectonic estimates the combined Group 2 PH population with HFpEF at over 600,000.

In patients with PH-HFpEF, chronic heart failure leads to increased blood pressure in the pulmonary arteries, exerting severe strain on the right side of the heart, which adapts poorly to the increased pressure. This increased pulmonary pressure gradually causes worsening exercise capacity, shortness of breath and right-sided heart failure which can lead to death. Although several Group 1 PH (Pulmonary Arterial Hypertension, PAH) medications have been explored in Group 2 PH, to date, no medications have been approved for its treatment.

## About Tectonic

Tectonic Therapeutic is a biotechnology company focused on the discovery and development of therapeutic proteins and antibodies that modulate the activity of G-protein coupled receptors (GPCRs). Leveraging its proprietary technology platform called GEODE™ (GPCRs Engineered for Optimal Discovery), Tectonic is focused on developing biologic medicines that overcome the existing challenges of GPCR-targeted drug discovery and harness the human body to modify the course of disease. Tectonic focuses on areas of significant unmet medical need, where therapeutic options are poor or nonexistent, and new medicines have the potential to improve patient quality of life. Tectonic is headquartered in Watertown, Massachusetts. For more information, please visit [www.tectonictx.com](http://www.tectonictx.com) and follow @TectonicTx on X (formerly Twitter) and LinkedIn.

## Forward-Looking Statements

This press release contains “forward-looking statements” within the meaning of the “safe harbor” provisions of the Private Securities Litigation Reform Act of 1995. All statements in this press release other than statements of historical facts are “forward-looking statements”. These statements may be identified by words such as “aims”, “anticipates”, “believes”, “could”, “estimates”, “expects”, “forecasts”, “goal”, “intends”, “may”, “plans”, “possible”, “potential”, “seeks”, “will” and variations of these words or similar expressions that are intended to identify forward-looking statements, although not all forward-looking statements contain these words. Forward-looking statements in this press release include, but are not limited to, statements regarding: the design, objectives, initiation, timing, progress and results of current and future clinical trials of Tectonic’s product candidate, TX45, including the ongoing Phase 1a and Phase 1b clinical trial in Group 2 PH-HFpEF; the proposed initiation of the Phase 2 clinical trial of TX45 in Group 2 PH-HFpEF including anticipated clinical trial design and study endpoints; and anticipated market opportunity of TX45 to address the unmet needs of patients living with PH-HFpEF. These forward-looking statements are based on Tectonic’s expectations and assumptions as of the date of this press release. Each of these forward-looking statements involves risks and uncertainties that could cause Tectonic’s clinical development programs, future results or performance to differ materially from those expressed or implied by the forward-looking statements. Many factors may cause differences between current expectations and actual results, including: the potential that success in preclinical testing and earlier clinical trials does not ensure that later clinical trials will generate the same results or otherwise provide adequate data to demonstrate the efficacy and safety of a product candidate; the impacts of macroeconomic conditions, including the conflict in Ukraine and the conflict between Israel and Hamas, heightened inflation and uncertain credit and financial markets, on Tectonic’s business, clinical trials and financial position; unexpected safety or efficacy data observed during preclinical studies or clinical trials; clinical trial site activation or enrollment rates that are lower than expected; Tectonic’s ability to realize the benefits of its collaborations and license agreements; changes in expected or existing competition; changes in the regulatory environment; the uncertainties and timing of the regulatory approval process; and unexpected litigation or other disputes. Other factors that may cause Tectonic’s actual results to differ from those expressed or implied in the forward-looking statements in this press release are identified in the section titled “Risk Factors” in the final prospectus on Form 424(b)(3) filed by AVROBIO with the SEC on May 3, 2024, and in other filings that Tectonic makes and will make with the SEC in the future. Tectonic expressly disclaims any obligation to update any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise, except as otherwise required by law. For more information, please visit [www.tectonictx.com](http://www.tectonictx.com) and follow @TectonicTx on X (formerly Twitter) and LinkedIn.

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# Transforming and Innovating the Discovery and Development of Novel, Class Leading GPCR-Targeted Therapies

July 2024





## DISCLAIMER

Statements contained in this presentation regarding matters that are not historical facts are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, as amended. Words such as "anticipates," "believes," "expects," "intends," "plans," "potential," "projects," "would" and "future" or similar expressions are intended to identify forward-looking statements. Each of these forward-looking statements involves substantial risks and uncertainties that could cause actual results to differ significantly from those expressed or implied by such forward-looking statements. Forward-looking statements contained in this presentation include, but are not limited to, statements regarding: the design, objectives, initiation, timing, progress and results of current and future preclinical studies and clinical trials of our product candidates, including the ongoing Phase 1a/b clinical trial for TX45, in Group 2 Pulmonary Hypertension and initiation of proposed Phase 2 clinical trial; candidate selection for our second program in HHT; the expected timing of program updates and data disclosures; the timing of filing INDs and other regulatory documents; the timing and likelihood of seeking regulatory approval for our product candidates including TX45; the competitive landscape for our product candidates; our ability to identify and develop additional product candidates; and our estimates regarding expenses, future revenue, capital requirements, cash runway and needs for additional financing.

These forward-looking statements reflect our current beliefs and expectations. Many factors may cause differences between current expectations and actual results, including the early stage of our development efforts; success in preclinical testing and earlier clinical trials does not ensure that later clinical trials will generate the same results or otherwise provide adequate data to demonstrate the efficacy and safety of a product candidates; clinical site activation rates or clinical trial enrollment rates that are lower than expected; changes in expected or existing competition; changes in the regulatory environment; the uncertainties and timing of the regulatory approval process; the impact of macroeconomic conditions, including the conflict in Ukraine and the conflict in the Middle East, heightened inflation and uncertain credit and financial markets, on our business, clinical trials and financial position; and unexpected litigation or other disputes. These and other risks are described more fully in our filings with the Securities and Exchange Commission ("SEC"), including the risks detailed in the prospectus filed with the SEC pursuant to Rule 424(b)(3) on May 3, 2024, and other documents we subsequently filed with or furnished to the SEC. All forward-looking statements contained in this presentation speak only as of the date on which they were made. Except as required by law, we assume no obligation to update any forward-looking statements contained herein to reflect any change in expectations, even as new information becomes available.

This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. Neither we nor any other person makes any representation as to the accuracy or completeness of such data or undertakes any obligation to update such data after the date of this presentation. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

## Agenda

- I. Company Overview
- II. GEODe™ Platform
- III. TX45 Relaxin in Group 2 Pulmonary Hypertension
  - i. Overview of Target and Indication
  - ii. Patient Journey
  - iii. Clinical Data
  - iv. Preclinical Data
  - v. Clinical Program
- IV. HHT Program
- V. Summary

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

## Validated GEODe™ Platform

- Validated platform to discover and optimize biologics that target GPCRs
- Prioritizing high value GPCR targets, where small molecules are not the right modality

## Phase 1 Best-In-Class Relaxin Agonist for PH, First-In-Class HHT Program

- First two assets address indications with no approved therapy
  1. RXFP1 agonist - potential therapy for Group 2 PH<sup>1</sup> in HFpEF<sup>2</sup>
    - >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 expected Sept-2024
    - Phase 1b hemodynamic proof of concept data expected in mid-2025,
    - Randomized Phase 2 data expected in 2026
  2. GPCR antagonist antibody addressing hereditary hemorrhagic telangiectasia (HHT)

## Team with a Track Record of “Firsts”

- Team with extensive track record of drug discovery and development success, resulting in 20 “first” approvals across multiple therapeutic areas

## Reverse Merger Closed June 2024

- Well capitalized by a syndicate of leading institutional funds
- **\$181M<sup>3</sup> post close cash (6/20/24) expected to provide runway into mid-2027**

<sup>1</sup>Pulmonary Hypertension; <sup>2</sup>Heart Failure with Preserved Ejection Fraction; <sup>3</sup>At transaction close (6/20/24), cash, cash equivalents and investments of approximately \$181 million, before payment of final transaction-related expenses, is expected to fund current operational plans into mid-2027

