# 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): January 13, 2025**

# Tectonic Therapeutic, Inc.
**(Exact name of registrant as specified in its charter)**

| **Delaware** | **001-38537** | **81-0710585** |
|---|---|---|
| **(state or other jurisdiction of incorporation)** | **(Commission File Number)** | **(I.R.S. Employer Identification No.)** |

| | |
|---|---|
| **490 Arsenal Way, Suite 210**<br>**Watertown, Massachusetts** | **02472** |
| **(Address of principal executive offices)** | **(Zip Code)** |

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

**Not applicable**
**(Former name or former address, if changed since last report.)**

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:

☐ 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, $0.0001 par value per share | TECX | The Nasdaq Stock Market LLC |

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 January 13, 2025, Tectonic Therapeutic, Inc. (the "Company") updated its corporate presentation for use in meetings with investors, analysts and others. The presentation is available through the Company's website and a copy is attached as Exhibit 99.1 to this Current Report on Form 8-K.

The information in this Current Report on Form 8-K, including Exhibit 99.1 attached hereto, is being furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act") or otherwise subject to the liabilities of that section. The information contained herein and in the accompanying exhibit is not incorporated by reference in any filing of the Company under the Securities Act of 1933, as amended, or the Exchange Act, whether made before or after the date hereof, regardless of any general incorporation language in such filing, except as shall be expressly set forth by specific reference in such filing.

**Item 9.01 Financial Statements and Exhibits.**

(d) Exhibits

| Exhibit No. | Description |
|---|---|
| 99.1 | Corporate Presentation dated January 2025. |
| 104 | Cover Page Interactive Data File (the cover page XBRL tags are embedded within the Inline XBRL document) |

**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.**

By: /s/ Daniel Lochner
Daniel Lochner
Chief Financial Officer

Dated: January 13, 2025

Exhibit 99.1

# Innovating GPCR-Targeted Therapies to Reach Large Untapped Market Opportunities

JANUARY 2025

TECTONIC Therapeutic

# 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 1b and Phase 2 clinical trial for TX45, in Group 2 Pulmonary Hypertension; 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; and our ability to identify and develop additional product candidates.

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 our Quarterly Report on Form 10-Q filed with the SEC on November 12, 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.

# Tectonic Tx: GPCR-Targeted Therapies for High-Value Opportunities

| | |
|---|---|
| **Clinical-Stage Biotech** | **TECX focused on discovery & development of GPCR-target biologics with significant unmet need**<br>• Founded in 2019 by Tim Springer and Andrew Kruse, TECX went public via reverse merger (AVROBIO) in June 2024 with a concurrent private placement of approximately $131 million |
| **Tenured Team** | **Executive team with numerous accomplishments, resulting in 20 "first" approvals** |
| **TX45 Lead Pipeline Asset** | **Long-acting relaxin in Phase 2, with de-risking Phase 1b topline results expected in Q1'25**<br>• Initial indication targeting Group 2 Pulmonary Hypertension (PH) associated with Heart Failure with Preserved Ejection Fraction (HFpEF), or PH-HFpEF<br>• Positive Phase 1a clinical trial results support best-in-class potential, including favorable safety profile<br>• Potential to target other indications, including other PH groups, heart failure and renal disease |
| **Relaxin Potentially Ideal for PH-HFpEF** | **Relaxin physiologic and hemodynamic effects demonstrated in prior clinical studies**<br>• Prior clinical development of relaxin by Novartis adds to clinical rationale for TX45 targeting PH-HFpEF |
| **PH-HFpEF Significant Market Potential** | **>1M+ patients in the U.S. with no approved therapy*; high 5-year mortality**<br>• Eli Lilly and Astra Zeneca also pursuing relaxin programs targeting heart failure indications and renal disease |
| **TX2100 Second Pipeline Asset** | **Targeting rare bleeding disorder called Hereditary Hemorrhagic Telangiectasia (HHT)**<br>• Significant market potential, no approved therapies for HHT, estimated ~75K patients in the U.S. alone (15-20% severe)<br>• Phase 1 clinical trial initiation expected in Q4'25 / Q1'26 |
| **Near-term Catalyst** | **TX45 Phase 1b, hemodynamic topline results in PH-HFpEF subjects (Part A) expected in Q1'25**<br>• Topline results from Part B of Phase 1b, hemodynamic trial evaluating PH-HFrEF subjects expected in 2H'25 |
| **Well-Capitalized** | **~$159 million in cash as of 9/30/24, expected to provide a cash runway into mid-2027** |

* *Estimates based on company sponsored market analysis conducted by Health Advances*

# This Accomplished Team Has Delivered for Patients and Investors

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

Celgene · MERCK · Columbia University · KEYTRUDA (pembrolizumab) Injection 100 mg

**Daniel Lochner**
CFO

VIATRIS · Goldman Sachs · OYSTER POINT · Columbia University

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

NOVARTIS · GNF · Penn · BRAFTOVI (encorafenib) 75 mg capsules

**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 · Washington University in St. Louis School of Medicine · DUPIXENT (dupilumab) injection 200mg · 300mg

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

Fusion · BAYER · Eisai · LEERINK SWANN · RBS

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

**FOUNDED MULTIPLE SUCCESSFUL COMPANIES**

LeukoSite · moderna · MORPHIC THERAPEUTIC · SEISMIC THERAPEUTIC · Scholar Rock

2022 Lasker Award

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

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

HARVARD MEDICAL SCHOOL · SEISMIC THERAPEUTIC

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

# Biologics Offer Advantages Over Small Molecules in Targeting GPCRs, Hold Potential to Transform Therapeutic Landscape

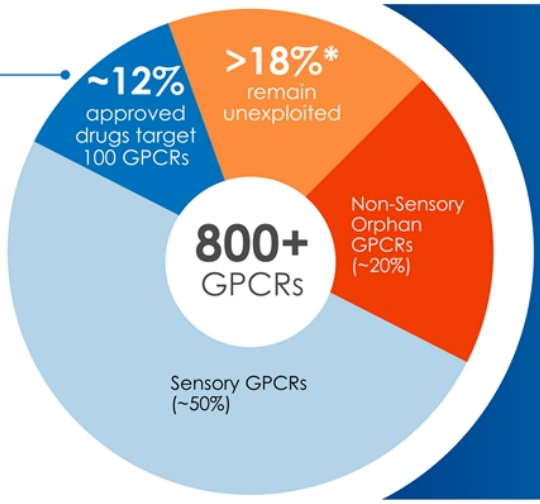
## Of the approved drugs that target GPCRs only three are antibodies

