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): September 19, 2024

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)**	**(IRS Employer Identification No.)**

490 Arsenal Way, Suite 210 **Watertown, MA**	**02472**
(Address of principal executive offices)	**(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 September 19, 2024, Tectonic Therapeutic, Inc. (the "Company") issued a press release titled "Tectonic Therapeutic Announces Favorable Phase 1a Safety, Tolerability and PK/PD Results for Lead Program TX45." 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 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 9.01. Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press release dated September 19, 2024.
99.2	Corporate Presentation dated September 2024.
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: September 19, 2024

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

Tectonic Therapeutic Announces Favorable Phase 1a Safety, Tolerability and PK/PD Results for Lead Program TX45

TX45 was well-tolerated with no observed immunogenicity, and demonstrated a favorable PK/PD relationship which was used to identify doses for the Phase 2 clinical trial

Results to be presented at the American Heart Association (AHA) Scientific Sessions in November 2024

Phase 1b single dose hemodynamic proof-of-concept clinical trial in Group 2 Pulmonary Hypertension in Heart Failure with Preserved Ejection Fraction (PH-HFpEF) escalated to the highest dose of TX45 (3 mg/kg) based on favorable tolerability profile observed at lower doses, with topline trial results expected in the second quarter of 2025

WATERTOWN, Mass., September 19, 2024 (GLOBENEWSWIRE) — 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 favorable Phase 1a topline data for its lead asset TX45, a long-acting, potentially best-in-class relaxin. TX45 is being developed for the treatment of Group 2 PH-HFpEF.

“These topline Phase 1a findings for TX45 validate the preliminary data previously presented at lower doses, and we look forward to sharing the full trial results at the AHA Scientific Sessions later this year,” said Alise Reicin, M.D., President and Chief Executive Officer of Tectonic. “Furthermore, the Phase 1a data reveal the successful translation of a robust preclinical model into the clinic. This allowed us to select doses for our global Phase 2 randomized, 6-month clinical trial evaluating the effect of TX45 on PH-HFpEF patients, enriched for those with combined pre- and post-capillary PH.”

The Phase 1a clinical trial is a single ascending dose study in healthy volunteers designed to assess the safety and tolerability of TX45 in addition to the pharmacokinetic (PK) and pharmacodynamic (PD) profile of TX45 based upon relaxin’s known ability to increase renal plasma flow. TX45 doses of 0.3, 1 and 3 mg/kg administered intravenously (IV) and 150, 300 and 600 mg given subcutaneously (SC) were examined. The trial demonstrated that TX45 had minimal adverse events and no evidence of immune-mediated clearance. By assessing the change in renal plasma flow from baseline at several timepoints after dosing, a robust PK/PD relationship was established to identify the Phase 2 doses and dosing regimens.

In a preclinical model of chronic pulmonary hypertension, trough exposures associated with maximal activity also demonstrated near peak increases in renal plasma flow. The PK/PD model created from the Phase 1a clinical data had a high concordance, when adjusted for differences in potency between species, with the PK/PD relationship observed in the preclinical studies. Tectonic has chosen dose regimens for the Phase 2 proof of concept clinical trial in patients with PH-HFpEF based upon these models. In the Phase 2 clinical trial, patients will be randomized to 300 mg SC (2ml injection) once monthly of TX45, 300 mg SC every other week of TX45, or placebo.

There are an estimated 6 million patients with heart failure in the U.S., with HFpEF representing up to approximately 50% of heart failure cases. The combined Group 2 PH population with HFpEF is conservatively estimated at over 600,000, and there are no currently available commercialized treatments.

Tectonic recently announced the U.S. Food and Drug Administration cleared its Investigational New Drug application for TX45. Screening for the Phase 2 APEX clinical trial has been initiated and topline results are anticipated in 2026.

In addition, Tectonic has an ongoing, single dose IV, open-label clinical trial evaluating the safety, tolerability and acute hemodynamic effects of TX45 in patients with PH-HFpEF. TX45 has already been administered at doses of 0.3 mg/kg and 1 mg/kg and is now being dosed at 3 mg/kg, based upon the favorable tolerability profile at lower doses. This trial is currently assessing TX45's acute effects on pulmonary capillary wedge pressure and pulmonary vascular resistance in addition to other hemodynamic assessments by right heart catheterization. Recruitment for this clinical trial has been better than expected and topline results are expected in the second quarter of 2025.

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 G-protein coupled receptor (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.

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 due to left-sided heart disease, specifically pulmonary hypertension secondary to left heart failure with preserved ejection fraction (PH-HFpEF).

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 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, often where therapeutic options are poor or nonexistent, as these are areas where 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 and follow @TectonicTx on X 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 preclinical studies and clinical trials of Tectonic's product candidates, including the ongoing Phase 1a and Phase1b clinical trial for its lead program, TX45, in Group 2 PH-HFpEF; the initiation of the Phase 2 clinical trial of TX45 in Group 2 PH-HFpEF including clinical trial design and endpoints; the 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 under the heading "Risk Factors" in Tectonic's quarterly report on Form 10-Q filed with the SEC on August 14, 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 and follow @TectonicTx on X (formerly Twitter) and LinkedIn.

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Exhibit 99.2

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

September 2024

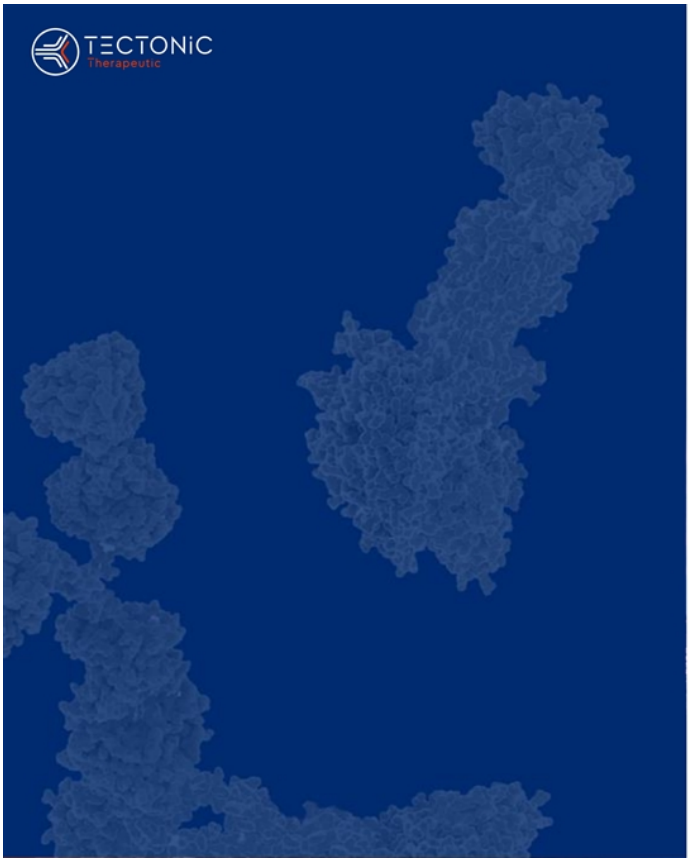
TECTONIC Therapeutic

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," "future," "planned" and "estimates" 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 and Phase1b clinical trial for its lead program, TX45, in Group 2 pulmonary hypertension secondary to left heart failure with preserved ejection fraction (PH-HFpEF); the proposed initiation of the Phase 2 clinical trial of TX45 in Group 2 PH-HFpEF, including anticipated trial design and endpoints; the anticipated market opportunity of TX45 to address the unmet needs of patients living with PH-HFpEF; 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 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 August 14, 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 2 Best-In-Class Relaxin Agonist for "Group 2 PH"

First-In-Class "HHT" Program

- First two assets address indications with no approved therapy
  1. **TX45**: RXFP1 agonist - potential therapy for Group 2 PH[1] in HFpEF[2]
     - >600,000 Patients in US alone (>20 times PAH)
     - Phase 1a trial complete. TX45 was well tolerated, no immunogenicity observed, and a favorable PK/PD relationship was demonstrated
     - Phase 1b hemodynamic proof of concept data expected in Q2-2025
     - Phase 2 randomized trial initiated in Aug '24, data expected in 2026
  2. **GPCR3**: 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
- **$185M[3] cash as of 6/30/24, expected to provide runway into mid-2027**

[1]Pulmonary Hypertension; [2]Heart Failure with Preserved Ejection Fraction; [3]Cash and cash equivalents as of June 30, 2024, prior to the payment of accrued transaction and related expenses of ~$14.4M, are expected to fund current operational plans into mid-2027

TECTONIC Therapeutic

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)

TECTONIC Therapeutic

Team Track Record: >20 1st Approvals with >$50B In Annual Sales

1st approvals and indication expansions shown below

ONCOLOGY/ IO

KEYTRUDA (pembrolizumab)
Abecma (idecabtagene vicleucel)
BAVENCIO (avelumab)
Breyanzi (lisocabtagene maraleucel)
Campath (Alemtuzumab For Intravenous Use Only)
BRAFTOVI (encorafenib)
VELCADE (bortezomib)
ZYKADIA (ceritinib)
TEPMETKO (tepotinib)
Odomzo (sonidegib)