# This Accomplished Team Has Delivered for Patients and Investors



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



**Daniel Lochner**  
CFO



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



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



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



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



**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)

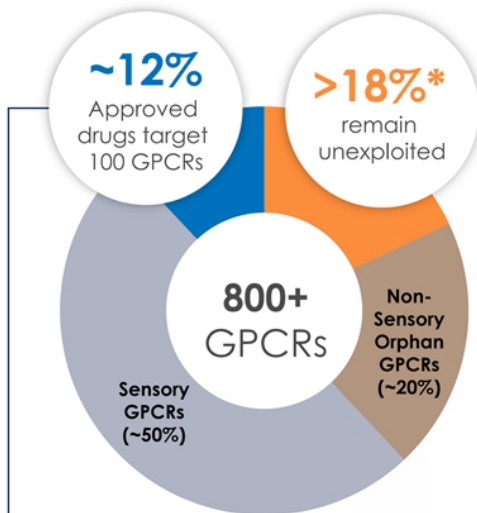


# Team Track Record: >20 1<sup>st</sup> Approvals with >\$50B In Annual Sales

1<sup>st</sup> approvals and indication expansions shown below

ONCOLOGY/ IO	IMMUNOLOGY/ INFLAMMATION	CARDIO/ METABOLISM	RESPIRATORY / ALLERGY	OTHER
<p><b>KEYTRUDA</b> (pembrolizumab) injection 100mg</p> <p><b>BAVENCIO</b> avelumab 30mg/100mL</p> <p><b>Campath</b> Alemtuzumab For Intravenous Use Only</p> <p><b>VELCADE</b> irinotecan</p> <p><b>TEPMETKO</b> tepotinib</p> <p><b>Odomzo</b> (sonidegib) capsules 200mg</p>	<p><b>Abecma</b> (idecabtagene vicleucel) <small>INDICATION EXPANSION</small></p> <p><b>Breyanzi</b> (lisocabtagene maraleucel) <small>INDICATION EXPANSION</small></p> <p><b>BRAFTOVI</b> (encorafenil)</p> <p><b>ZYKADIA</b> ceritinib tablets</p> <p><b>DUPIXENT</b> (dupilumab)</p> <p><b>Amevive</b> (alefacept)</p> <p><b>Entyvio</b> vedolizumab</p> <p><b>MAVENCLAD</b> (cladribine) tablets 10 mg</p> <p><b>ARCOXIA</b> (etoricoxib)</p> <p><b>MAYZENT</b> (siponimod) 1 mg - 2 mg tablets</p> <p><b>Simponi</b> golimumab</p> <p><b>Remicade</b> INFLIXIMAB</p> <p><b>ZEPOSIA</b> fexanimod</p> <p><b>RAPTIVA</b> efalizumab</p> <p><b>VIOXX</b> (rofecoxib, MSD)</p>	<p><b>Entresto</b> (sacubitril/valsartan) tablets 24/26mg - 48/51mg - 97/103mg</p> <p><b>Praluent</b> (alirocumab) injection 300mg/10mL</p> <p><b>CAMZYOS</b> (mavacamten) capsules</p>	<p><b>DUPIXENT</b> (dupilumab)</p> <p><b>Claritin</b></p> <p><b>SINGULAIR</b> (indirina maleate), MSD</p> <p><b>Nasonex</b> (mometasone furoate nasal spray)</p> <p><b>GRASTEK</b> Timothy Grass Pollen Allergen Extract Tablet for Sublingual Use Z800/BAU</p>	<p><b>Reblozyl</b> (lusipatercept-aamt) for injection 25mg - 75mg</p> <p><b>INREBIC</b></p> <p><b>EMEND</b>  Aprepitant</p>

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



- **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

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

(\*) 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)

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

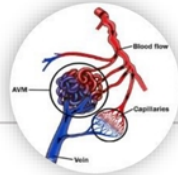


## GROUP 2 PULMONARY HYPERTENSION (Group 2 PH)

### Potential Best-in-Class

RXFP1 Agonist<sup>1</sup>

Supporting clinical data

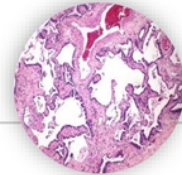


## HEREDITARY HEMORRHAGIC TELANGIECTASIA (HHT)

### First in Class & Indication

GPCR Antagonist<sup>2</sup>  
(anti-angiogenic)

Target pathway linked to disease genetics



## FIBROSIS

### Bi-specific Approach

GPCR Modulator<sup>2</sup>  
(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 therapeutics discovered internally using GEODE platform

# Pipeline of GPCR-Targeted Biologics with Multiple Potential Value Infection Points Ahead

Program	Preclinical	Phase 1	Phase 2	Phase 3	Indication
RXFP1 Agonist (TX45 – Fc-relaxin)	Phase 1a (ongoing) PK/PD data Sept-2024 Phase 1b (ongoing) Hemodynamic data mid-2025		Initiation Planned Q3'24 Randomized Phase 2 Data 2026		Group 2 PH <sup>(1)</sup> in Patients with Heart Failure with Preserved Ejection Fraction (HFpEF)
GPCR Antagonist	Development Candidate Selection	Initiation Planned Q4'25/Q1'26			Hereditary Hemorrhagic Telangiectasia (Osler Weber Rendu Syndrome)
Bi-functional GPCR Modulator	Discovery				Fibrosis
GPCR Modulators	Discovery				Multiple Indications

(1) Pulmonary Hypertension





## **GEODe™ PLATFORM**

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Proprietary, validated platform, enables reproducible discovery and optimization of GPCR targeted biologics

# Solving 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*

# Proprietary GEODE™ platform spans three enabling technologies to identify and optimize potent GPCR targeted biologics

1.

## EXPRESSION AND PURIFICATION TECHNOLOGY

Produce Sufficient Quantities and Stabilize Them in the Correct Conformation

Native ECD



Strategic Tagging

Stabilizing Fusions

Stabilizing Chimeras

Native

Artificial



Membrane Fragments



Synthetic Nanodiscs

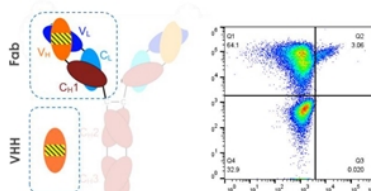


Scaffold-based Nanodisc

2.

## IN-VITRO YEAST DISPLAY LIBRARIES

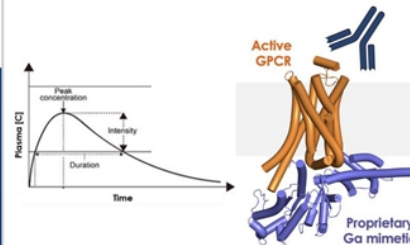
Efficiently Screen Diverse Antibody Libraries Against GPCRs



3.

## PROTEIN ENGINEERING

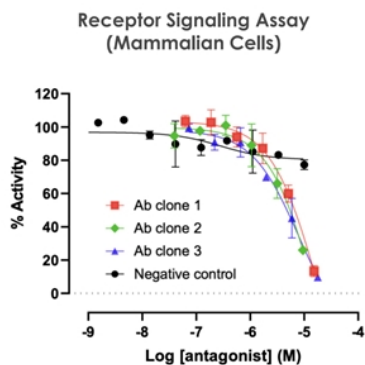
- Optimize Protein Pharmacology
- Engineer Proprietary Scaffolds for Agonist Discovery



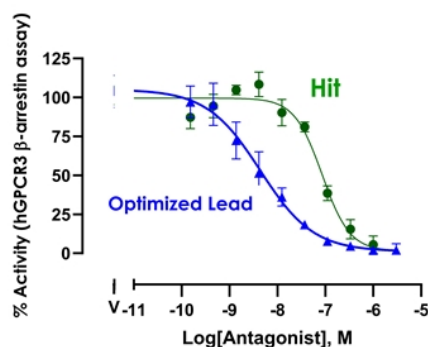
Large toolbox of biochemical methods, engineering tools, and assays

# GEODE™ Platform Discovery Capabilities Deliver Selective, Ligand Competitive Orthosteric Antagonists

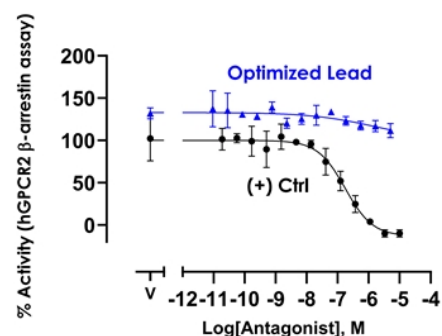
## PURIFIED ANTIBODIES ARE FUNCTIONAL ANTAGONISTS\*



## OPTIMIZATION IMPROVES ORIGINAL POTENCY BY ~20X



## SELECTIVE (NO EFFECT ON OFF-TARGET GPCR)

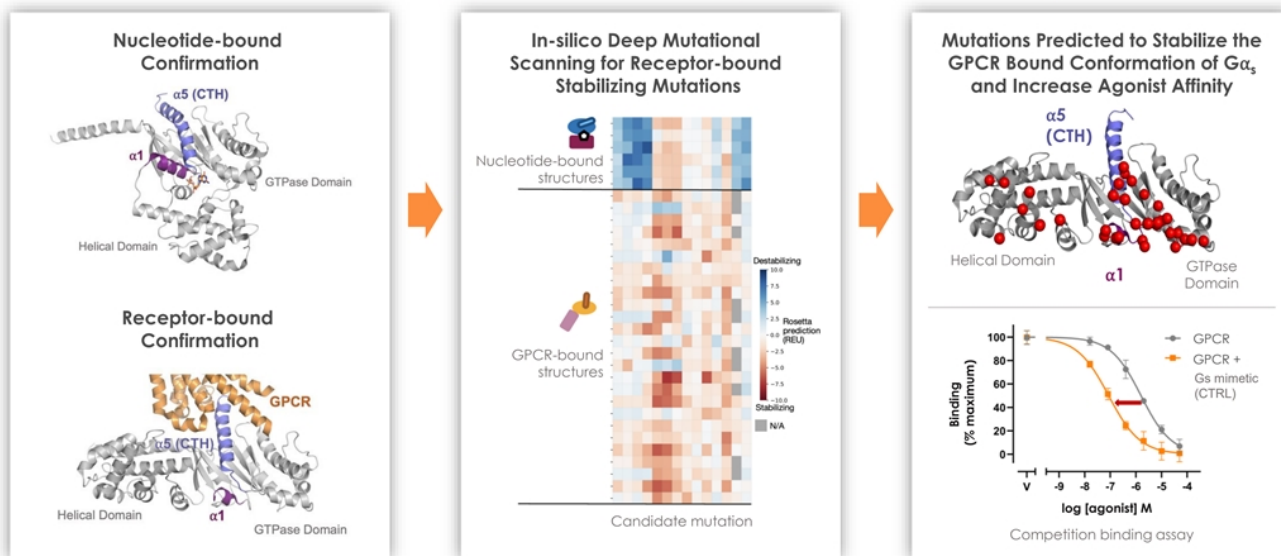


\*Latest generation proprietary libraries delivering initial hits with >10X potency

# Our Proprietary Antigen Formats Enable Screening for Biologics with Agonist Activity



# Design of Our Proprietary G $\alpha$ Mimetics Is Driven by the Latest in Machine Learning and Energy Prediction Algorithms