**>470**
approved drugs
(~33% of all)

**>$180B**
In annual sales

Predominantly small molecules

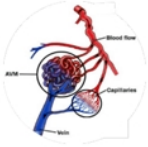
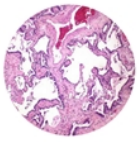
Address broad range of therapeutic areas




- When difficult to target with small molecule, biologic captures complexity of ligand/receptor engagement
- Biologic minimizes off-target binding to improve safety/tolerability
- Engineer biologic to target or exclude tissue or compartment
- Bispecific approach enables dual target engagement when multi-modal action is required

*(*) 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

| | | | |
|---|---|---|---|
|  | Long-Acting Relaxin to Target RXFP1[1] | **Group 2 Pulmonary Hypertension (PH) due to HFpEF in Phase 2**<br>Positive Phase 1a clinical data | **Potential Best-in-Class Profile** |
|  | GPCR Antagonist[2] (anti-angiogenic) | **Hereditary Hemorrhagic Telangiectasia (HHT)**<br>Target pathway linked to disease pathway | **Potential First-in-Class** |
|  | GPCR Modulator[2] (anti-fibrotic) | **Fibrosis**<br>Supporting clinical data for one component of bispecific | **Bispecific Approach** |

**Scale of proof-of-concept studies:** ~50-200 subjects per indication; 3-6 months treatment endpoints

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

# Unique Pipeline of GPCR-Targeted Biologics Underpinned By TX45 Targeting PH-HFpEF with P1b Results Expected Q1'25


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


# TX45: Long-acting relaxin to address large, unmet need in Group 2 PH

RXFP1 agonist with differentiated profile

# TX45: Potential Best-in-class Treatment for Group 2 PH-HFpEF

| | |
|---|---|
| **Relaxin with optimized PK** | • Protein engineering has extended pharmacologic half-life to support monthly dosing<br>• Rigorous Phase 1 PK/PD model enabled robust Phase 2 dose selection |
| **High unmet need** | • Group 2 PH-HFpEF* has no approved therapy<br>• >1M+ patients in US** and high 5-year mortality |
| **Mechanism appears ideal to address disease pathology** | • Pulmonary and systemic vasodilator; improves cardiac relaxation during diastole<br>• Reversal of fibrosis in pulmonary vasculature and heart<br>• Anti-inflammatory |
| **Supporting clinical and pre-clinical data** | • Serelaxin demonstrated clinical and hemodynamic benefits in acute heart failure<br>• Clear benefit observed with TX45 in rodent PH and congestive heart failure models |
| **Streamlined and differentiated clinical strategy** | • Enrichment strategy for CpcPH patients where there is the greatest unmet need<br>• No outcome study needed<br>• Enables potential early launch relative to broad heart failure indication |
| **Potential to expand market** | • Other PH Groups, heart failure, renal disease |

** Heart Failure with preserved Ejection Fraction, ** US prevalence numbers for Class 2 and 3, estimates based on company sponsored market analysis conducted by Health Advances*

# Significant Pharma Interest in Relaxin

## Tectonic has potential best-in-class molecule

| Company | Format | Formulation | Half Life in NHV | Dosing* | Patient Population | Phase 2 Endpoints |
|---|---|---|---|---|---|---|
| TECTONIC Therapeutic | Fc-Fusion (TX45) | Sub Q | 14-20 days | Q4 Weeks | Group 2 PH / HFpEF (enriched for CpcPH) | Change in pulmonary vascular resistance (PVR) |
| AstraZeneca | Fc-Fusion (AZD3427) | Sub Q | 7-9 days** | Q2 Weeks* | Group 2 PH / HFpEF *and* HFrEF | Change in pulmonary vascular resistance (PVR) |
| AstraZeneca | Small Molecule (AZD5462) | PO | 3-6 hours | QD* | CHF | Change in echocardiography parameters |
| Lilly | h-Albumin-mAb-Fusion (LY3540378) | Sub Q *Injection site reactions* | 8-10 days | Q Weekly* | HFpEF | Change in left atrial reservoir strain (LARS) |

** Expected dosing frequency, AZN and LLY based on dosing frequency in Phase 2 studies listed in clinical trials database*
*** Half life of 13-14 days reported in patients with CHF based on sparse PK profiling*

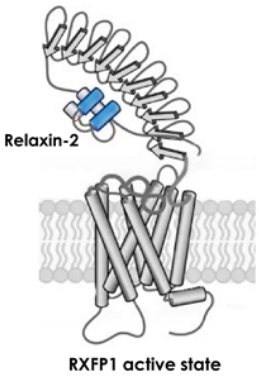
# Hemodynamic and Anti-fibrotic Properties of Relaxin Demonstrated by its Role in Pregnancy

## Pharmacology

**AGONIST**
Natural Ligand of RXFP1 Receptor

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

Relaxin upregulated in pregnancy



RXFP1 active state

## 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

## Background

- Program sponsored by Novartis
- Serelaxin half life <9 hours, a major hurdle for development for chronic disease
- 2–day continuous IV dosing in patients with acute heart failure

## Results and Insights

- Serelaxin demonstrated safety in greater than 6,000 patients
- Meta-analysis showed significant benefit
- Development halted after pivotal study, AHF-2, failed to achieve co-primary endpoints
  - Trial design and operational challenges may have contributed to failure
  - More recently, Biomarker sub-study (N=1020) accepted Nov. 12, 2024 showed 45% improvement in 5-day worsening heart failure (p= 0.025) and biomarker changes, including reduction in NT-proBNP and Troponin replicated prior studies[1]
- RXFP1 agonism is beneficial in cardiovascular disease
- A long-acting relaxin in the ideal indication could benefit patients

