TX45 Phase 1b PH-HFpEF Interim Data Release for Single Dose Hemodynamic Trial

January 2025

TECTONIC Therapeutic

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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 and market potential of our product candidates; and our ability to identify and develop additional product candidates as well as pursue additional indications.

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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

- 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 trial, supported by Phase 1b interim results

- Initial indication targeting Group 2 Pulmonary Hypertension (PH) associated with Heart Failure with Preserved Ejection Fraction (HFpEF), or PH-HFpEF, with Phase 2 trial enriched for CpcPH
- Positive Phase 1a clinical trial results support best-in-class potential, including favorable safety profile
- Positive interim Phase 1b clinical trial results achieved or exceeded all hemodynamic goal targets, supporting Phase 2 trial

Relaxin Potentially Ideal for PH-HFpEF

Relaxin physiologic and hemodynamic effects further demonstrated in prior clinical studies

- Prior clinical development of relaxin by Novartis adds to clinical rationale for TX45 targeting PH-HFpEF

PH-HFpEF Significant Market Potential

~1.4M+ Group 2 PH-HFpEF patients in the U.S. with no approved therapy*; high 5-year mortality

- Potential peak multi-billion-dollar* revenue potential for Group 2 PH-HFpEF patients with EF > 40%
- Astra Zeneca is pursuing a Group 2 PH relaxin program targeting both HFpEF and HFrEF patients

TX2100 Second Pipeline Asset

Targeting rare bleeding disorder called Hereditary Hemorrhagic Telangiectasia (HHT)

- Significant market potential, no approved therapies for HHT, estimated ~75K patients in the U.S. alone (15-20% severe)
- Phase 1 clinical trial initiation expected in Q4'25 / Q1'26

Potential to Broaden TX45 to HFrEF Patients

TX45 Phase 1b, hemodynamic topline results in PH-HFrEF subjects expected in 2H'25

- Positive PH-HFrEF results could potentially expand the addressable TX45 patient population by ~1.1M patients in the U.S. *

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*

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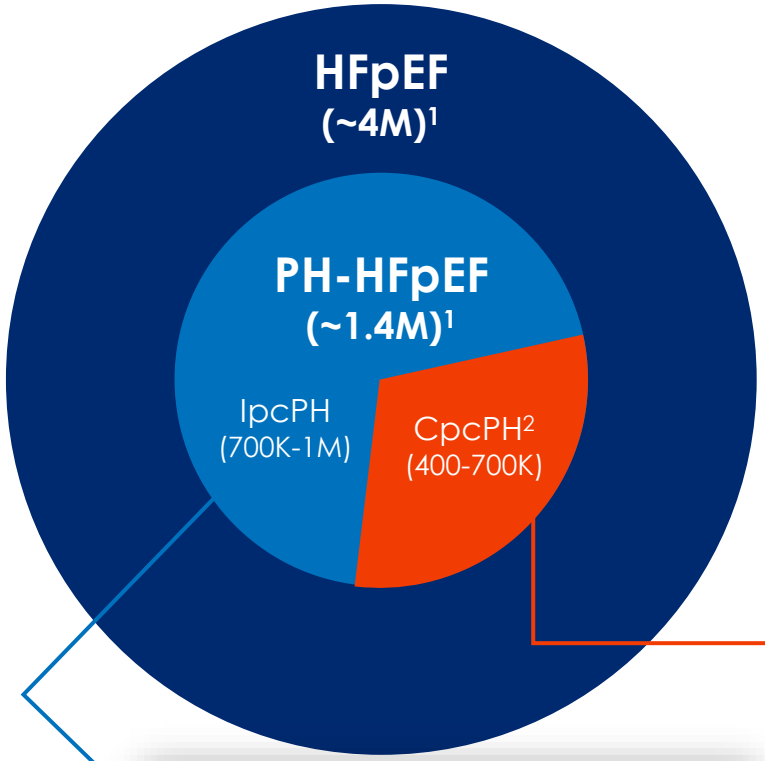
Initial Focus on Group 2 PH due to Heart Failure with Preserved EF (PH-HFpEF), Enriched for CpcPH Patients