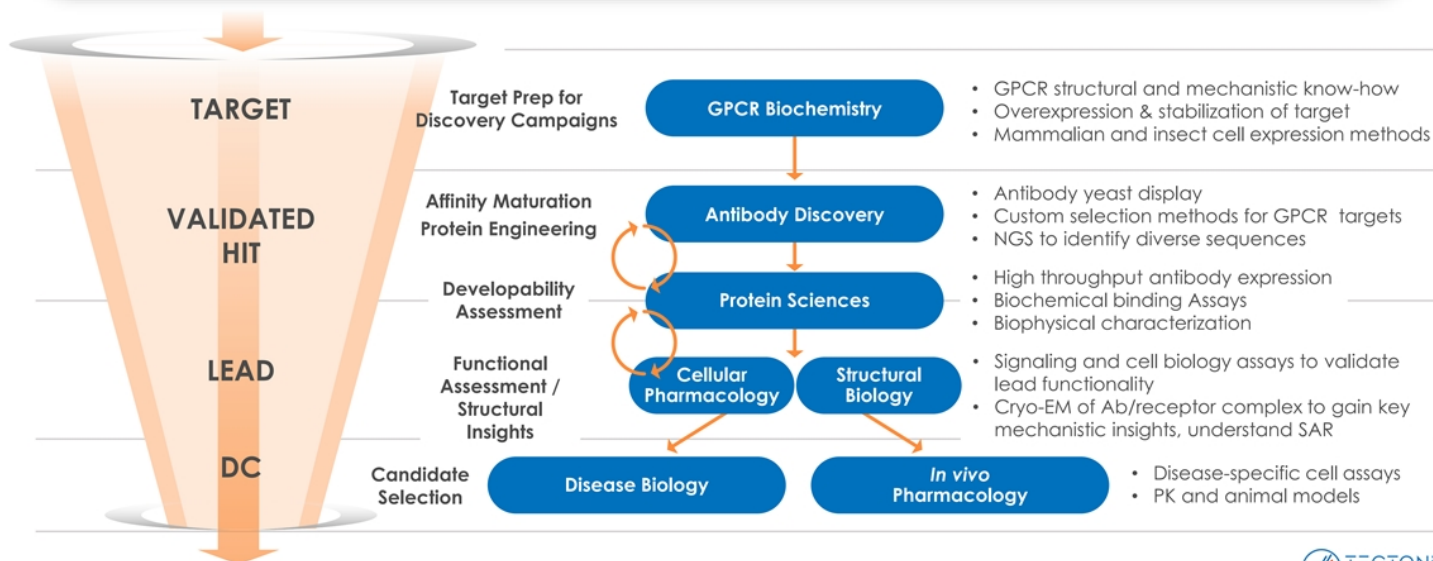


Ongoing enhancement of our ability to screen for biologics with agonist activity

# End-to-end Capabilities in Place at Tectonic for Continued Discovery of Optimal DCs



## Suite of Ab Discovery, Optimization and Characterization Capabilities





## **TX45: Fc-RELAXIN FUSION PROTEIN**

RXFP1 agonist with differentiated profile



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

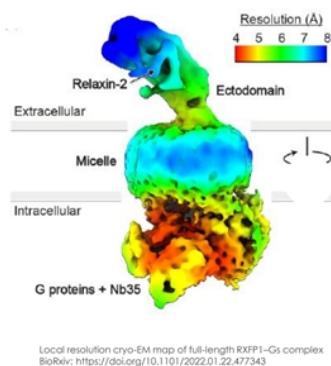
## Pharmacology

### AGONIST

Natural Ligand of RXFP1 Receptor

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

Relaxin upregulated in pregnancy



## 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



# The First Recombinant Relaxin (serelaxin) Demonstrated Safety and Benefit in Acute Heart Failure (AHF) in Trials of >11,000 Patients

-Note: trials only included a two-day relaxin infusion

Study (WHF Day 5)	Relative Risk [95% CI]	N(drug)	N(pbo)
Pre-RELAX AHF	0.56 [0.22 – 1.45]	42	61
RELAX-AHF	0.54 [0.37 – 0.78]	581	580
RELAX-AHF-2	0.90 [0.76 – 1.07]	3274	3271
RELAX-AHF-EU	0.71 [0.52 – 0.98]	1756	894
RELAX-AHF-ASIA	0.42 [0.21 – 0.84]	437	433
<b>Meta Analysis</b>	<b>0.77 [0.67 – 0.89]</b> <b>p = 0.0002</b>	6090*	5239

Effects of serelaxin on worsening heart failure (WHF) – fixed-effect (FE) meta-analysis; serelaxin 30 µg/kg/day vs. placebo, CI, confidence interval.

PK limitations of relaxin a major hurdle to its development for chronic diseases

Our GEODe Protein Engineering capabilities address this challenge

- One of two pivotal studies included 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

\*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



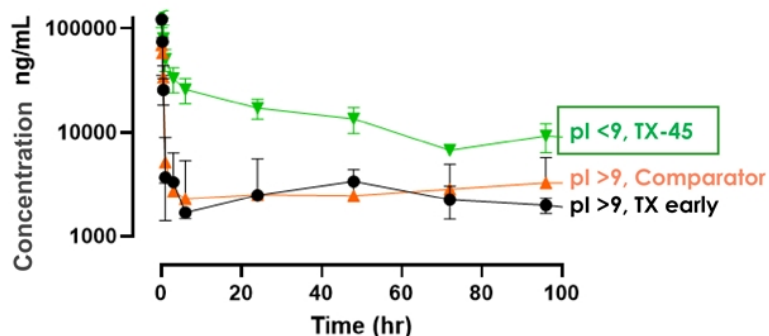
Relaxin Fc-fusions **have steep decline in exposure after dosing (>90%)** because of glyocalyx binding due to high pI<sup>1</sup>



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



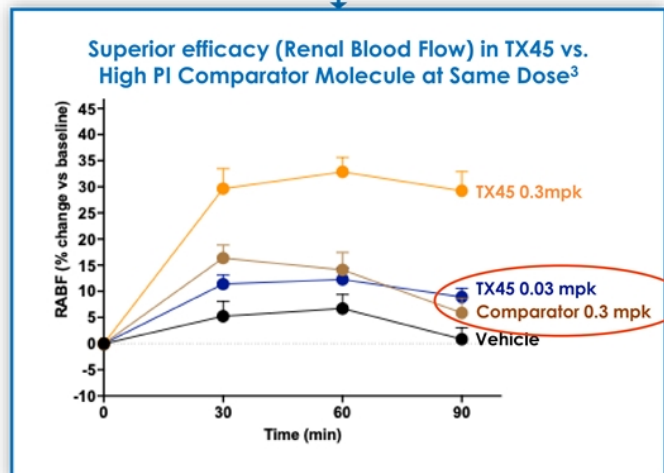
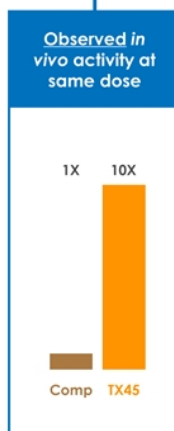
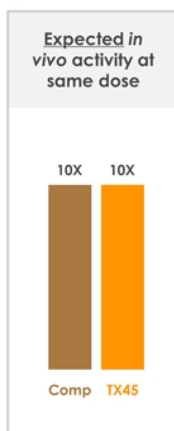
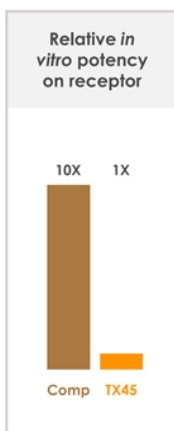
**TX45 EXHIBITS SUPERIOR PROFILE vs. PARENT COMPOUND AND COMPARATOR<sup>2</sup> MOLECULE<sup>3</sup>**  
Preclinical Rat Pharmacokinetic Data



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 over comparator<sup>1</sup> molecule than predicted based on PK and *in vitro* activity<sup>2</sup> – potentially from reduced trapping of drug in glycocalyx, resulting in increased free drug available to activate RFXP1 in tissues



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

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

3. Source: Tectonic internal data

## TX45 – Optimized RXFP1 Agonist for Group 2 PH in HFpEF

- |  |  |
|--|--|
| ✓ <b>Potential Best-in-Class Relaxin Agonist with Optimized PK</b> | <ul style="list-style-type: none"><li>• Protein engineering has extended pharmacologic half-life to support monthly dosing</li></ul>   |
| ✓ <b>High Unmet Need in Group 2 PH with HFpEF<sup>1</sup></b>      | <ul style="list-style-type: none"><li>• No approved therapy</li><li>• &gt;600,000 patients in US</li><li>• High 5-year high mortality</li></ul>  |
| ✓ <b>Mechanism may be Ideal to Address Group 2 PH</b>              | <ul style="list-style-type: none"><li>• Pulmonary + systemic vasodilation, cardiac relaxation</li><li>• Reversal of fibrosis in pulmonary vasculature and heart</li><li>• Anti-inflammatory</li></ul>                              |
| ✓ <b>Supporting Clinical and Pre-clinical Data</b>                 | <ul style="list-style-type: none"><li>• Hemodynamic benefit in studies of serelaxin in AHF</li><li>• Clear benefit observed with TX45 in rodent PH and CHF models</li></ul>  |
| ✓ <b>Streamlined Development Strategy</b>                          | <ul style="list-style-type: none"><li>• No outcome study needed</li><li>• Enrichment strategy for CpcPH where there is greatest unmet need</li><li>• Enables potential early launch relative to congestive heart failure</li></ul> |
| ✓ <b>Potential to Expand Indications</b>                           | <ul style="list-style-type: none"><li>• Other PH Groups, Heart failure, renal disease</li></ul>  |