IMMUNOLOGY/ INFLAMMATION

DUPIXENT (dupilumab)
Amevive (alefacept)
Entyvio (vedolizumab)
MAVENCLAD (cladribine) tablets 10 mg
ARCOXIA (etoricoxib)
MAYZENT (siponimod)
Simponi (golimumab)
Remicade (INFLIXIMAB)
ZEPOSIA (ozanimod)
RAPTIVA (efalizumab)
VIOXX (rofecoxib, MSD)

CARDIO/ METABOLISM

Entresto (sacubitril/valsartan) tablets
Praluent (alirocumab) Injection
CAMZYOS (mavacamten)

RESPIRATORY / ALLERGY

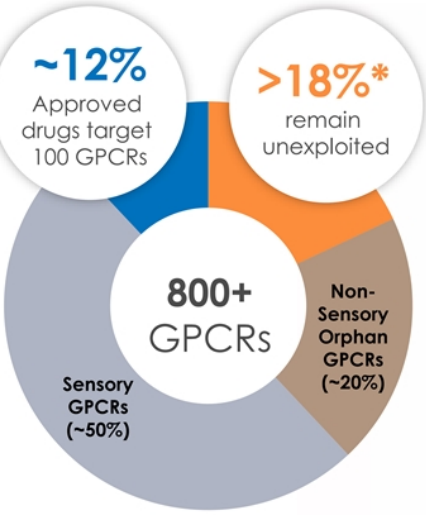
DUPIXENT (dupilumab)
Claritin
SINGULAIR
Nasonex
GRASTEK (Timothy Grass Pollen Allergen Extract Tablet for Sublingual Use 2800 BAU)

OTHER

Reblozyl (luspatercept-aamt) for injection 25mg • 75mg
INREBIC
EMEND (Aprepitant)

TECTONIC Therapeutic

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



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

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

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

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

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

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

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

TECTONiC Therapeutic

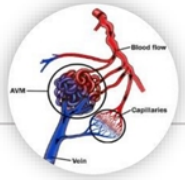
Our Unique Pipeline Opportunities are Enabled by Biologic Targeting of GPCRs

GROUP 2 PULMONARY HYPERTENSION (Group 2 PH) IN PHASE 2

Potential Best-in-Class

RXFP1 Agonist[1]

Supporting clinical data

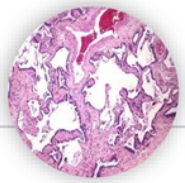


HEREDITARY HEMORRHAGIC TELANGIECTASIA (HHT)

First in Class & Indication

GPCR Antagonist[2] (anti-angiogenic)

Target pathway linked to disease genetics



FIBROSIS

Bi-specific Approach

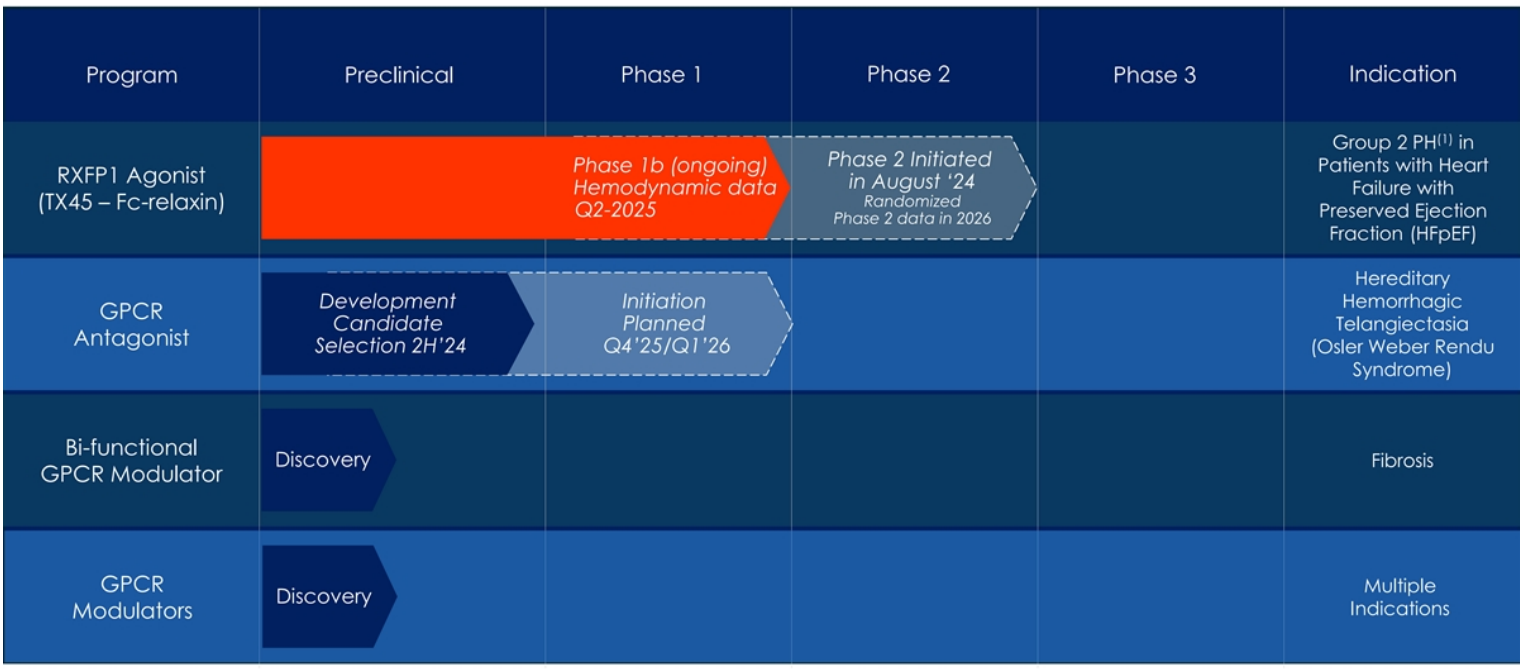
GPCR Modulator[2] (anti-fibrotic)

Supporting clinical data for one component of bispecific

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

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

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



(1) Pulmonary Hypertension

GEODe™ 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

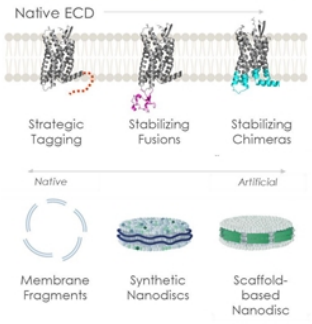
2.
In-vitro Yeast Display Libraries
provide high-diversity, without immune editing

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

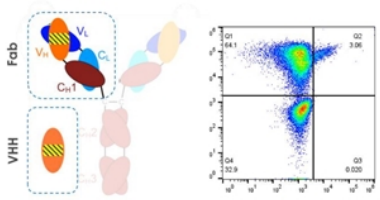
1. EXPRESSION AND PURIFICATION TECHNOLOGY

Produce Sufficient Quantities and Stabilize Them in the Correct Conformation



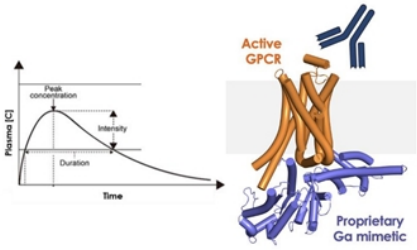
2. IN-VITRO YEAST DISPLAY LIBRARIES

Efficiently Screen Diverse Antibody Libraries Against GPCRs



3. PROTEIN ENGINEERING

- **Optimize Protein Pharmacology**
- **Engineer Proprietary Scaffolds for Agonist Discovery**

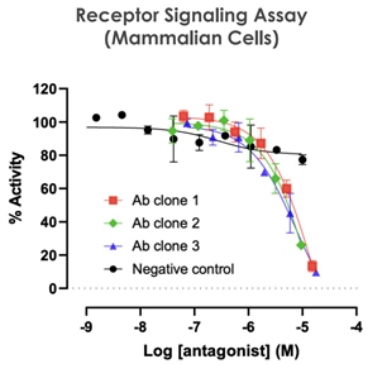


Large toolbox of biochemical methods, engineering tools, and assays

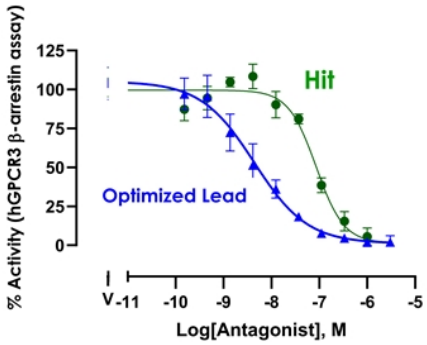
TECTONIC Therapeutic

GEODe™ Platform Discovery Capabilities Deliver Selective, Ligand Competitive Orthosteric Antagonists