**META ANALYSIS: Serelaxin was Efficacious in AHF**

| Study (WHF Day 5) | Relative Risk [95% CI] | N (Drug) | N (PBO) |
|---|---|---|---|
| **Meta Analysis** | **0.77 [0.67 – 0.89] p = 0.0002** | **6,090*** | **5,239** |
| 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] | 3,274 | 3,271 |
| RELAX-AHF-EU | 0.71 [0.52 – 0.98] | 1,756 | 894 |
| RELAX-AHF-ASIA | 0.42 [0.21 – 0.84] | 437 | 433 |

1. *A.A. Voors et al., European Journal of Heart Failure 2024*
* *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

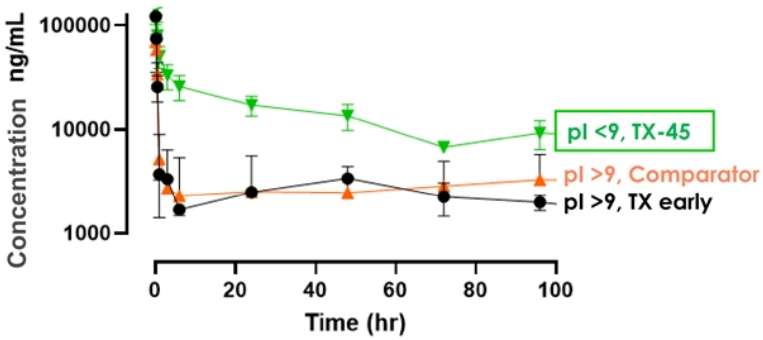
Relaxin has **very short *in vivo* half-life** Fc-fusion needed to improve PK

**Half-life extended relaxins 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 Molecules [2,3]**

**Preclinical Rat Pharmacokinetic Data**




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

# TX45 Initial Indication: Group 2 Pulmonary Hypertension (PH)

## Pulmonary hypertension consists of 5 distinct diseases, or groups

| | |
|---|---|
| **Group 1** PAH | • Idiopathic, hereditary or drug-induced<br>• Connective tissue disease-associated<br>• Congenital heart disease-associated |
| **Group 2** PH | • **Due to left heart failure (HFpEF, HFrEF*) or valvular heart disease**<br>• **CAD, HTN, T2DM**, high cholesterol are risk factors**<br>• **Two Subtypes: CpcPH & IpcPH** |
| **Group 3** | • Due to lung disease or hypoxia<br>• May be due to COPD, interstitial lung disease (i.e., IPF) or obstructive sleep apnea |
| **Group 4** CTEPH | • Chronic thrombo-embolic pulmonary hypertension – i.e., as a consequence of blood clots |
| **Group 5** Misc. | • Miscellaneous group including sickle cell, polycythemia vera, and sarcoidosis |

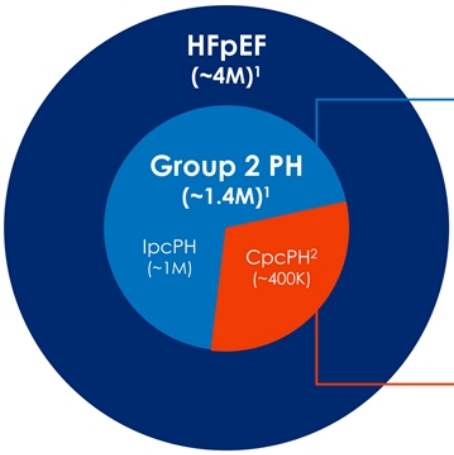
### Group 2 PH is chronic, progressive and the largest category of Pulmonary Hypertension

- Elevated blood pressure in the pulmonary arteries
- Chronically elevated pulmonary arterial pressures taxes the right side of the heart
- Pulmonary artery narrowing and muscularization
- Over time, the disease can lead to right heart failure and death
- No approved therapies

** Heart Failure with reduced Ejection Fraction*
*** CAD: Coronary Artery Disease, HTN: Hypertension, T2DM: Type 2 Diabetes Mellitus*

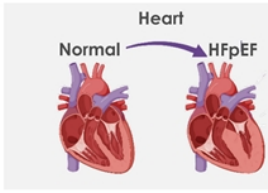
# Initial Focus on Group 2 PH due to Heart Failure With Preserved EF (HFpEF), Enriched for CpcPH Patients

## Clinical program designed to enable evaluation of efficacy in overall population and CpcPH



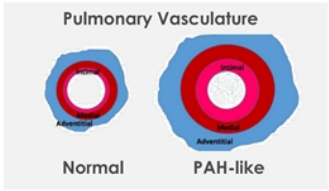

**IpcPH** (**I**solated, **p**ost **c**apillary **PH**)

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

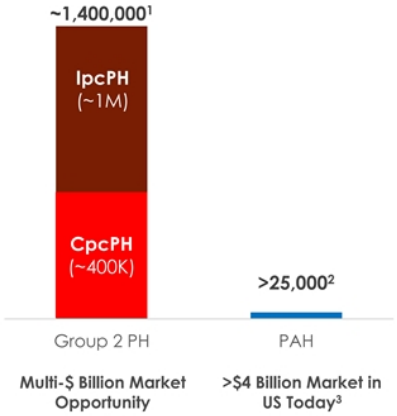



1. *US prevalence numbers for Class 2 and 3, estimates based on company sponsored market analysis conducted by Health Advances*
2. *Assumes diagnosis based on pulmonary vascular resistance (PVR) of > or equal to 3 wood units*