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

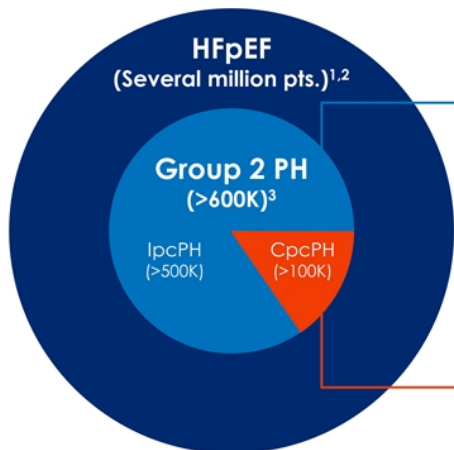
Group 1 ("PAH") (~25,000 <sup>1</sup> )	Group 2 (>600,000 <sup>1</sup> )	Group 3	Group 4 ("CTEPH")	Group 5 (Misc.)
<ul style="list-style-type: none"> <li>• Idiopathic</li> <li>• Hereditary</li> <li>• Connective tissue disease-associated</li> <li>• Congenital heart disease-associated</li> <li>• Drug-induced</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Due to left heart disease (HFpEF, HFrEF) or valvular heart disease</b></li> <li>• <b>CAD, HTN, T2DM<sup>2</sup>, high cholesterol are risk factors</b></li> <li>• <b>Two Subtypes: CpcPH / lpcPH</b></li> </ul>	<ul style="list-style-type: none"> <li>• Due to lung disease or hypoxia</li> <li>• May be due to COPD, interstitial lung disease (i.e., IPF) or obstructive sleep apnea</li> </ul>	<ul style="list-style-type: none"> <li>• Chronic thrombo-embolic pulmonary hypertension –i.e., as a consequence of blood clots</li> </ul>	<ul style="list-style-type: none"> <li>• Miscellaneous group with causes unclear or multiple underlying factors</li> </ul>

1. US Prevalence

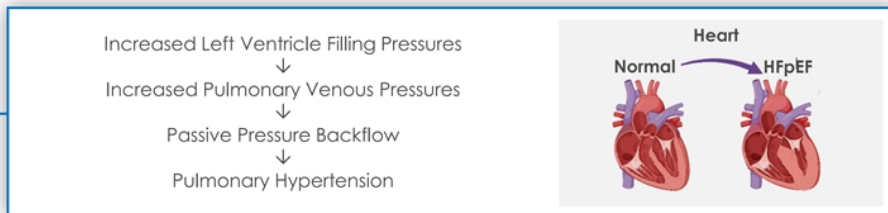
2. CAD: Coronary Artery Disease, HTN: Hypertension, T2DM: Type 2 Diabetes Mellitus  
Nat. Pul. Hypertension Unit, Ireland

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

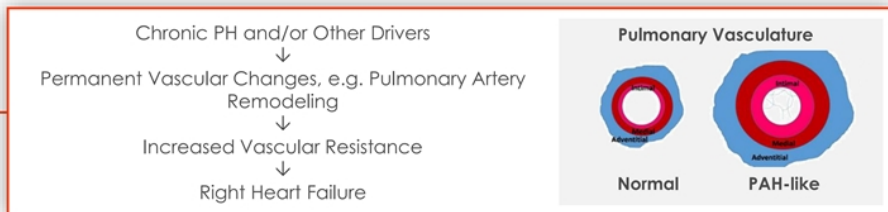
Clinical Program Designed to Enable Evaluation of Efficacy in Overall Population and CpCPH



## IpcPH (I)solated, post capillary PH



## CpcPH (C)ombined, pre- and post capillary PH



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





## **Group 2 PH: Patient Journey**

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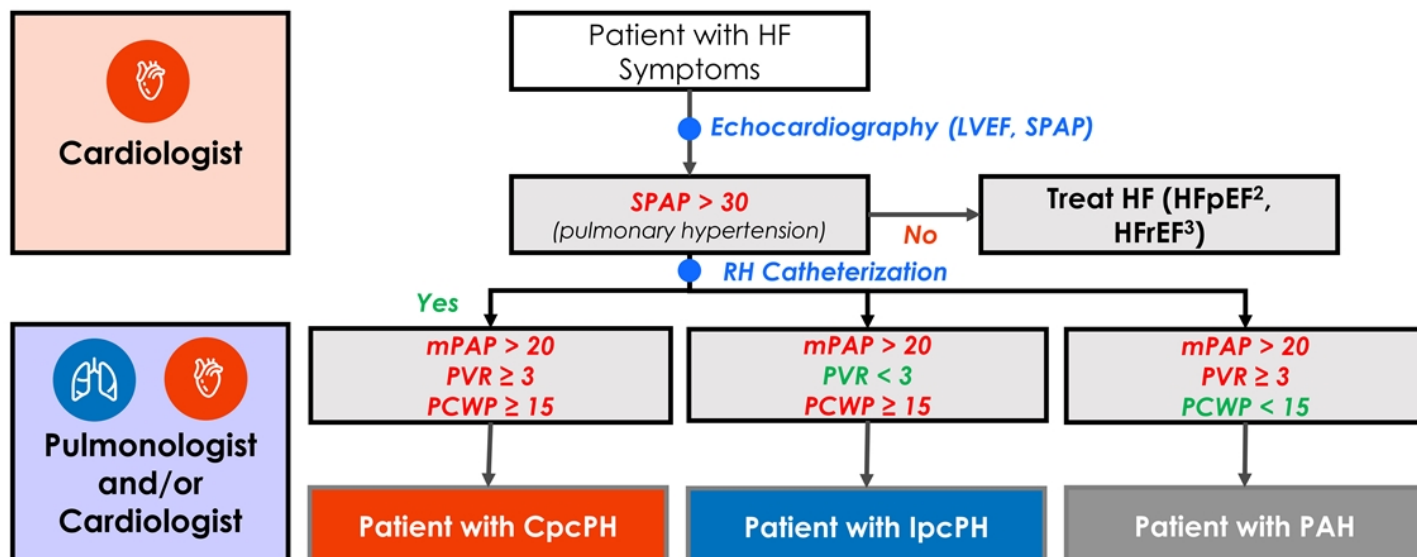




## Key Hemodynamic Measures in Pulmonary Hypertension

Measure	Definition	Detection Method(s) / Formulas	Clinical Significance
 <b>mPAP</b> Mean Pulmonary Arterial Pressure (mm Hg)	Fluid pressure in the lung arteries	Directly measured by RHC sPAP estimated by echo	Key parameter for diagnosing pulmonary hypertension of all causes (Groups I-V)
<b>PVR</b> Pulmonary Vascular Resistance (Wood Units)	Resistance to blood flow in pulmonary arteries ("narrowness of pipes")	Calculated from mPAP, PCWP, and CO obtained by RHC $PVR = (mPAP - PCWP) / CO$	Provides information about disease/narrowing specifically in pulmonary arteries
 <b>PCWP</b> Pulmonary Capillary Wedge Pressure (mm Hg)	Fluid pressure in lung capillaries – measure of left atrial pressure	Directly measured by RHC	Used to assess left ventricular filling abnormalities – elevated in left sided heart failure ("hard to fill pump")
<b>CO</b> Cardiac Output (L / min)	Amount of blood pumped per unit time	CO directly measured by RHC thermodilution	CO is a key measure of heart function and is depressed in heart failure

## Group 2 Pulmonary Hypertension (PH) Patient Journey

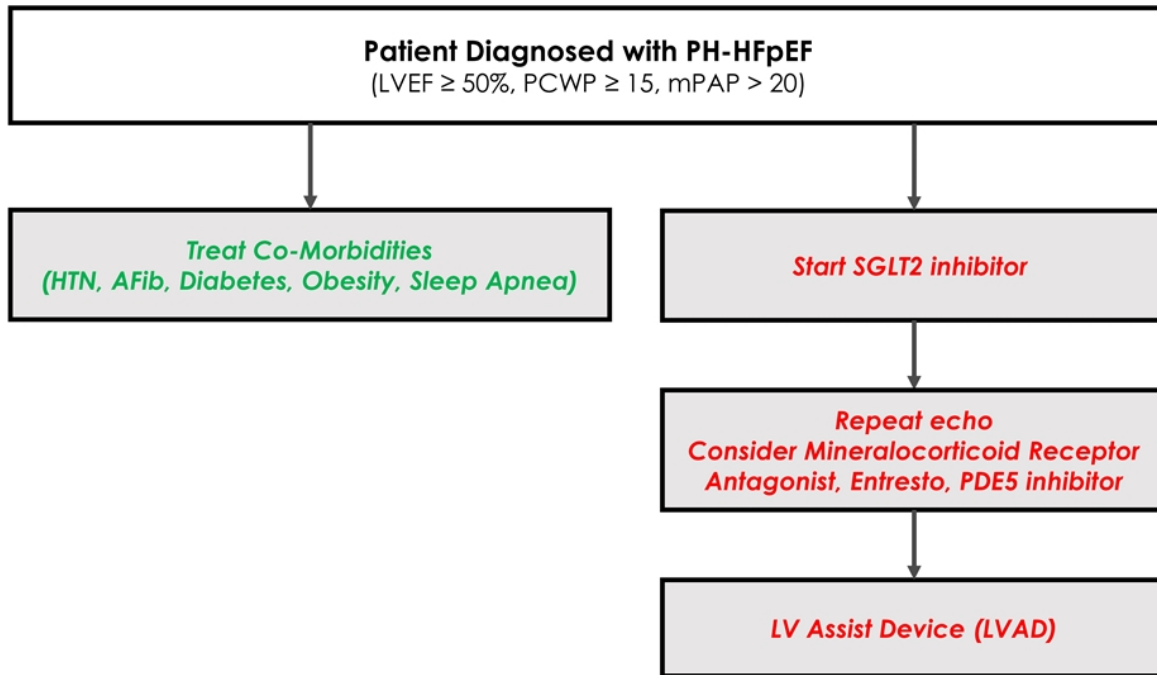


(1) LVEF: left ventricular ejection fraction; SPAP: estimated systolic pulmonary artery pressure by echo; mPAP: mean pulmonary artery pressure; PVR: pulmonary vascular resistance; PCWP: pulmonary capillary wedge pressure; CpcPH: combined pre-and post-capillary pulmonary hypertension; lpcPH: isolated post-capillary PH