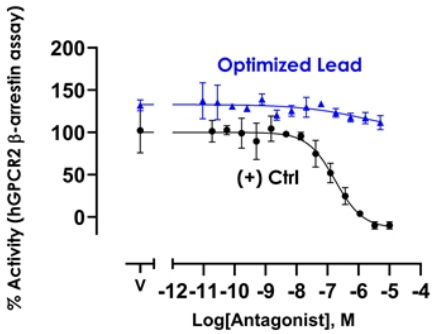
PURIFIED ANTIBODIES ARE FUNCTIONAL ANTAGONISTS*



OPTIMIZATION IMPROVES ORIGINAL POTENCY BY ~20X



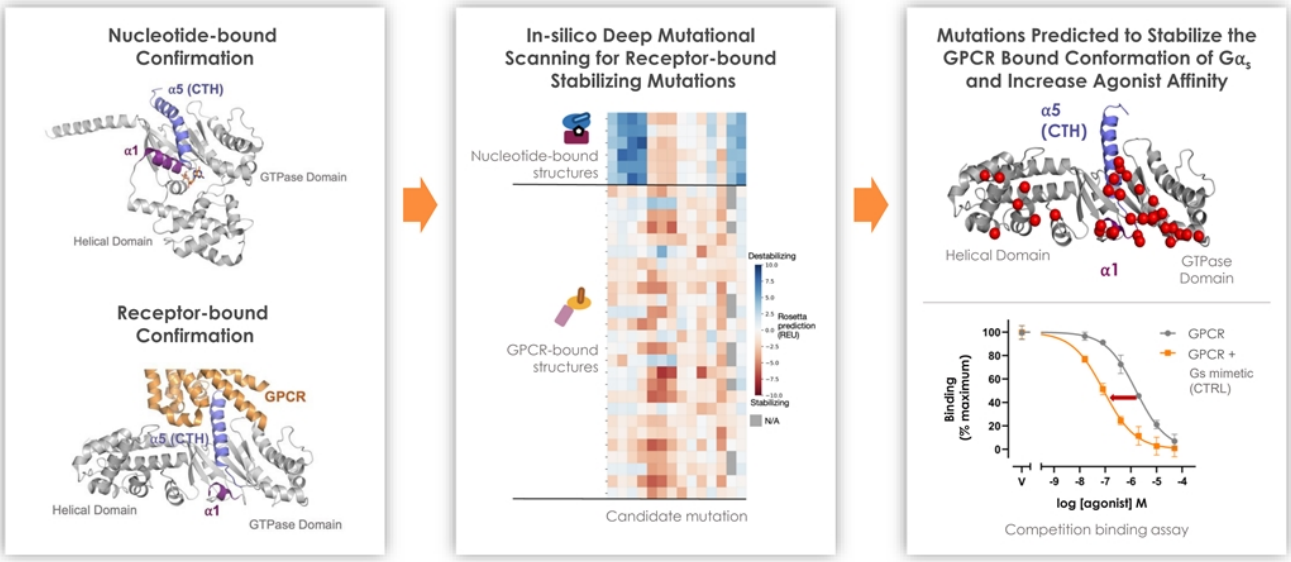
SELECTIVE (NO EFFECT ON OFF-TARGET GPCR)



**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 Gα Mimetics Is Driven by the Latest in Machine Learning and Energy Prediction Algorithms



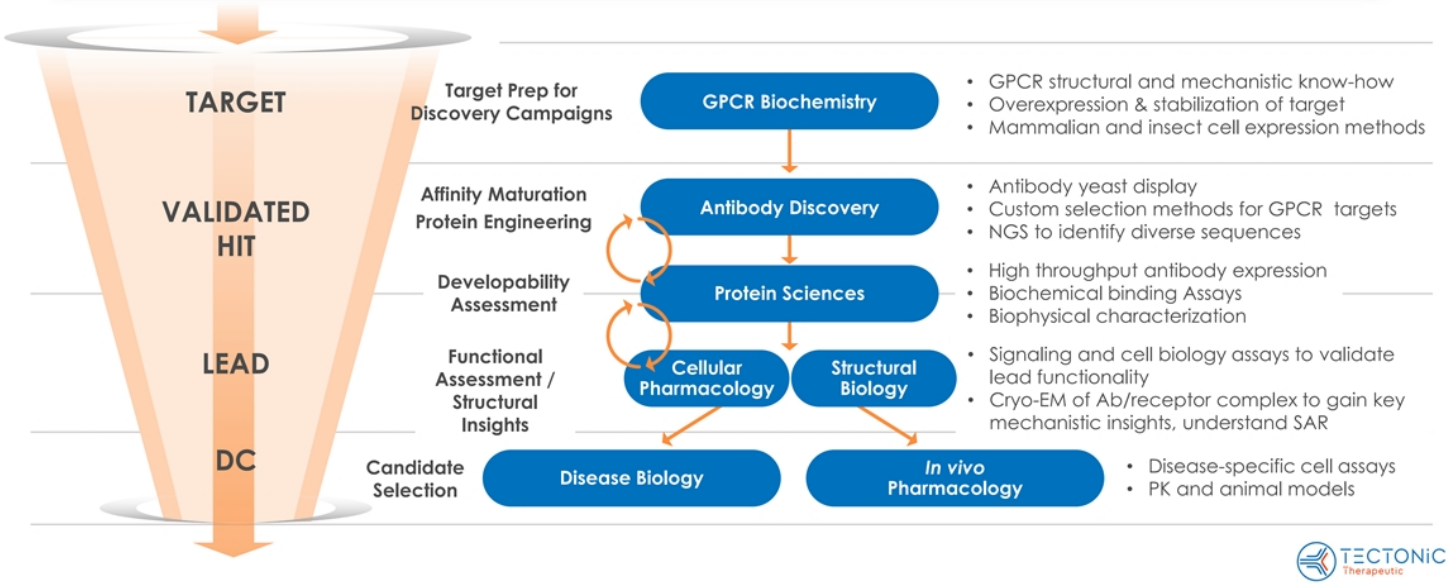
Ongoing enhancement of our ability to screen for biologics with agonist activity

TECTONiC Therapeutic

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

TECTONiC Therapeutic

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

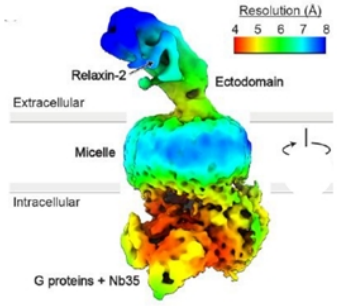
Pharmacology

AGONIST

Natural Ligand of RXFP1 Receptor

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

Relaxin upregulated in pregnancy



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

Facilitates Gestation

PULMONARY AND SYSTEMIC VASODILATOR

Increases cardiac output to accommodate the increased demand from developing fetus

ANTIFIBROTIC

Prepares musculoskeletal tissues for pregnancy and childbirth

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
Meta Analysis	**0.77 [0.67 – 0.89] p = 0.0002**	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 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

TECTONIC Therapeutic

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

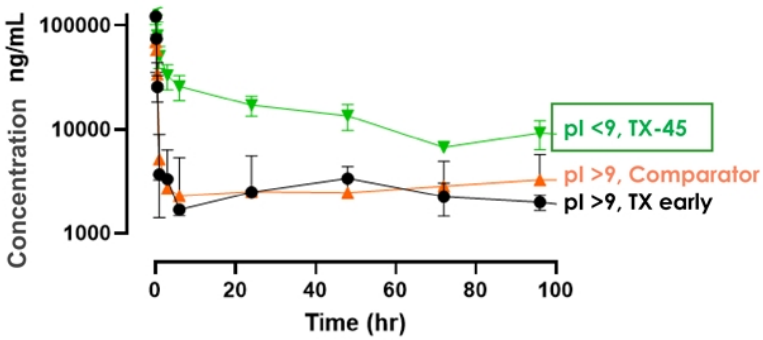
Relaxin has **very short *in vivo* half-life** Fc-fusion needed to improve PK