# Group 2 PH vs. PAH (Group 1)

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

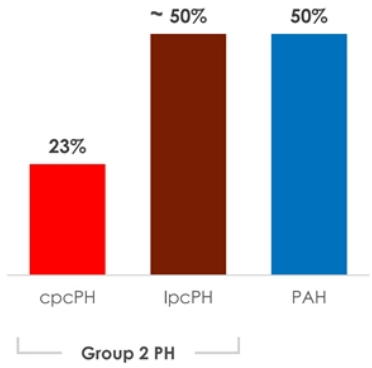
### US Prevalence >> PAH




**Multi-$ Billion Market Opportunity**

**>$4 Billion Market in US Today[3]**

### 5-Year Survival ≤ PAH[4]

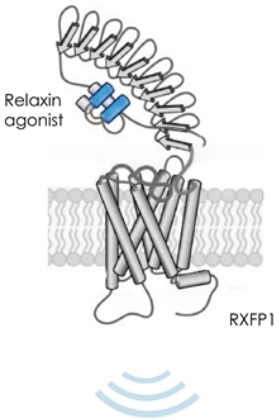


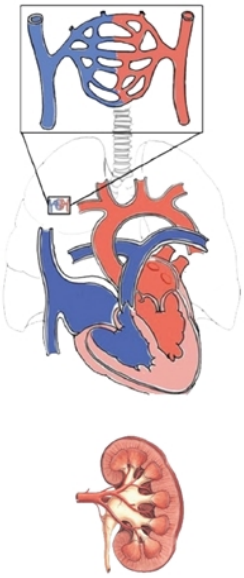

### No Therapeutic Options For Group 2 PH

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

1. US prevalence numbers for Class 2 and 3, estimates based on company sponsored market analysis conducted by Health Advances
2. www.pahinitiative.com
3. GlobalData
4. 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

# Relaxin Agonism of RXFP1 Elicits Changes in Multiple Organs and Organ Systems Important in PH-HFpEF





| | |
|---|---|
| ↑ **Vasodilation**<br>Pulmonary & Systemic<br>↑ NO ↓ Endothelin-1 | ↓ RV / LV*<br>Afterload |
| ↑ **LV Relaxation**<br>↑ SERCA2 function | Improved LV<br>Diastolic Function |
| ↓ **Fibrosis**<br>Anti-Inflammatory<br>↑ MMPs ↓ TGFβ | RV / LV and<br>Pulmonary Artery<br>Reverse Remodeling |
| ↑ **Renal Blood Flow** | ↑ $Na^+$ Excretion<br>↓ RV / LV Preload |

** RV: right ventricle; LV: left ventricle*

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

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

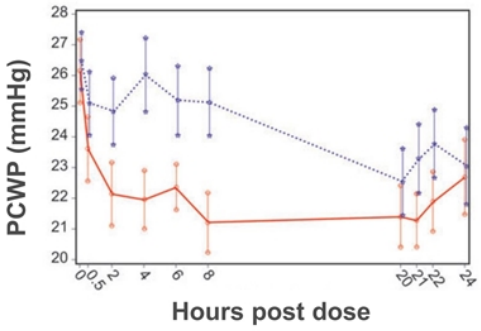
| CHARACTERISTICS OF PH-HFpEF | ANTICIPATED RELAXIN EFFECTS |
|---|---|
| Pulmonary artery narrowing, thickening, stiffening, fibrotic remodeling | **Pulmonary Vasodilation**<br>**Anti-inflammatory, anti-fibrotic** |
| Thickening and stiffening of Left Ventricle | **Peripheral vasodilation, improved cardiac relaxation, left ventricular remodeling** |
| Compromised kidney function | **Improvement in kidney function, natriuresis** |

**Combined decrease in pulmonary pressure and increased cardiac function are expected to be needed for efficacy in PH-HFpEF**

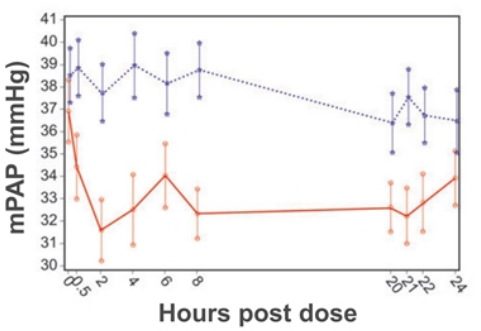
# In Acute Heart Failure (AHF), Serelaxin Improves LV Function (Lowering PCWP), and Lowers Pulmonary Pressures and Resistance (mPAP, PVR)[1]

## Furosemide given 4h prior to serelaxin infusion, and 8h after initiation of serelaxin

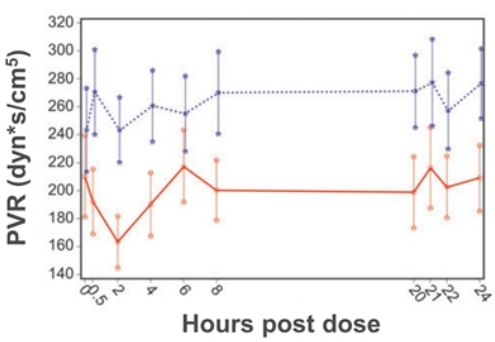
**PCWP**
Lung capillary pressure – measure of left atrial pressure