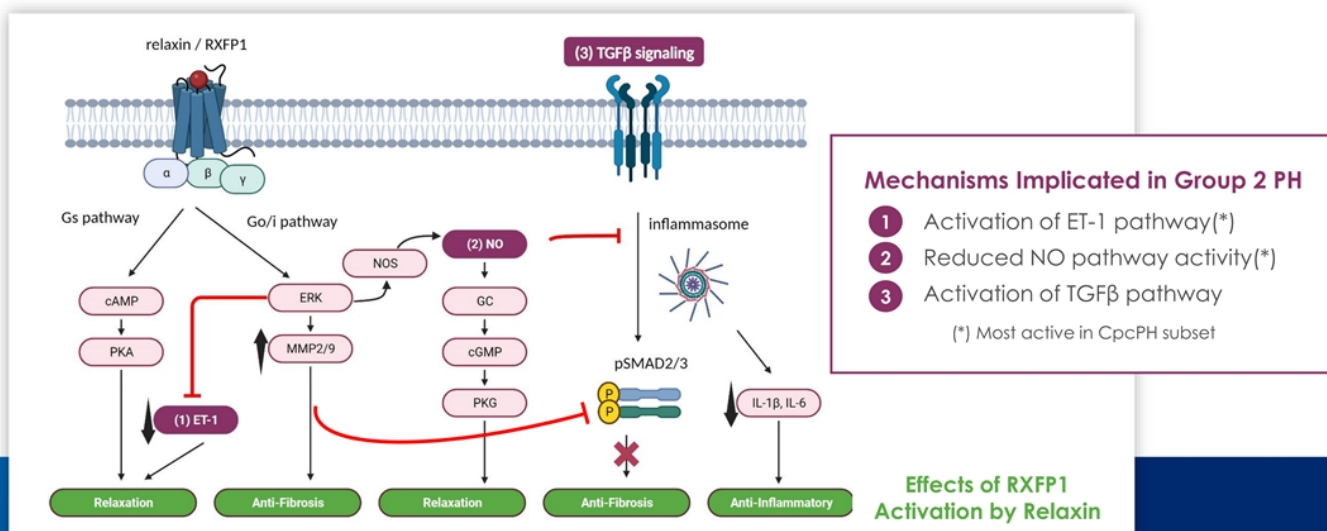
(2) Heart Failure with preserved Ejection Fraction

(3) Heart Failure with reduced Ejection Fraction

# Treatment of Pulmonary Hypertension (PH) in the Setting of Heart Failure with Preserved Ejection Fraction (HFpEF)



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



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

## 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

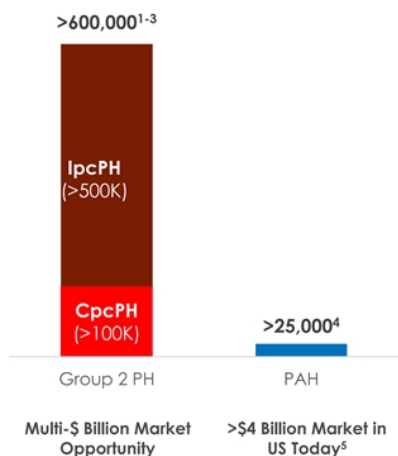
CHARACTERISTICS OF GROUP 2 PH	IpcPH	CpcPH	ANTICIPATED RELAXIN EFFECTS
Pulmonary artery narrowing, thickening, stiffening, fibrotic remodeling		✓	Pulmonary Vasodilation Anti-inflammatory, anti-fibrotic
Right Ventricular Dysfunction	✓	✓	Right ventricular remodeling
Thickening and stiffening of Left Ventricle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

**Reducing pulmonary pressures and improvement of left heart function are both key to providing efficacy**

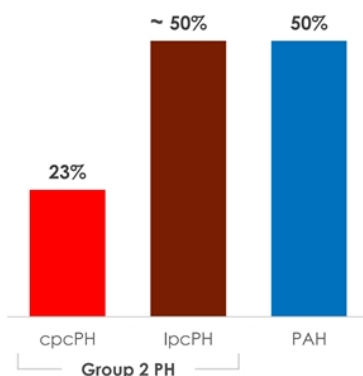
# Group 2 PH vs. PAH

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

## US PREVALENCE >> PAH



## 5 YEAR SURVIVAL ≤ PAH<sup>6</sup>

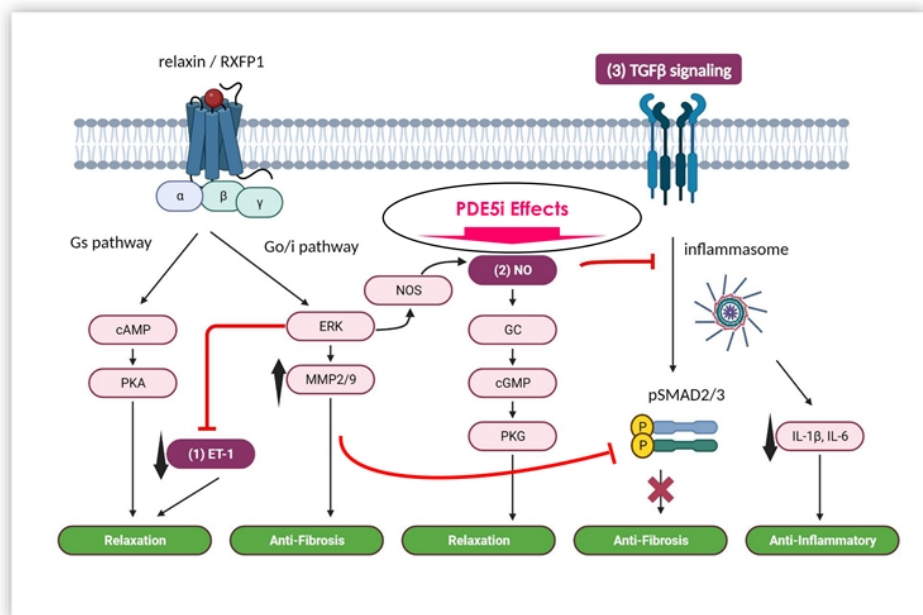


## NO THERAPEUTIC OPTIONS

<p><b>No approved therapies</b></p> <p>...</p> <p>Limited pipeline</p> <p><i>PAH Drugs have not demonstrated convincing efficacy in Group 2 PH with the exception of PDE5i in CpcPH</i></p>	<p><b>Multiple drugs/mechanisms approved</b></p> <p>ET1R antagonists</p> <p>PDE5 inhibitors</p> <p>GC stimulators</p> <p>Prostacyclins</p> <p>ACTRII-Trap</p>
<b>Group 2 PH</b>	<b>PAH</b>

1. US prevalence numbers. Estimates based on data from  
 2. Kapellios, 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

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



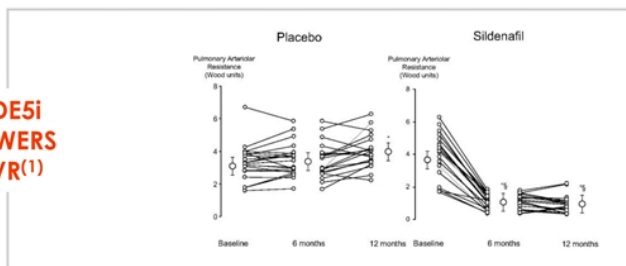
TX45 anticipated to be effective in both Cpc-PH and lpc-PH because it targets additional anti-fibrotic and anti-inflammatory mechanisms on top of activation of the NO pathway

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

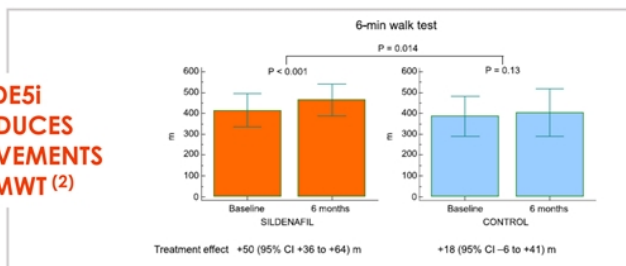
# PDE5 Inhibitors Show Significant Benefit in CpcPH and HFpEF Despite Limited Mechanism of Action Compared with Relaxin