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

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

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

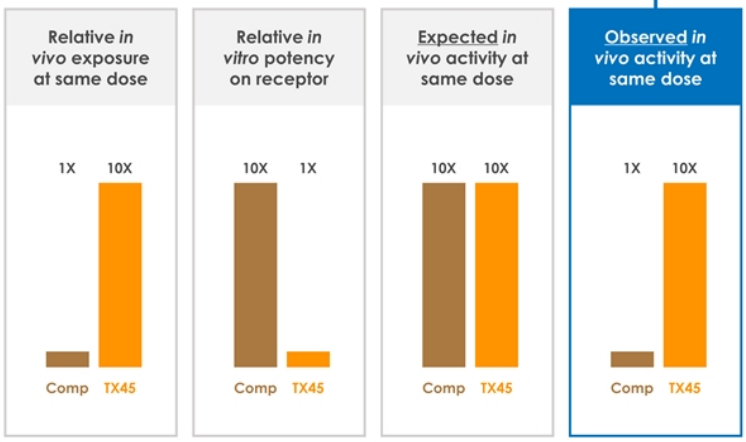
Preclinical Rat Pharmacokinetic Data

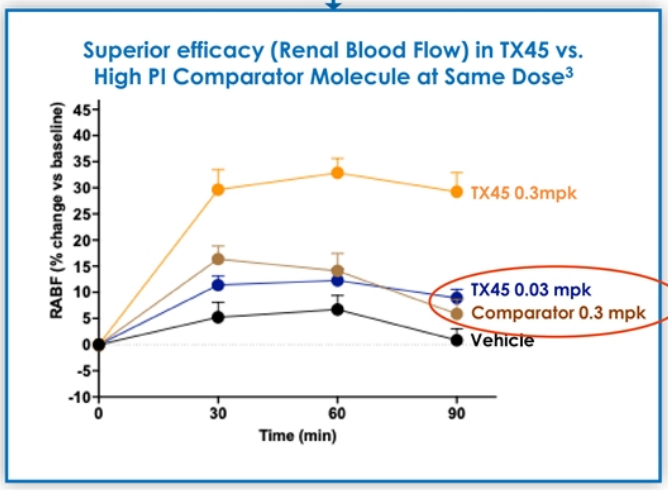


1. Isoelectric Point
2. High pI Fc-relaxin fusion protein described in literature
3. Source: Tectonic internal data

TX45 Reflects Significant Protein Engineering to Optimize Its Pharmacology

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





1. High pI Fc-relaxin fusion protein described in literature
2. ~0.03 mpk of TX45 has similar efficacy as 0.3 mpk of Comparator
3. Source: Tectonic internal data

TECTONIC Therapeutic

TX45 – Optimized RXFP1 Agonist for Group 2 PH in HFpEF

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

1. Heart Failure with preserved Ejection Fraction

Pulmonary Hypertension Consists of 5 Distinct Diseases

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

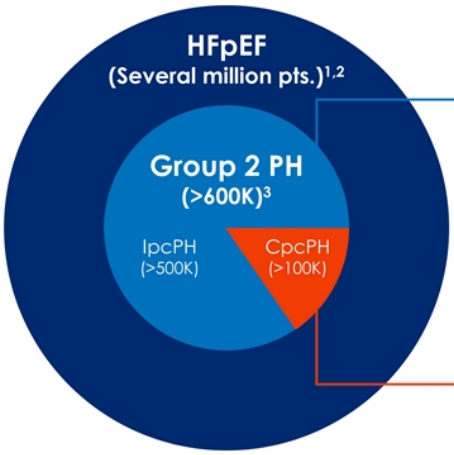
Group 1 ("PAH") (~25,000[1])	Group 2 (>600,000[1])	Group 3	Group 4 ("CTEPH")	Group 5 (Misc.)
• Idiopathic • Hereditary • Connective tissue disease-associated • Congenital heart disease-associated • Drug-induced	• **Due to left heart disease (HFpEF, HFrEF) or valvular heart disease** • **CAD, HTN, T2DM[2],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

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

TECTONIC Therapeutic

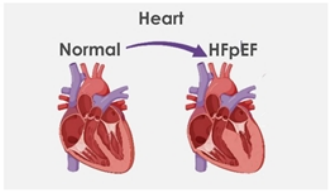
Our Focus is on the Group 2 PH Subset of Heart Failure with Preserved EF (HFpEF)

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



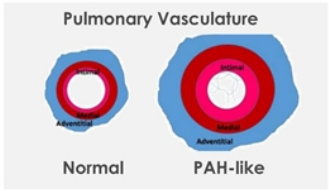
IpcPH (**I**solated, **p**ost **c**apillary **PH**)

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



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

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



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

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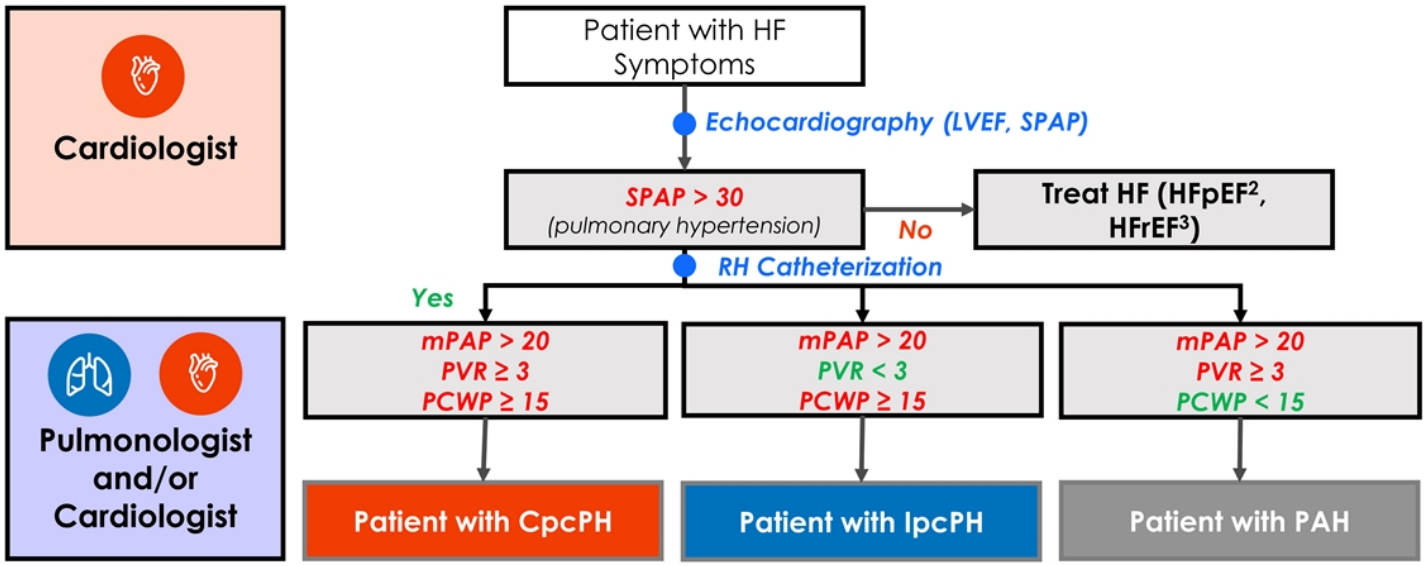
Group 2 PH: Patient Journey

Key Hemodynamic Measures in Pulmonary Hypertension

Measure	Definition	Detection Method(s) / Formulas	Clinical Significance
mPAP 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)**
PVR 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**
PCWP 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")**
CO 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; IpcPH isolated post-capillary PH
(2) HFpEF: Heart Failure with preserved Ejection Fraction
(3) HFrEF: Heart Failure with reduced Ejection Fraction

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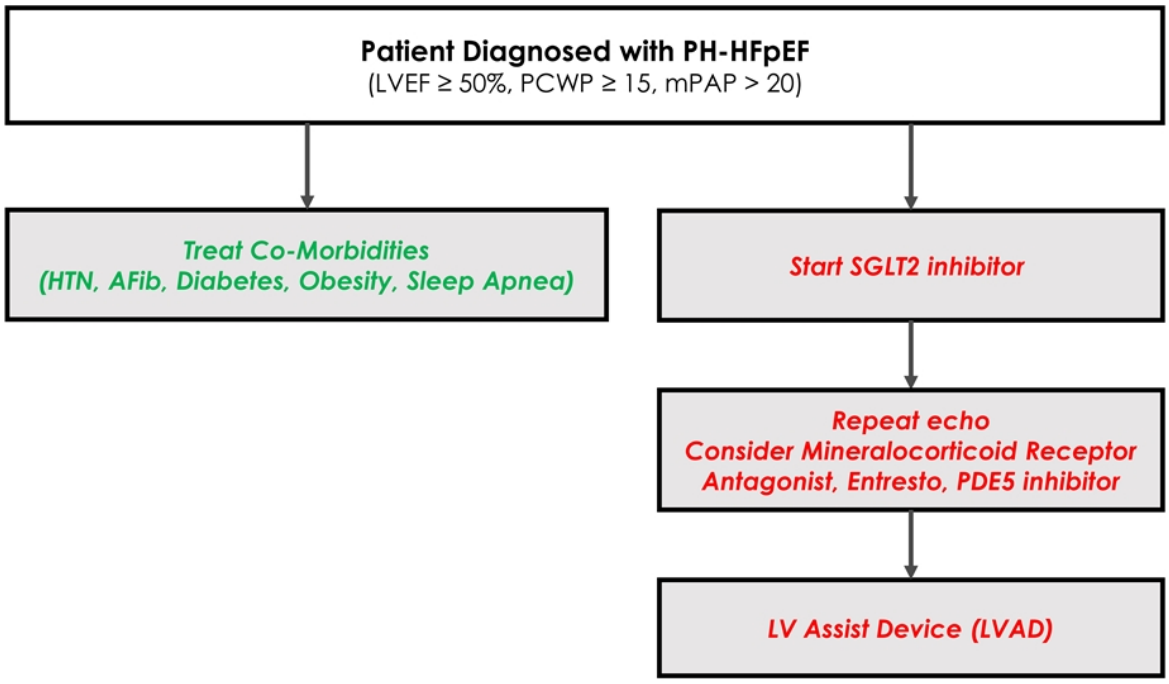
Treatment of Pulmonary Hypertension (PH) in the Setting of Heart Failure with Preserved Ejection Fraction (HFpEF)