**mPAP**
Pulmonary (lung) artery pressure




**PVR**
Blood flow resistance in pulmonary arteries

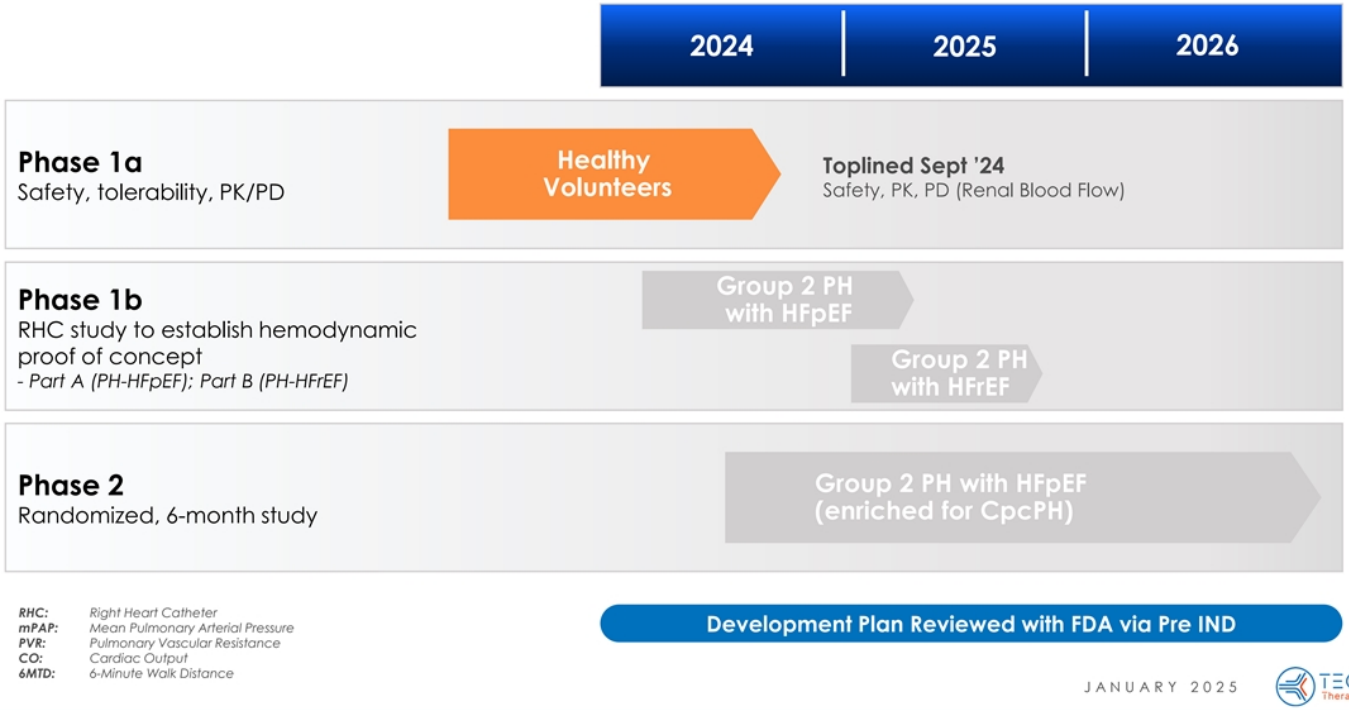



Treatment group — Serelaxin ····☆···· Placebo

In a similar study in patients with chronic heart failure, **a reduction in PCWP and an increase in cardiac output** was demonstrated[2]

1. Ponikowski P. et al. Eur. Heart J. 2014
2. Dschietzig T. et. Al. Ann NY Acad Sci 2009

# TX45 Development Program Overview

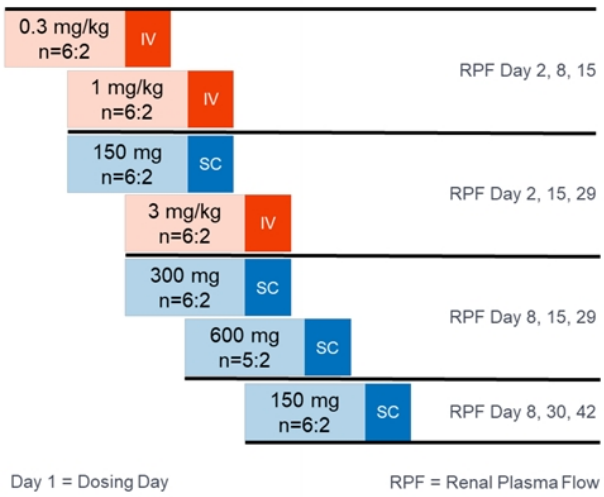



**RHC:** *Right Heart Catheter*
**mPAP:** *Mean Pulmonary Arterial Pressure*
**PVR:** *Pulmonary Vascular Resistance*
**CO:** *Cardiac Output*
**6MTD:** *6-Minute Walk Distance*

**Development Plan Reviewed with FDA via Pre IND**

# Phase 1a Clinical Study Complete

## Positive results support on-going development




### Benefits of the Study Design

- Exposure-response model developed with over 200 data points
- Overcomes impact of outlier values on mean values based on 6 patients per dose cohort
- Enables more robust dataset with which to choose doses for Phase 2

# TX45 Shows Favorable Safety Profile

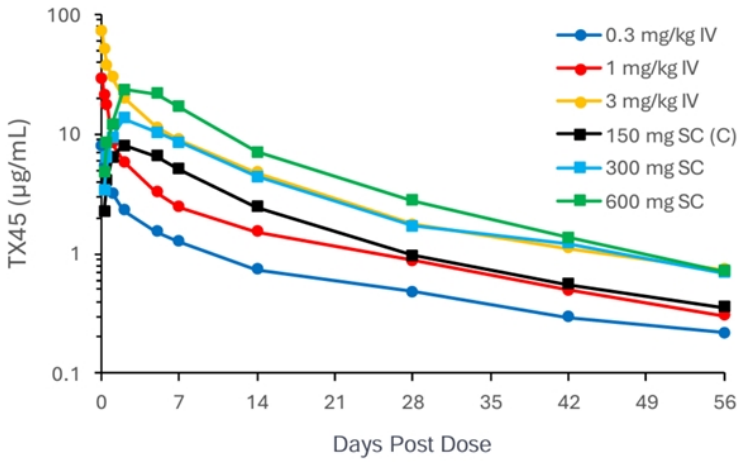
- No discontinuations or treatment-related SAEs
- No observed injection site reactions, immunogenicity, or detection of anti-drug antibodies
- Most common AE was transient orthostatic tachycardia (increases in heart rate with standing)
  - Placebo: 17% vs TX45: 23%
  - Not associated with drops in blood pressure
- No clinically meaningful changes in vital signs or labs

# TX45 Single Dose Demonstrates Extended Half-Life in Subjects

## TX45 Pharmacokinetics (PK) Profile

- Potential best-in-class terminal elimination half life of 14-20 days
- PK was dose proportional with subcutaneous bioavailability of ~50%
- Modeled accumulation at steady state after multiple doses is predicted to be 1.5X for 300 mg SC every 4 weeks (Q4W) and 2X for 300 mg SC every 2 weeks (Q2W)