Expected to Increase POS of Relaxin in HFpEF and CpcPH

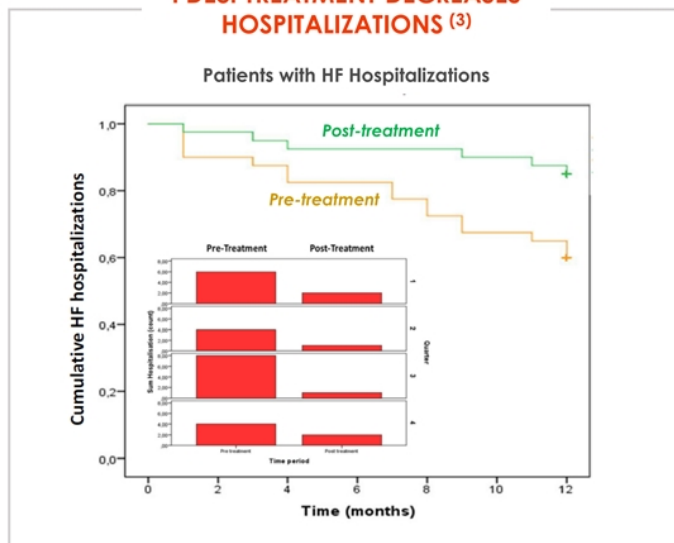
**PDE5i LOWERS PVR<sup>(1)</sup>**



**PDE5i PRODUCES IMPROVEMENTS IN 6MWT<sup>(2)</sup>**



**PDE5i TREATMENT DECREASES HOSPITALIZATIONS<sup>(3)</sup>**



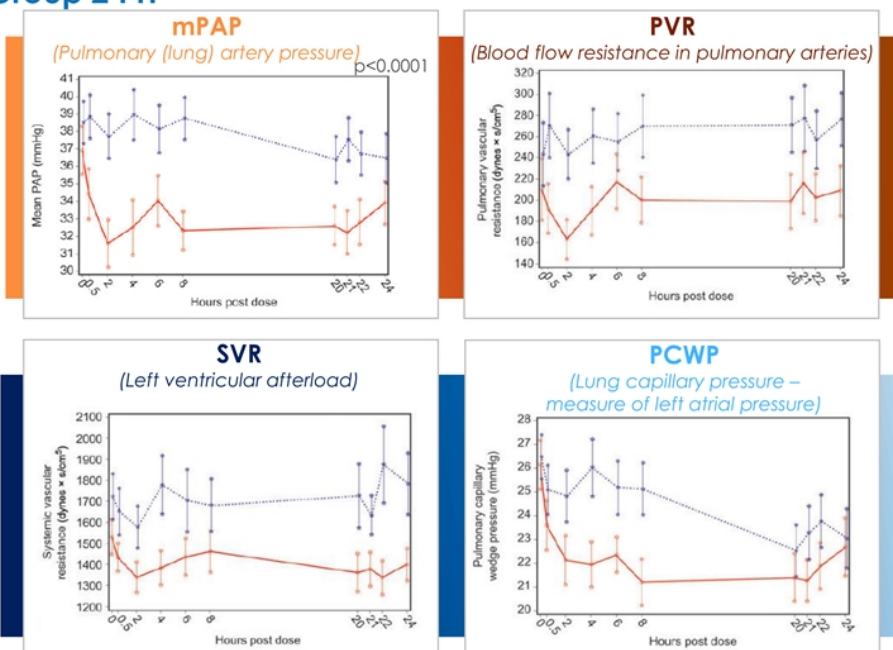
1. Guozzi et al. 2011  
 2. Belyavskiy et al. 2020  
 3. Kramer et al. 2019



# Relaxin Improves Hemodynamics in Heart Failure

Balanced pulmonary and peripheral vasodilation, and improved heart function  
(decreased PCWP) relevant to Group 2 PH

- Panels: 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), pulmonary capillary wedge pressure (PCWP)\*\***
- Not shown: serelaxin also improved **right atrial pressures (RAP), and renal function\***
- 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

\*\* Diuretics were allowed after the first 8 hours



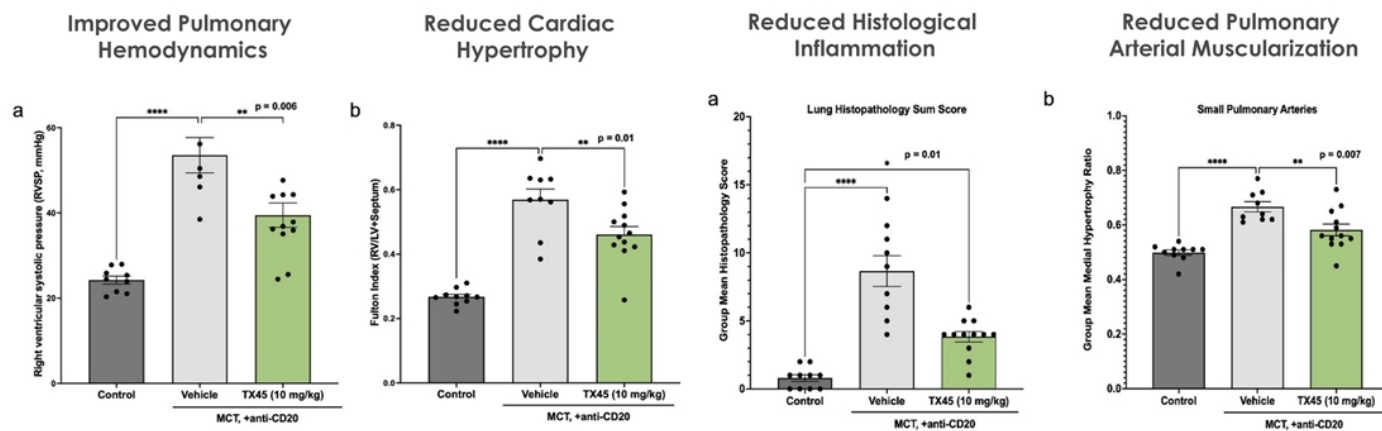
## **TX45 and Other Relaxin Preclinical Data**

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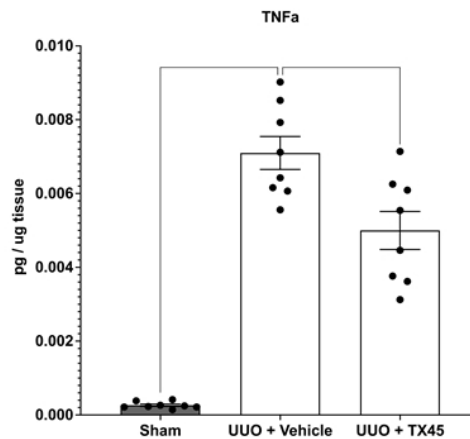
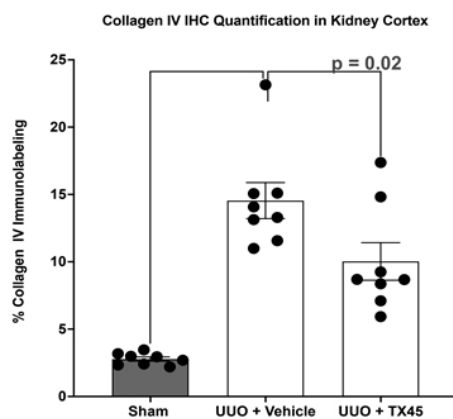
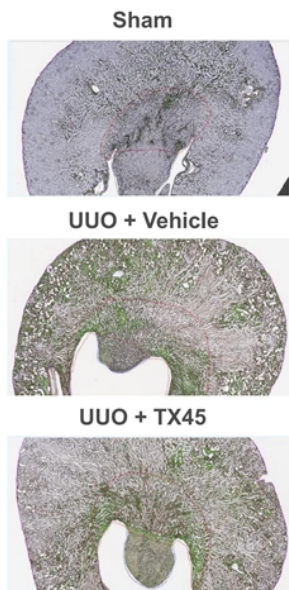
Preclinical validation  
Anti-fibrotic effects of relaxin  
observable across broad range of  
studies

# TX45 Efficacy in Monocrotaline-Induced Model of Pulmonary Hypertension in Rats

TX45 Significantly Reduces Right Ventricular Systolic Pressure, Fulton's Index and Muscularization of Small Pulmonary Arteries in Tx Model of PH