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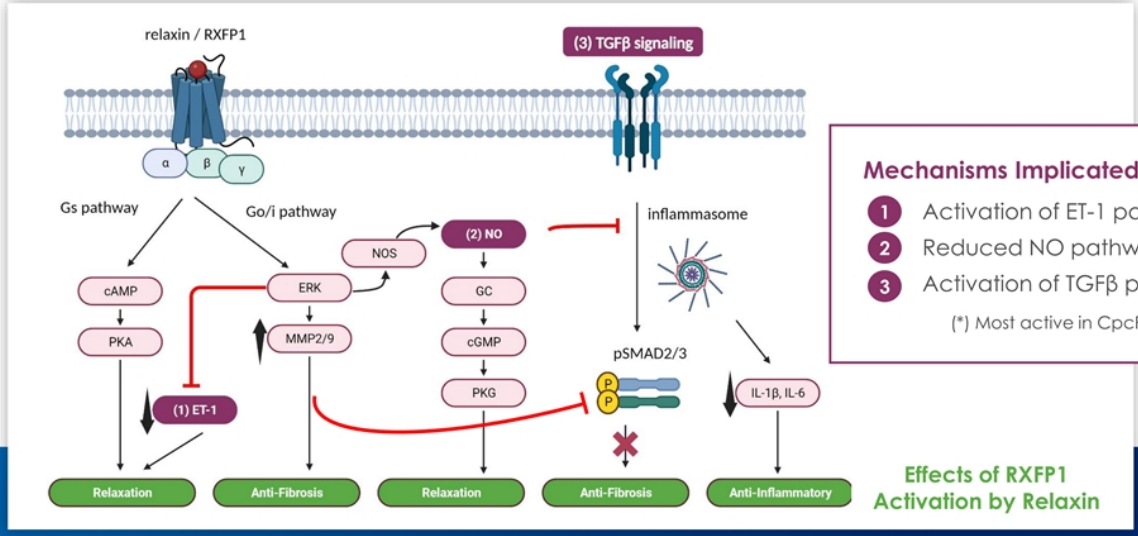
Relaxin Multimodal MOA Addresses Pathways Implicated in Group 2 PH Pathophysiology



Mechanisms Implicated in Group 2 PH

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

(*) Most active in CpcPH subset

Effects of RXFP1 Activation by Relaxin

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

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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

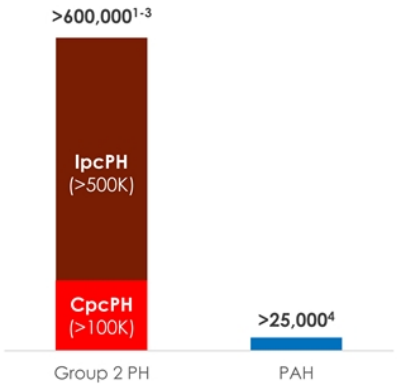
CHARACTERISTICS OF GROUP 2 PH	IpcPH	CpcPH	ANTICIPATED RELAXIN EFFECTS
Pulmonary artery narrowing, thickening, stiffening, fibrotic remodeling		✓	Pulmonary Vasodilation Anti-inflammatory, anti-fibrotic
Right Ventricular Dysfunction	✓	✓	Right ventricular remodeling
Thickening and stiffening of Left Ventricle	✓	✓	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

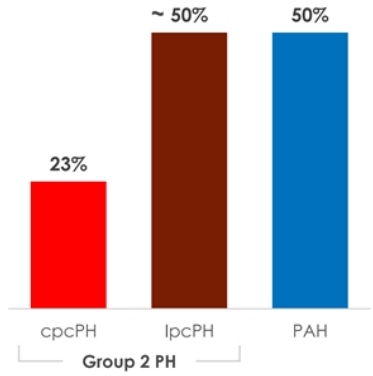
US PREVALENCE >> PAH



Multi-$ Billion Market Opportunity

>$4 Billion Market in US Today[5]

5 YEAR SURVIVAL ≤ PAH[6]



NO THERAPEUTIC OPTIONS

No approved therapies

...

Limited pipeline

PAH Drugs have not demonstrated convincing efficacy in Group 2 PH with the exception of PDE5i in CpcPH

Group 2 PH

Multiple drugs/ mechanisms approved

ET1R antagonists
PDE5 inhibitors
GC stimulators
Prostacyclins

ACTRII-Trap

PAH

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

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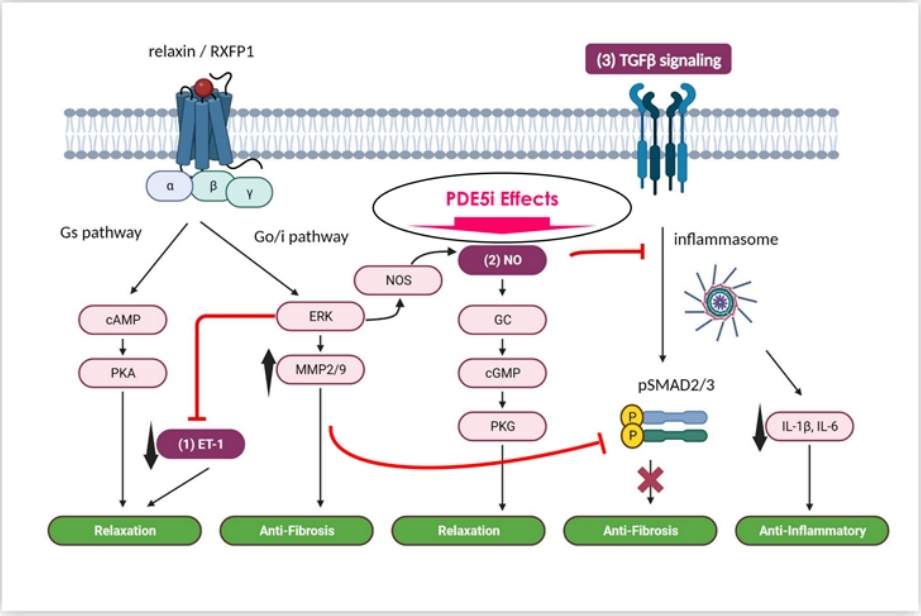
PDE5 Inhibitors Affect Only One of Several Pathways Addressed by Relaxin



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

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

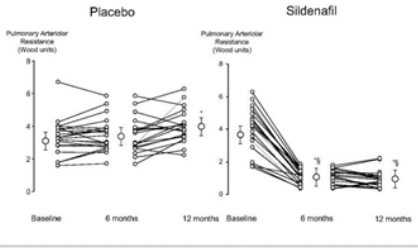
TX45 anticipated to be effective in both Cpc-PH and Ipc-PH because it targets additional anti-fibrotic and anti-inflammatory mechanisms on top of activation of the NO pathway

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

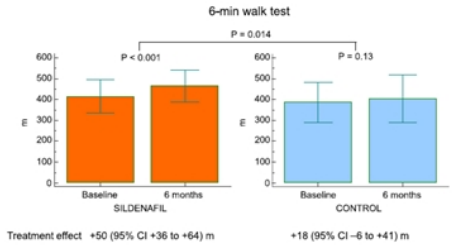
PDE5 Inhibitors Show Significant Benefit in CpcPH and HFpEF Despite Limited Mechanism of Action Compared with Relaxin

Expected to Increase POS of Relaxin in HFpEF and CpcPH

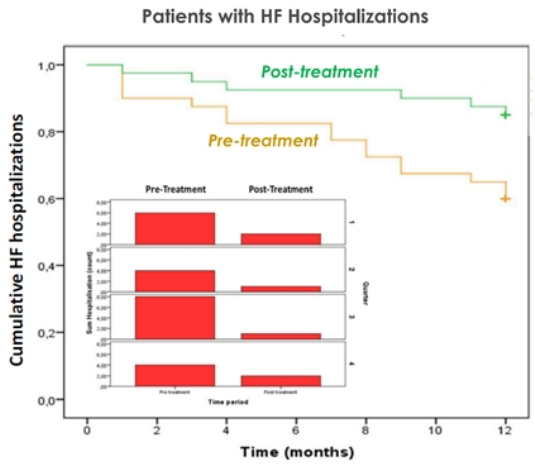
PDE5i LOWERS PVR(1)



PDE5i PRODUCES IMPROVEMENTS IN 6MWT (2)



PDE5i TREATMENT DECREASES HOSPITALIZATIONS (3)