**Single Dose TX45 Pharmacokinetics**



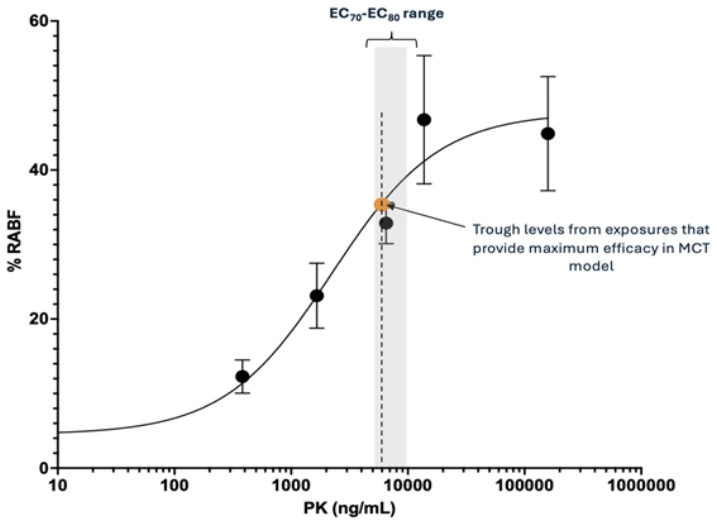
# Preclinical PK/PD from Acute Renal Blood Flow (RBF) Model Informs Target Plasma Concentration Levels at Trough for Maximum Therapeutic Effect

## 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 provide ~ $EC_{70}$ response in the RBF model and predict a trough exposure of 2 ug/ml in humans *




* *The exposure necessary for human EC70 is predicted to be 2ug i.e. 3-fold lower than in rats given the 3x greater potency of TX45 on human RXFP1 compared to rat RXFP1*

# Robust Human-Exposure Model Allows for Phase 2 Dose Selection

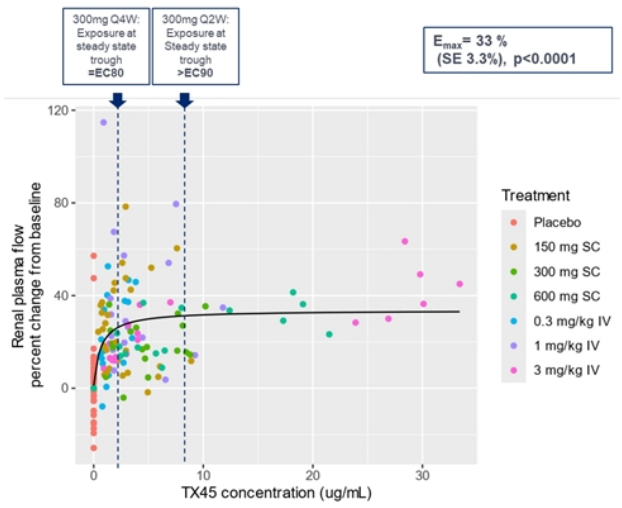
## Phase 1a Renal Plasma Flow (RPF)

- Mean dose cohort effects (n=6 per cohort) demonstrated increased renal plasma flow of up to 42%
- Incorporation of all exposure-response data across all doses and time points post dose resulted in a modeled Emax = 33% (SE 3.3%, p-value < 0.0001)

## Phase 2 Dose Selection

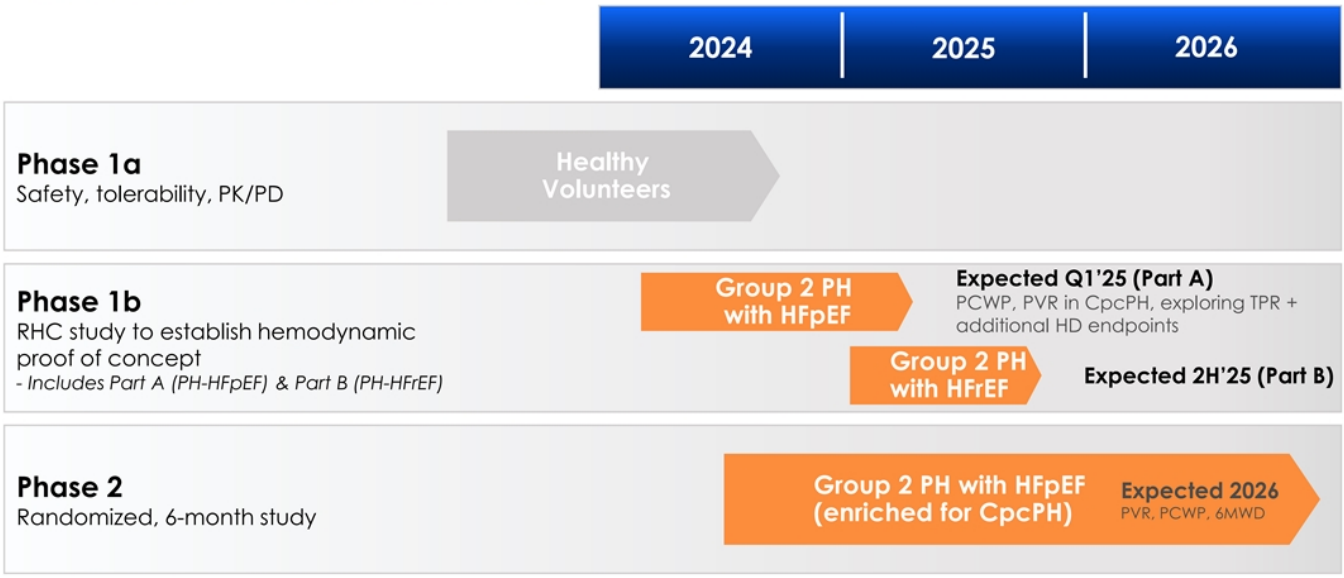
- 300 mg SC monthly: Steady state trough of 2.6 ug/ml ($EC_{80}$) slightly higher than preclinical predicted exposures associated with maximal efficacy
  - Preclinical studies predicted 2 ug/ml at trough would result in maximal efficacy
- 300 mg SC every 2 weeks: Steady state trough of 8.7 ug/ml (>$EC_{90}$), to evaluate whether increased exposure translates to greater efficacy

**TX45-RPF $E_{max}$ model**



# TX45 Development Program Overview

## Planned readouts in 2025 and 2026

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**Development Plan Reviewed with FDA via Pre IND**