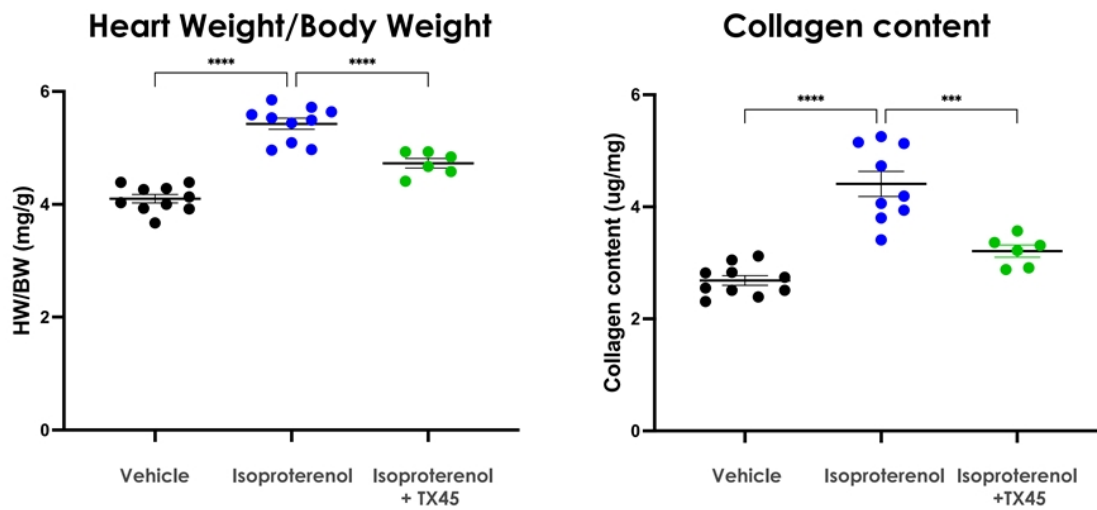


# TX45 Significantly Reduces Collagen and TNF $\alpha$ levels in Mouse UO Model of Renal Fibrosis



\* Dotted red line defines the cortex region

# TX45 Reduces Cardiac Hypertrophy and Fibrosis in the Mouse Isoproterenol Induction Model

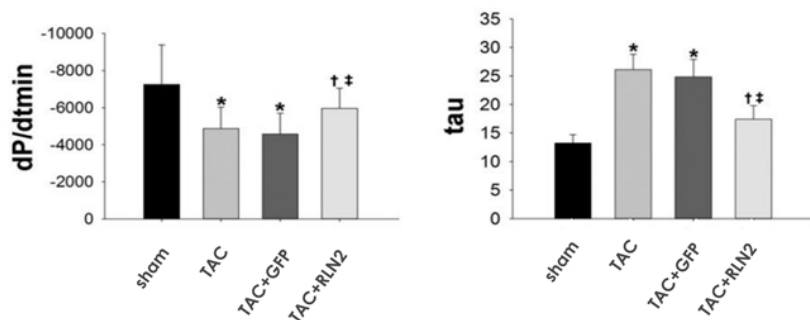


# Relaxin Prevents Diastolic Dysfunction in a Model of HFpEF and Reverse Cardiac Fibrosis

Relaxin Prevents TAC (transverse aortic constriction) -Induced Cardiac Diastolic Dysfunction in Rats & Reverses Diabetes-Induced Cardiac Fibrosis and Diastolic Dysfunction in mRen-2 Rats.

## Human relaxin-2 Improves Diastolic Dysfunction

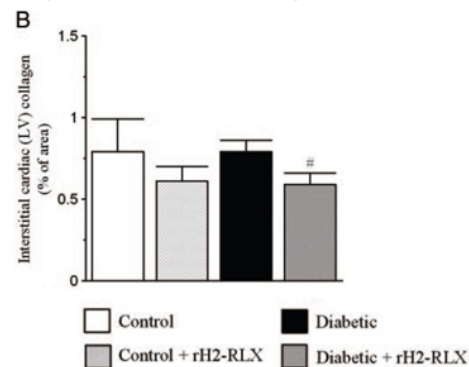
gene therapy administered with 28 days follow-up  
(Shuai X.X. et al. 2016)



\* GFP = green fluorescent protein (adenovirus used as negative control)

## Human relaxin-2 reverses cardiac fibrosis

2 wk infusion in STZ-treated diabetic/HTN mRen-2 rats  
(Samuel C.S. et al. 2008)



# Additional Anti-Fibrotic Effects of Relaxin Demonstrated in Preclinical Animal Models of Heart Failure

In other rodent models of heart failure, Relaxin has been shown to also:

- ✓ **Inhibit** TGF $\beta$  or ANG-II induced collagen synthesis in cardiac fibroblasts<sup>1</sup>
- ✓ **Prevent** interstitial and perivascular fibrosis, with effect superior to enalapril<sup>2</sup>
- ✓ **Prevent** diastolic dysfunction<sup>3</sup>
- ✓ **Prevent** and **Reverse** cardiac hypertrophy<sup>3</sup>
- ✓ **Reverse** cardiac inflammatory gene expression<sup>4</sup>

Findings consistent across models and studies published by different investigators



1. **Relaxin knockout** model of cardiac fibrosis (mouse) - Samuel C.S. et al. 2004
2. **Isoproterenol Infusion** model of heart failure (mouse) - Samuel C.S. et al. 2014
3. **Transverse aortic constriction** model of HFpEF (rat) - Shuai X.X. et al. 2016, Lapinskas T. et al. 2020
4. **Aging-induced** cardiac inflammation (rat) - Martin B. et al. 2018



## **TX45 Clinical Program and Preliminary Phase 1 Data**

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# TX45 Development Program Overview

Planned readouts in Q3'2024, 2025, 2026



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

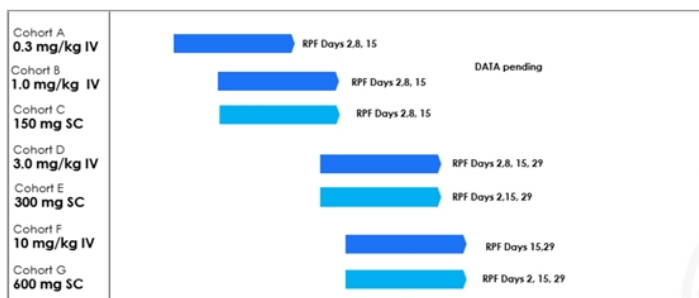
Development Plan Reviewed with FDA via Pre IND



# TX45 Single Ascending Dose Study : Summary of preliminary data<sup>1</sup>

- Well tolerated with minimal adverse events, no drug-related SAEs
- **Pharmacokinetics**
  - Low intersubject variability in serum concentrations ( $\leq 20\%$ )
  - 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
  - Magnitude of effect consistent with serelaxin's effect
  - Meets "go criteria"

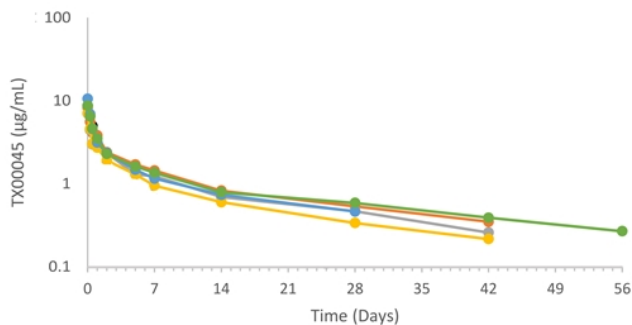
## TX45 SAD Dose Escalation Plan



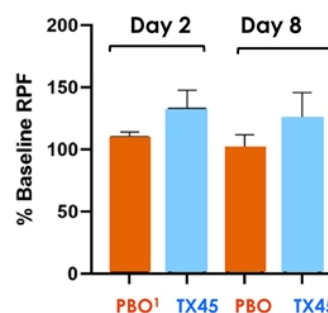
RPF= Renal Plasma Flow  
\*Cohorts F and G are optional

# Phase 1a Study: Preliminary Single Dose TX45 Pharmacokinetic/Pharmacodynamic Data (lowest dose)

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



Based on Preliminary Data, We Anticipate Potentially Monthly Dosing at Optimal SC Dose

1. Placebo

# Preclinical PK/PD from Acute RBF Model Informs Target Plasma Concentration Levels at Trough for Therapeutic Effect

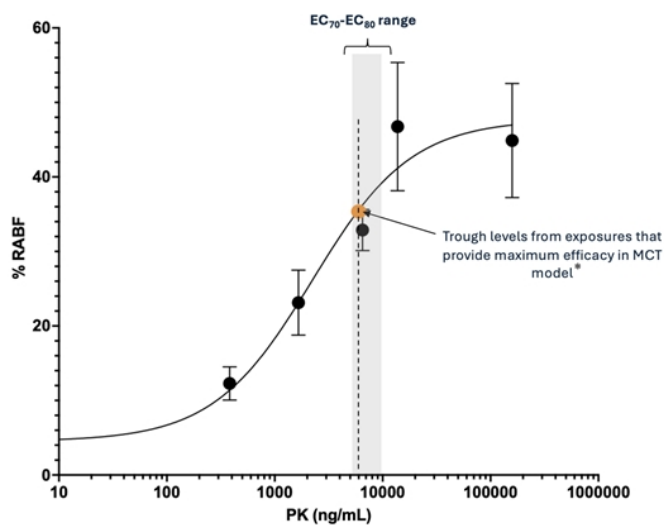
## RBF Model

Used to assess pharmacodynamic response to TX45 administration based on acute vasodilatory effects of relaxin, as measured by increased rat renal blood flow (RBF)

## MCT Model

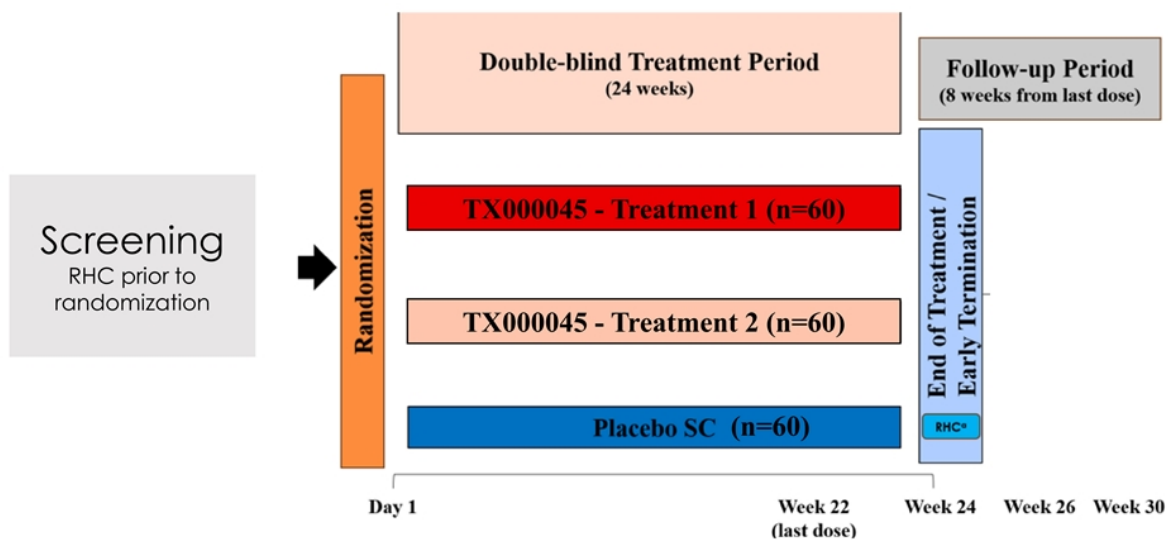
Used to assess the therapeutic anti-inflammatory/anti-proliferative efficacy of TX45 in a rat model of pulmonary hypertension