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

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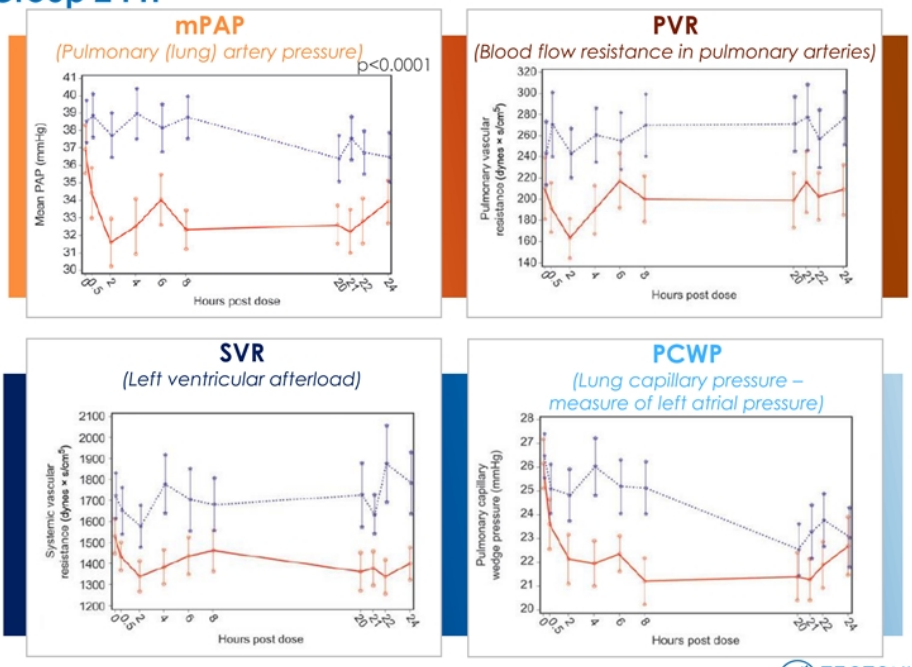
Relaxin Improves Hemodynamics in Heart Failure

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

TECTONiC Therapeutic

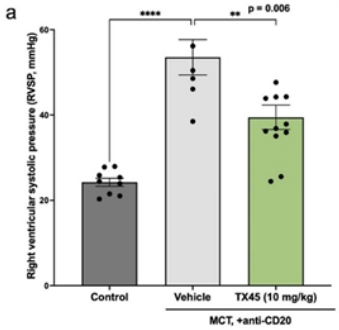
TX45 and Other Relaxin Preclinical Data

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

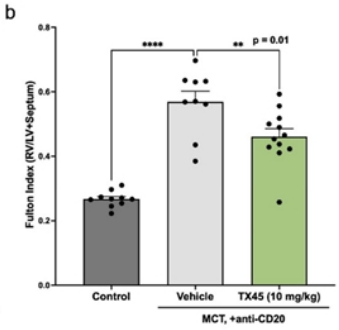
TX45 Efficacy in Monocrotaline-Induced Model of Pulmonary Hypertension in Rats

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

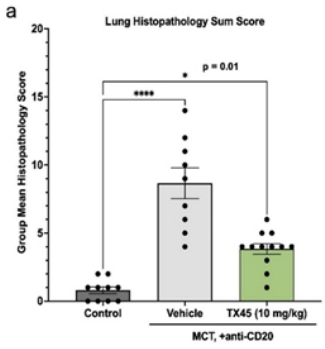
Improved Pulmonary Hemodynamics



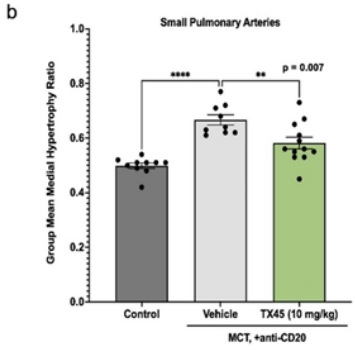
Reduced Cardiac Hypertrophy



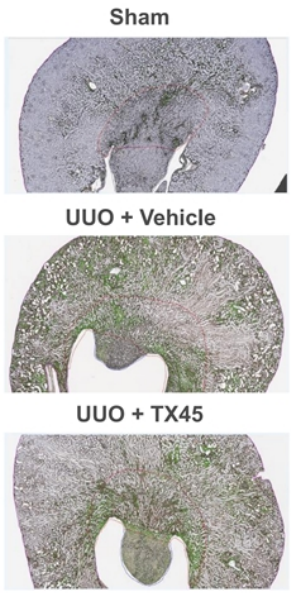
Reduced Histological Inflammation

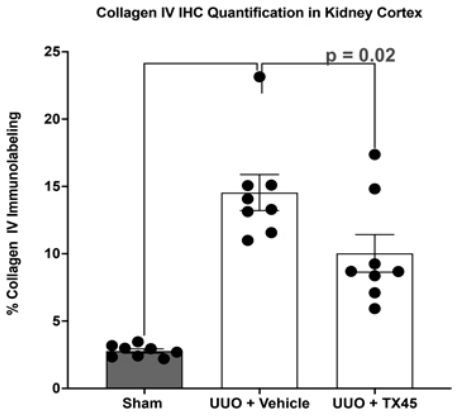


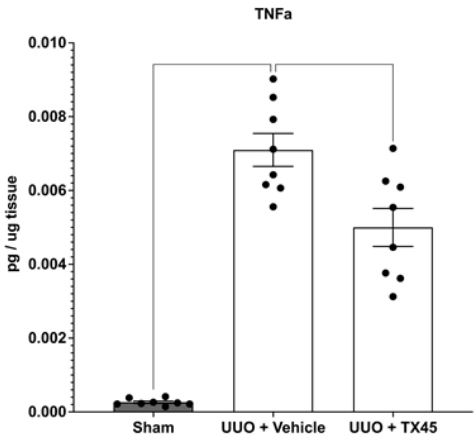
Reduced Pulmonary Arterial Muscularization



TX45 Significantly Reduces Collagen and TNFa levels in Mouse UUO Model of Renal Fibrosis







* Dotted red line defines the cortex region

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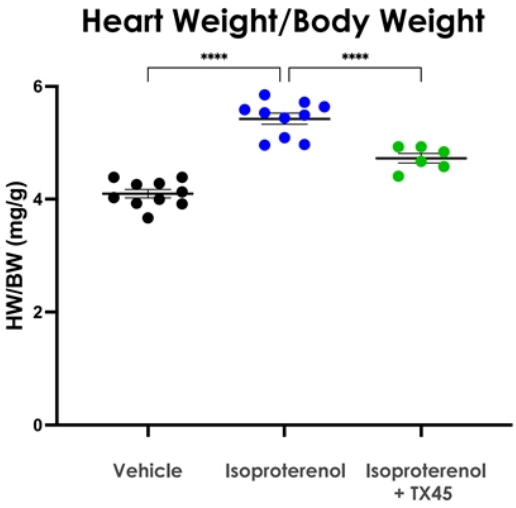
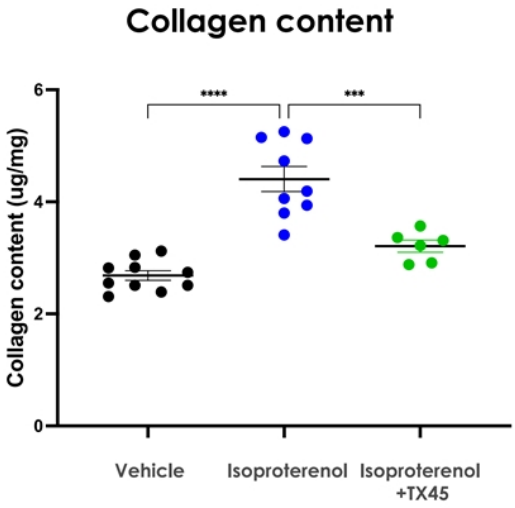
TX45 Reduces Cardiac Hypertrophy and Fibrosis in the Mouse Isoproterenol Induction Model



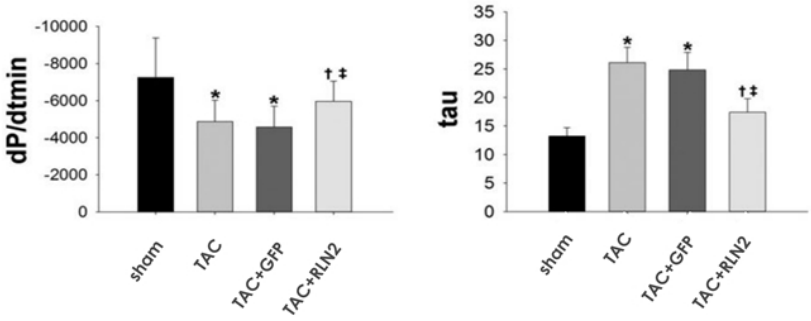


Relaxin Prevents Diastolic Dysfunction in a Model of HFpEF and Reverse Cardiac Fibrosis