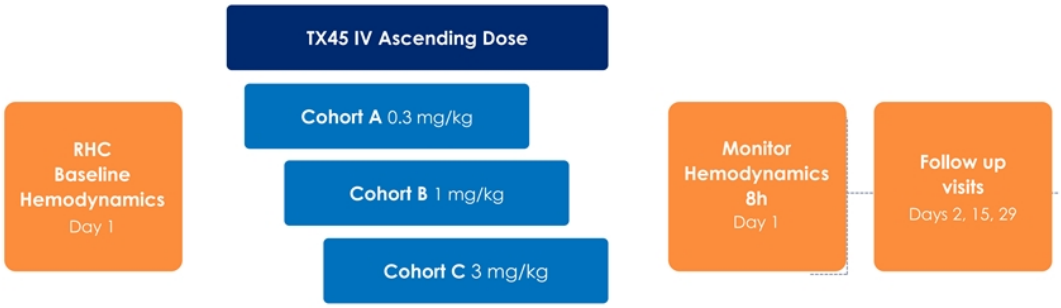
# TX45 Phase 1b Trial Design (Part A)

## Open label single dose safety and hemodynamics trial in PH-HFpEF

**Study Goals:**

- Establish single dose safety in patients
- Demonstrate relevant acute hemodynamic changes consistent with improvement in **both** LV function as well as pulmonary vascular dysfunction

- **Primary Endpoint:** Safety and Tolerability
- **Key Secondary Endpoints:** PCWP in all patient and PVR in CpcPH subgroup




**New Part B added, evaluating PH-HFrEF subjects, initiating in Q1'25 (3mg/kg dose); data expected 2H'25**

# Positive TX45 Phase 1b Trial Expected to Improve Probability of Success of TX45 in Later Stage Development

## GOAL: Treatment for PH-HFpEF needs to *both* increase LV function and improve pulmonary vascular component of the disease

- **Decrease (~15-20%) in pulmonary capillary wedge pressure (PCWP) in overall patient population**
  - PCWP provides insight into left ventricular function and correlates with exercise capacity in HFpEF and HFrEF[1]
- **Decrease (~15-20%) in pulmonary vascular resistance (PVR) in patients with CpcPH**
  - PVR is normal in IpcPH, so a floor effect is likely in this subgroup
  - In PAH, a lowering of PVR is associated with improvement in 6MWD[2]
- **Reduction in total pulmonary resistance (TPR) in overall patient population**

1. Wolsk E et al. Eur. J. Heart Fail. 2018
2. www.accessdata.fda.gov/drugsatfda_docs/nda/2017/209279Orig1s000MedR.pdf

# APEX Phase 2 Efficacy Trial Design for TX45

## Clinical trial in subjects with PH-HFpEF enriched for subjects with CpcPH subgroup

- Global multicenter, double-blind, randomized, placebo-controlled proof-of-concept clinical trial to evaluate the efficacy of TX45


- **Primary Endpoint:**
  Change from baseline in PVR
- **Secondary Endpoints:**
  Change from baseline in PCWP, 6MWD, KCCQ*

* *Kansas City cardiomyopathy questionnaire*


## HHT program

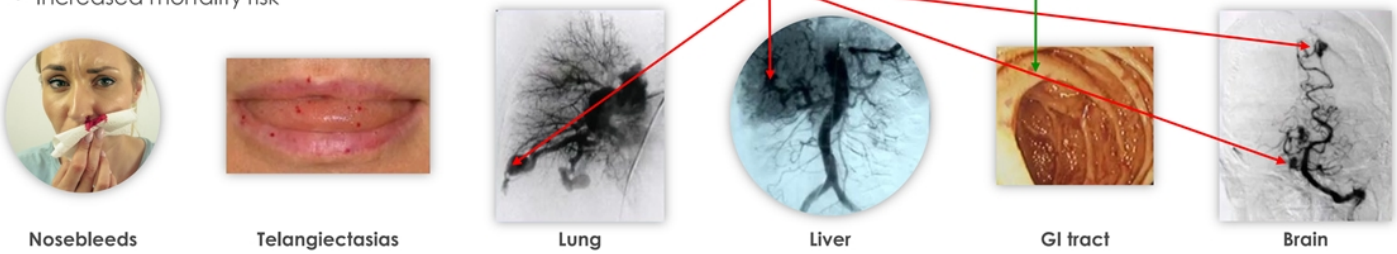
Potential first-in-class and indication opportunity for 2nd most common genetic bleeding disorder

# 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

**No currently approved therapies for HHT**




Nosebleeds | Telangiectasias | Lung | Liver | GI tract | Brain

**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**

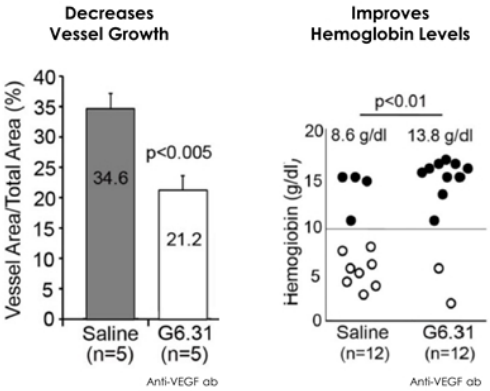
- Iron and transfusion dependent anemia (10-30% of patients)
- High output CHF 2nd to Liver AVM → liver transplant
- Stroke
- Brain abscesses and other deep tissue abscesses
- Venous thromboembolism (VTE)
- Pulmonary Hypertension
- Migraines

*AVM= arterial venous malformation

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

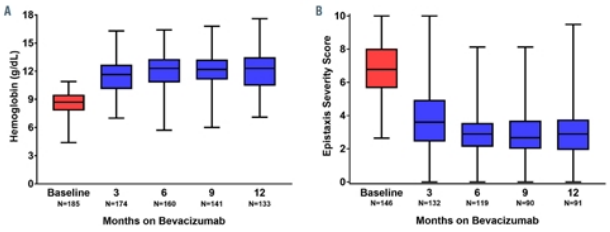
## Anti-VEGF mAb suppresses AVM formation, visceral hemorrhage in HHT model