The trough levels required for maximal efficacy in the MCT model fall between the  $EC_{70}$  and  $EC_{80}$  response in the RBF model







\* The exposure in humans that falls between the  $EC_{70}$ - $EC_{80}$  are expected to be 3-fold lower than in rats given the greater potency of TX45 on human RXFP1 compared to rat RXFP1

## Summary of Projected TX45 Phase 2 Study Design



# Significant Pharma Interest in Relaxin

## Tectonic has Potential Best-in-Class Molecule

Company	Format	Formulation	Expected Dosing Frequency	Population	Timing
	<b>Fc-Fusion</b> <i>Engineered for optimal PK, biodistribution, high [C] formulation</i>	<b>SubQ</b> <i>High [C] achievable</i>	<b>Q4 Weeks</b>	<b>Group 2 PH / HFpEF (enriched for CpcPH)</b>	<b>Start in Q3'24 Data in 2026</b>
	Fc-Fusion	SubQ	Q2 Weeks*	Group 2 PH / HFpEF and HFREF	Start: Q1 2023 1 <sup>st</sup> completion: Q2 2025
	Small Molecule	PO	QD*	CHF	Start: Q2 2024 1 <sup>st</sup> completion: Q4 2025
	h-Albumin-mAb-Fusion	SubQ <i>Injection site reactions</i>	Q Weekly*	HFpEF	Start: Q1 2023 1 <sup>st</sup> completion: Q4 2025

\* Based on dosing frequency in Phase 2 studies listed in clinical trials database



## HHT Program

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First-in- indication opportunity for 2<sup>nd</sup> most common genetic bleeding disorder

# Hereditary Hemorrhagic Telangiectasia (HHT)

## Autosomal Dominant Disease that Causes Abnormal Blood Vessel Formation

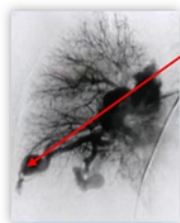
- Rare, autosomal dominant disease: ~ 75,000 patients in US
  - Mutations in the BMP9/10 pathway
- High degree of phenotypic variability (15-20% severe)
- Increased mortality risk



Nosebleeds



Telangiectasias



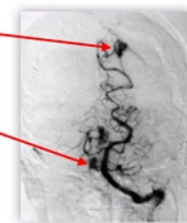
Lung



Liver



GI tract



Brain

AVMs

Telangiectasias

No currently approved therapies for HHT

### FREQUENCY OF ABNORMAL HHT VESSELS

- **>95%** Nose (epistaxis)
- **>90%** Skin (Telangiectasia)
- **50%** Lungs (pulmonary AVMs\*)
- **50%** Liver (hepatic AVMs)
- **20%** Gastrointestinal tract
- **10%** Brain (cerebral AVMs)

### INCREASED FREQUENCY OF THE FOLLOWING

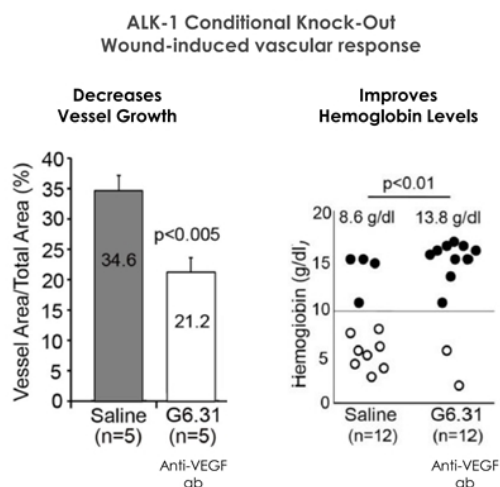
- Iron and transfusion dependent anemia (10-30% of patients)
- High output CHF 2nd to Liver AVM → liver transplant
- Stroke
- Brain abscesses and other deep tissue abscesses
- Venous thromboemboli (VTE)
- Pulmonary Hypertension
- Migraines

\*AVM= arterial venous malformation



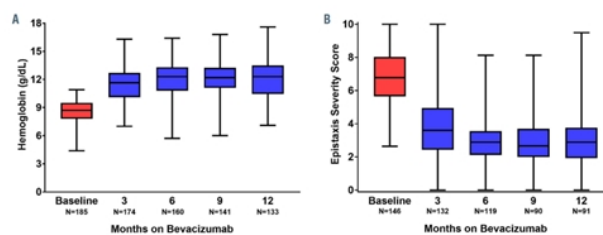
# Anti VEGF: Mouse HHT Model Predictive of Efficacy in Patients

## ANTI-VEGF mAb SUPPRESSES AVM FORMATION, VISCERAL HEMORRHAGE IN HHT MODEL



Angiogenesis. 2014 Oct; 17(4): 823-830

## ANTI-VEGF THERAPY REDUCES EPISTAXIS SEVERITY, IMPROVES HEM. PARAMETERS IN PATIENTS

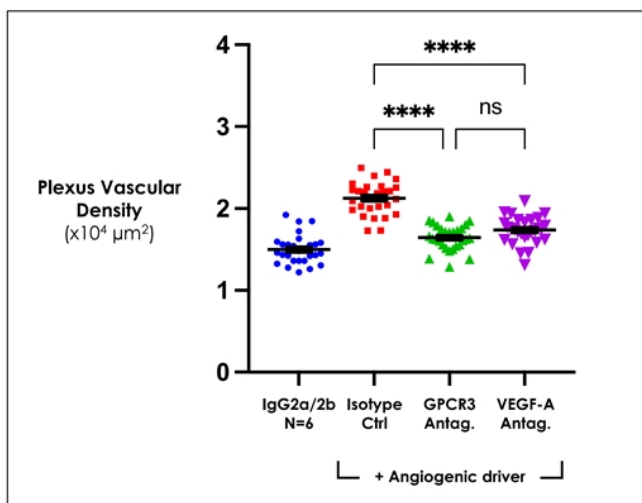
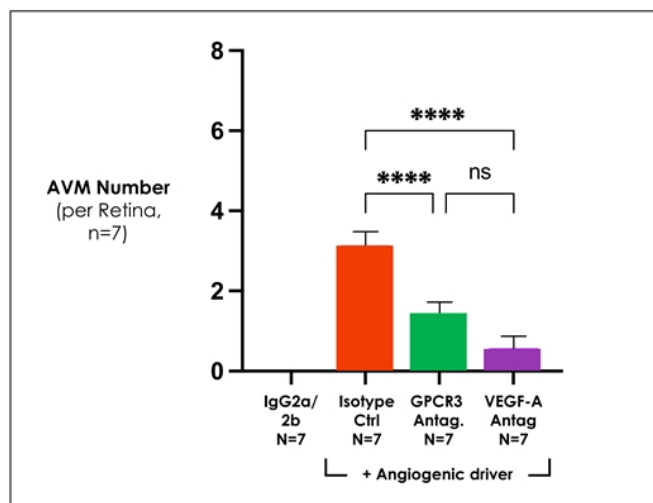


- No rigorous clinical studies ever conducted – only evidence is from IITs
  - Patent expiration on anti-VEGF mab lowered incentive to investment in label expansion
  - Dose and Dosing interval not well explored
- Treating physicians concerned about side effects

Haematologica. 2021 Aug 1; 106(8): 2161-2169

# A GPCR3 Antagonist Significantly Reduces AVMs and Retinal Vascular Density in Animal Model of HHT

Effects of anti-GPCR3 antagonist mAb in mouse HHT model generated by immunoblocking of BMP9 and BMP10<sup>(1,2)</sup>



1. Ruiz, S. et al., Scientific Reports, 2016; 6:37366, doi: 10.1038/srep37366  
2. Ruiz, S. et al., J. Clin. Invest., 2020; 130(2):942-957, doi.org/10.1172/JCI127425

## Projected HHT Development Program Overview





## Summary

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## AVROBIO/Tectonic Merger Overview

<b>Company Ticker</b>	NASDAQ: TECX
<b>Private Placement Investors</b>	Major mutual fund, TAS Partners, 5AM Ventures, EcoR1 Capital, Polaris Partners, Farallon Capital (managed funds), Vida Ventures, Pags Group and other investors
<b>Cash at Close (6/20/24)</b>	~\$181 million <sup>1</sup>
<b>Expected Cash Runway</b>	Into Mid-2027
<b>Reverse Stock Split:</b>	1 for 12
<b>Merger Close Date</b>	6/20/2024

1. As of 6/20/24, Before final transaction expenses



## Uniquely Positioned to Deliver on Value Creating Milestones

### Strong Balance Sheet Post Transaction

**~\$181 Million\*** (as of 6/20/24)  
**Runway Into Mid-2027**

Well positioned  
to execute

### Pipeline of Uniquely Differentiated Assets

**Multiple Inflection Points**  
**2024, 2025, 2026, 2027**

Address important clinical  
problems, underserved  
patient populations

### Accomplished Team World-leader Founders

**20 1<sup>st</sup> Approvals**  
**>\$50B in Annual Sales**

Leadership with  
Proven Track Record

\*At transaction close (6/20/24), cash, cash equivalents and investments of approximately \$181 million, before payment of final transaction-related expenses, is expected to fund current operational plans into mid-2027



## Thank you

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