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

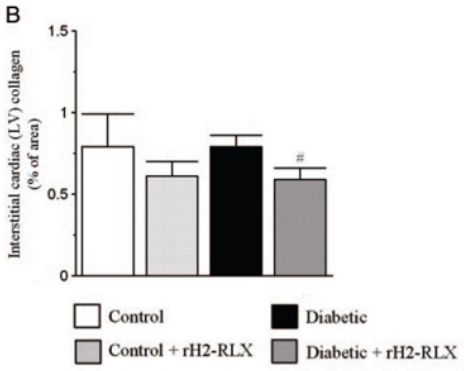
Human relaxin-2 Improves Diastolic Dysfunction

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



Human relaxin-2 reverses cardiac fibrosis

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



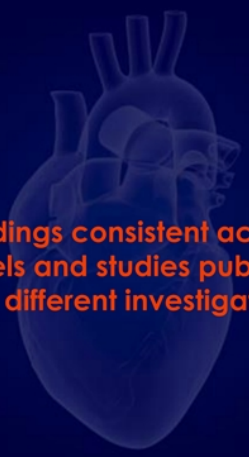
* GFP = green fluorescent protein (adenovirus used as negative control)

TECTONiC Therapeutic

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** TGFβ or ANG-II induced collagen synthesis in cardiac fibroblasts[1]
- ✓**Prevent** interstitial and perivascular fibrosis, with effect superior to enalapril[2]
- ✓**Prevent** diastolic dysfunction[3]
- ✓**Prevent** and **Reverse** cardiac hypertrophy[3]
- ✓**Reverse** cardiac inflammatory gene expression[4]



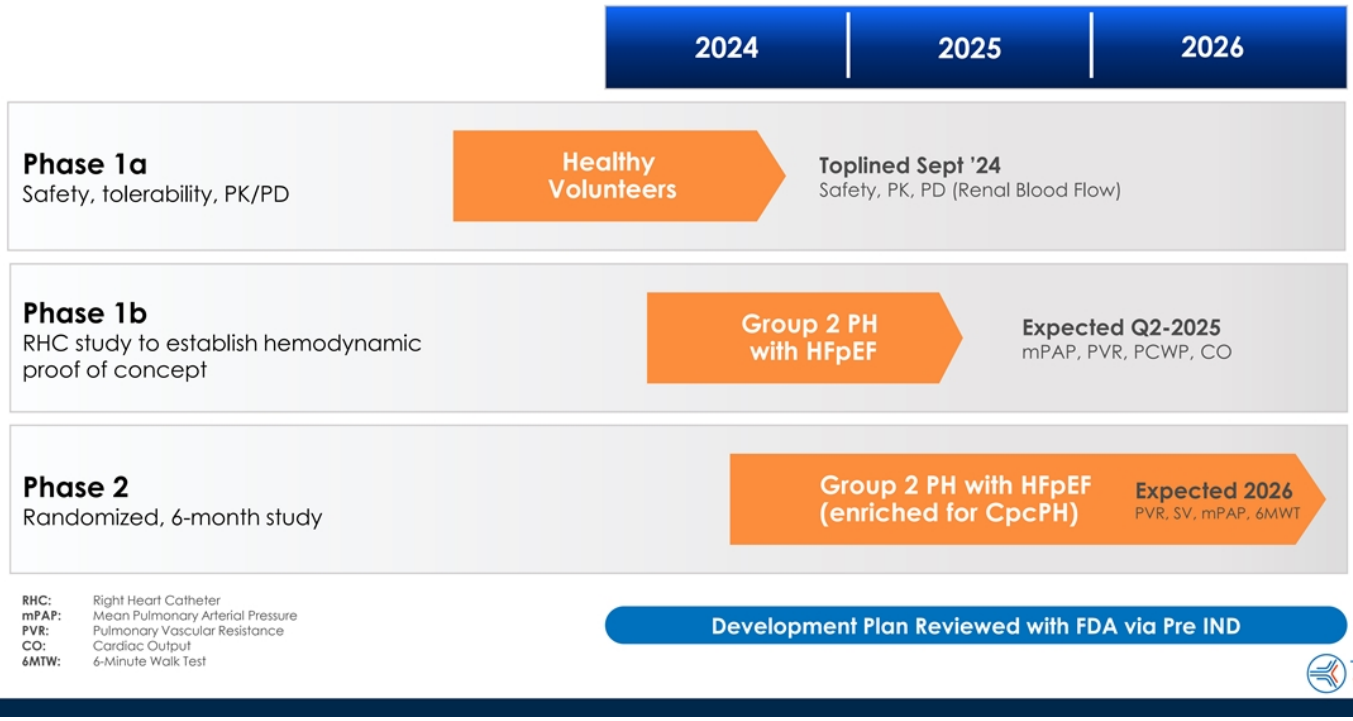
Findings consistent across models and studies published by different investigators

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

TX45 Development Program Overview

Planned readouts in 2025 and 2026



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

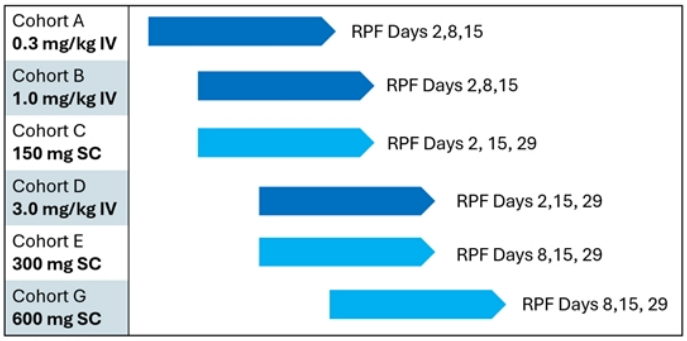
Development Plan Reviewed with FDA via Pre IND

TECTONIC Therapeutic

TX45 Phase 1a Single Ascending Dose Study

- **Study has completed**
- **TX45 was well tolerated with minimal adverse events, no drug-related SAEs**
- **Pharmacokinetics**
  - PK is dose proportional
  - 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"**