ALK-1 Conditional Knock-Out
Wound-induced vascular response




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

## Anti-VEGF therapy reduces epistaxis severity, improves hem. Parameters in patients

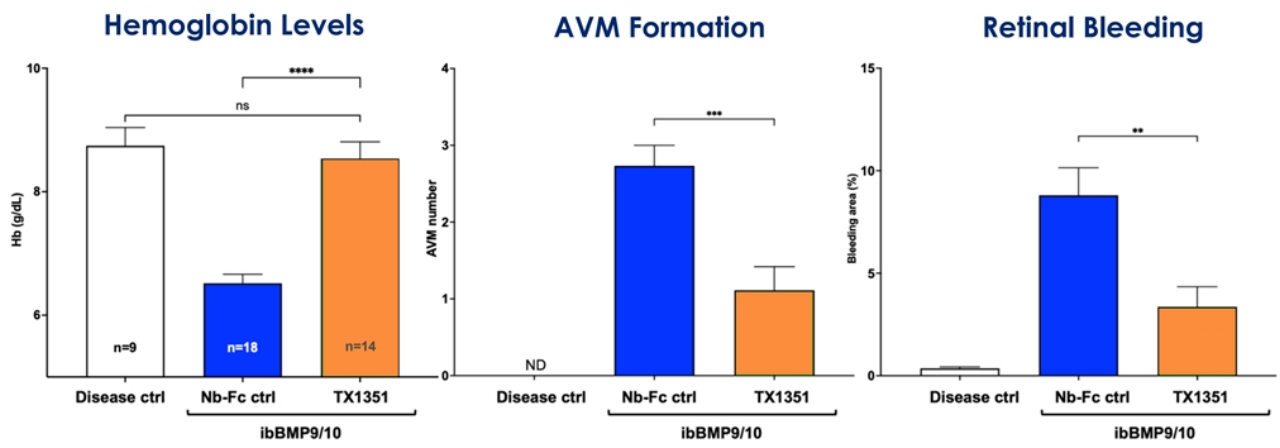



- No rigorous clinical studies ever conducted – only evidence is from IITs
  - Patent expiration on anti-VEGF mab lowered incentive to investment in label expansion
  - Dose and Dosing interval not well explored
- Treating physicians concerned about side effects

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

# A GPCR3 Antagonist Significantly Reduces AVM Formation and Bleeding in Animal Model of HHT

## Effects of anti-GPCR3 antagonist mAb in mouse HHT model generated by immuno-blocking of BMP9 and BMP10[1,2]




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
Angiogenesis. 2014 Oct; 17(4): 823–830
Haematologica. 2021 Aug 1; 106(8): 2161–2169

# Projected HHT Development Program Overview


## Platform

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 Antibody Discovery**
*Optimized high-diversity Fab and VHH libraries*
*Selection protocols optimized for membrane embedded GPCRs*

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

# Tectonic Tx: Positioned to Deliver on Value-Creating Milestones

## Two pipeline candidates addressing untapped markets with significant market potential

- Lead candidate, TX45, long-acting relaxin in Phase 2, with de-risking Phase 1b trial results expected in Q1'25
- TX45 has best-in-class potential for >1M+ patients with Group 2 Pulmonary Hypertension with HFpEF; potential to expand to other indications in heart failure and renal disease
- Second pipeline candidate for HHT, a rare bleeding disorder with no approved therapy

## Steady cadence of inflection points for 2025 and 2026

- Q1'25: TX45 Phase 1b, hemodynamic topline results in PH-HFpEF subjects (Part A)
- 2H'25: TX45 Phase 1b, hemodynamic topline results in PH-HFrEF subjects (Part B)
- 2026: TX45 Phase 2 topline trial results; HHT Phase 2 initiation late Q4'26 / early Q1'27

## Proven leadership team well-positioned to execute with strong balance sheet

- Executive team with proven track record
- ~$159 million in cash as of 9/30/24, expected to provide a cash runway into mid-2027


# Thank You

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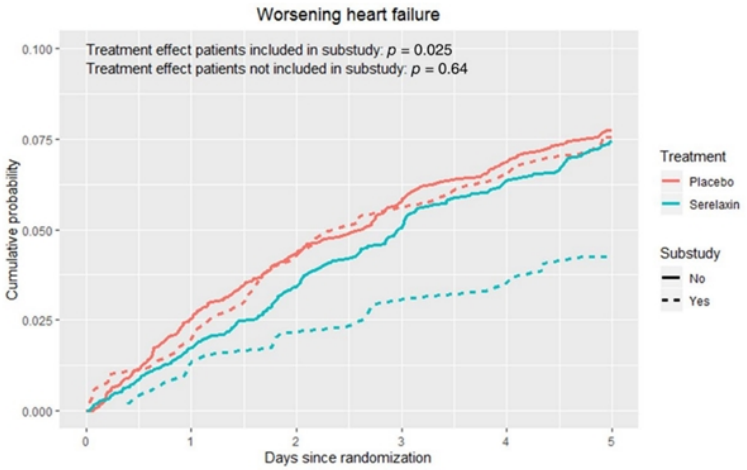
# Results of Serelaxin Pre-specified Substudy of RELAX-AHF-2 Demonstrated Multi-Organ Protection

## Background

- In RELAX-AHF-2, no benefit shown on 5-day heart failure worsening or 180d mortality with 48h IV serelaxin treatment
- Recent prospective, pre-specified substudy of RELAX-AHF-2 of 1,020 patients (503 randomly assigned to placebo, 517 to serelaxin) assessed changes in biomarkers of cardiac, renal and hepatic damage

## Results

- Serelaxin treatment led to significant Improvement in cardiac and renal injury biomarkers, including NT-proBNP, Troponin T, cystatin C, creatinine and uric acid
- In this sub-group, serelaxin treatment associated with 45% reduction in 5d heart failure worsening (p = 0.025), but no change in 180d mortality
- Improvement in biomarkers correlated with 180d survival




*Eur J Heart Fail. 2024 Dec 12. doi: 10.1002/ejhf.3551.*