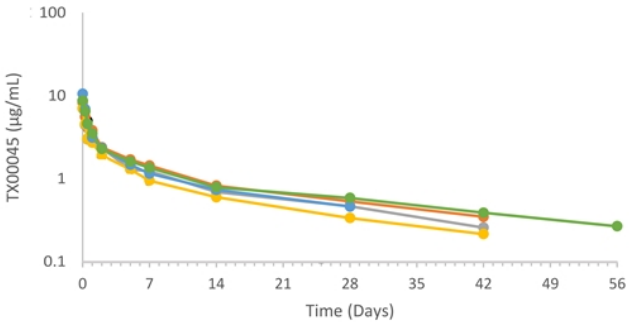
TX45 SAD Dose Escalation Plan



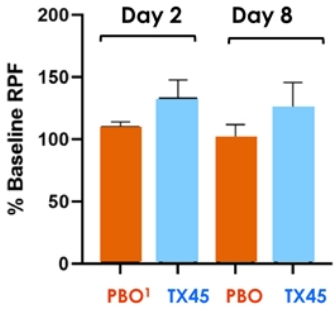
RPF = Renal Plasma Flow

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

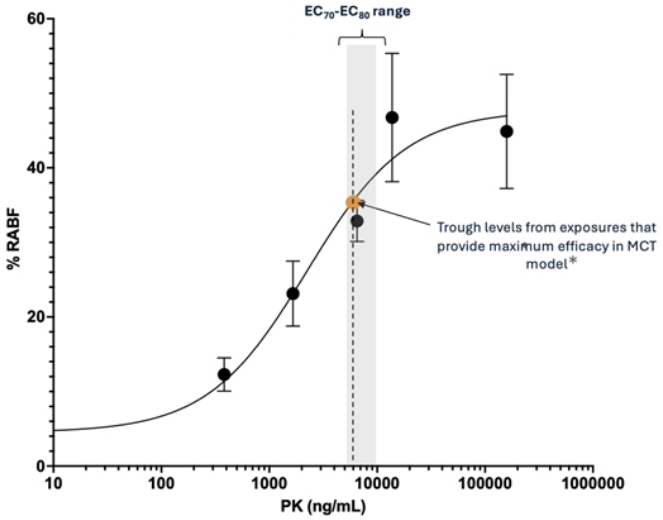
RBF Model

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

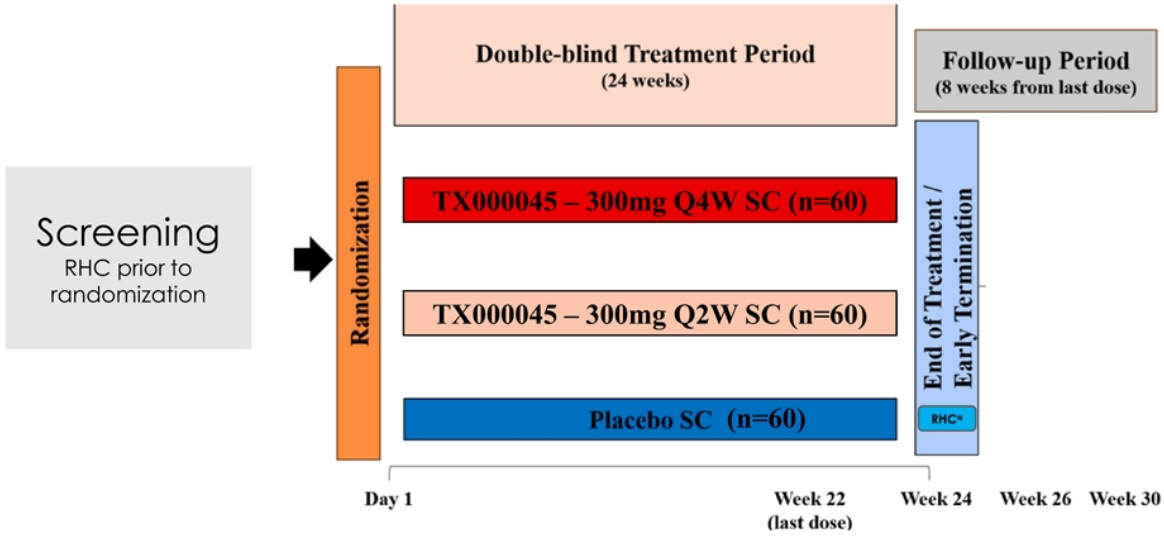
Used to assess the therapeutic anti-inflammatory/anti-proliferative efficacy of TX45 in a rat model of pulmonary hypertension

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 necessary for human EC70-80 is predicted to be 3-fold lower than in rats given the 3x greater potency of TX45 on human RXFP1 compared to rat RXFP1*

Summary of Planned 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
TECTONIC Therapeutic	**Fc-Fusion** *Engineered for optimal PK, biodistribution, high [C] formulation*	**SubQ** *High [C] achievable*	**Q4 Weeks**	**Group 2 PH / HFpEF (enriched for CpcPH)**	**Start in August '24 Data in 2026**
AstraZeneca	Fc-Fusion	SubQ	Q2 Weeks*	Group 2 PH / HFpEF *and* HFrEF	Start: Q1 2023 1st completion: Q2 2025
AstraZeneca	Small Molecule	PO	QD*	CHF	Start: Q2 2024 1st completion: Q4 2025
Lilly	h-Albumin-mAb-Fusion	SubQ *Injection site reactions*	Q Weekly*	HFpEF	Start: Q1 2023 1st completion: Q4 2025

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

HHT Program

First-in- indication opportunity for 2nd most common genetic bleeding disorder

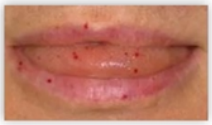
Hereditary Hemorrhagic Telangiectasia (HHT)

Autosomal Dominant Disease that Causes Abnormal Blood Vessel Formation

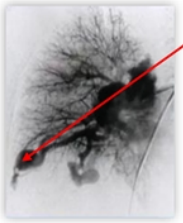
- Rare, autosomal dominant disease: ~ 75,000 patients in US
  - Mutations in the BMP9/10 pathway
- High degree of phenotypic variability (15-20% severe)
- Increased mortality risk

No currently approved therapies for HHT

Nosebleeds

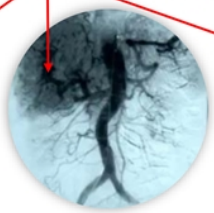


Telangiectasias



Lung

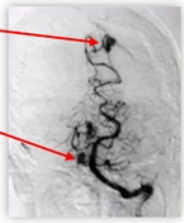
AVMs



Liver

Telangiectasias

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 thromboemboli (VTE)
- Pulmonary Hypertension
- Migraines

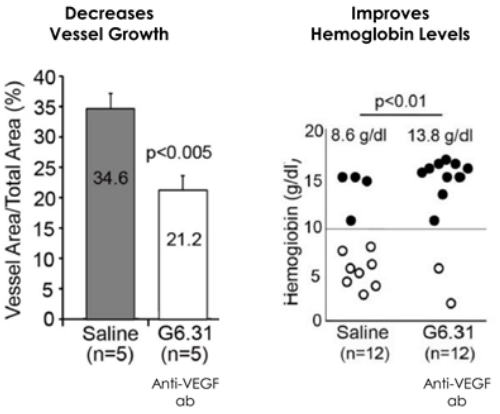
*AVM= arterial venous malformation

TECTONIC Therapeutic

Anti VEGF: Mouse HHT Model Predictive of Efficacy in Patients

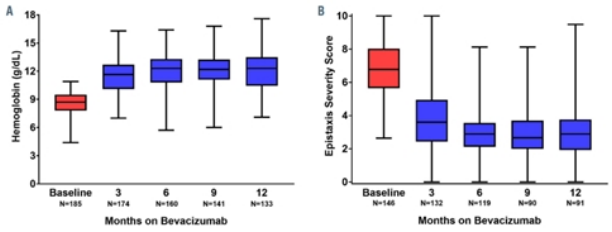
ANTI-VEGF mAb SUPPRESSES AVM FORMATION, VISCERAL HEMORRHAGE IN HHT MODEL

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



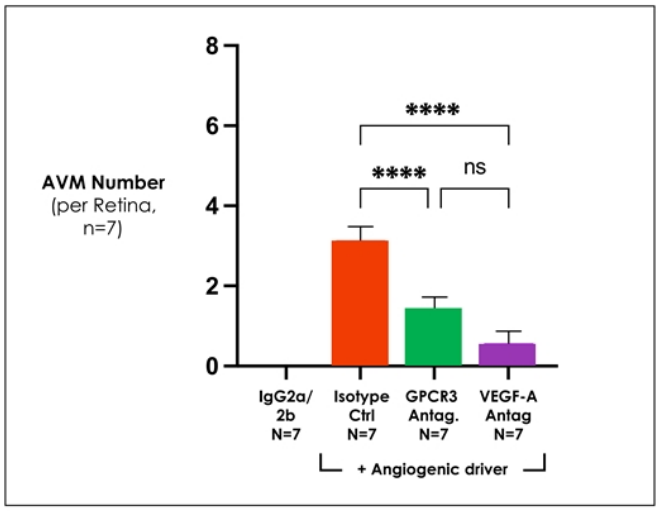
- No rigorous clinical studies ever conducted – only evidence is from IITs
  - Patent expiration on anti-VEGF mab lowered incentive to investment in label expansion
  - Dose and Dosing interval not well explored
- Treating physicians concerned about side effects

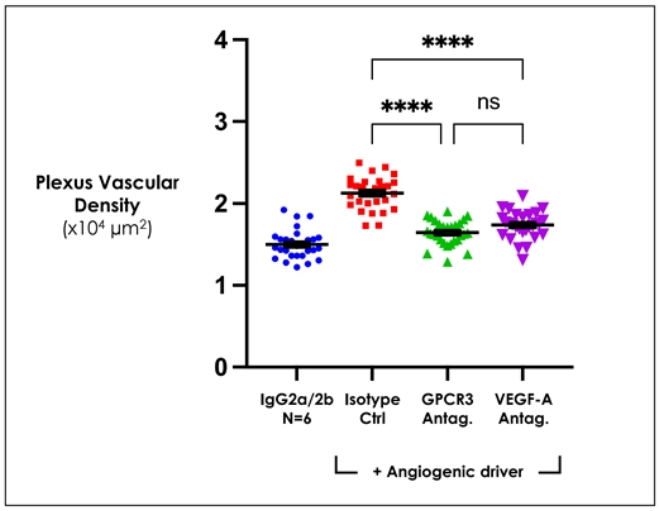
Haematologica. 2021 Aug 1; 106(8): 2161–2169

TECTONiC Therapeutic

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[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

Projected HHT Development Program Overview

Summary

Financial Overview

Company Ticker	NASDAQ: TECX
Investor Participation from June 2024 Private Placement	Major mutual fund, TAS Partners, 5AM Ventures, EcoR1 Capital, Polaris Partners, Farallon Capital (managed funds), Vida Ventures, Pags Group and other investors
Cash as of 6/30/24	~$185 million[1]
Expected Cash Runway	Into Mid-2027
Common Stock Outstanding (6/30/24):	~14.7M[2]

[1]Cash and cash equivalents as of June 30, 2024, prior to the payment of accrued transaction and related expenses of ~$14.4M
[2]As of 6/30/24

TECTONIC Therapeutic

Uniquely Positioned to Deliver on Value Creating Milestones

Strong Balance Sheet Post Transaction	Pipeline of Uniquely Differentiated Assets	Accomplished Team World-leader Founders
~$185 Million* (as of 6/30/24) **Runway Into Mid-2027**	**Multiple Inflection Points 2025, 2026, 2027**	**20 1st Approvals** **>$50B in Annual Sales**
Well positioned to execute	Address important clinical problems, underserved patient populations	Leadership with Proven Track Record

* Cash and cash equivalents as of June 30, 2024, prior to the payment of accrued transaction and related expenses of ~$14.4M, are expected to fund current operational plans into mid-2027

Thank you

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