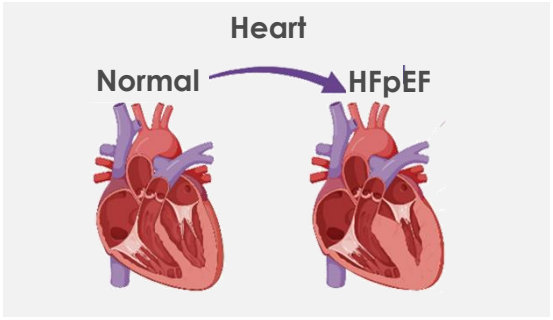
Clinical program designed to enable evaluation of efficacy in overall population and CpcPH



Group 2 PH-HFrEF could add ~1.1M[1] on top of the ~1.4M for PH-HFpEF

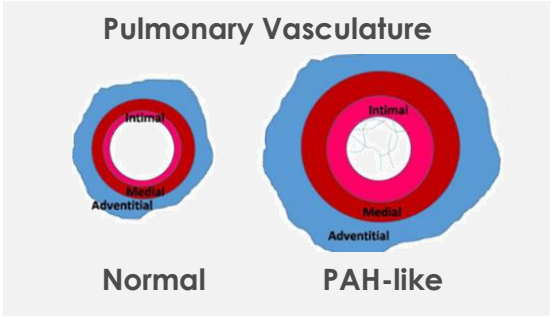
IpcPH (**I**solated, **p**ost **c**apillary **PH**)

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, HF, 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. 400K CpCPH and 1M IpcPH assumes diagnosis based on PVR≥3; 700K CpCPH and 700K IpcPH assumes diagnosis based on PVR≥2.

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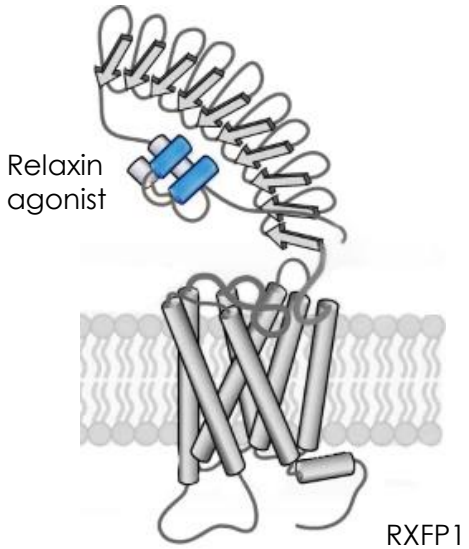
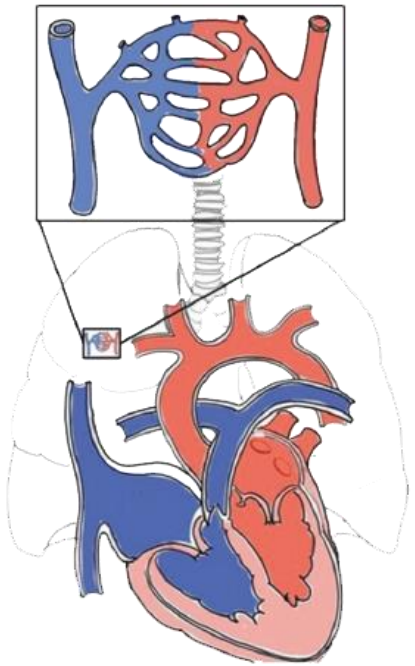
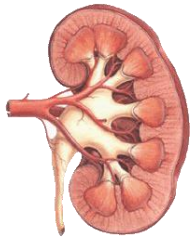
Relaxin Addresses Multiple Organ System Pathologies in PH-HFpEF

Phase 1b data is anticipated to capture the acute impact of vasodilation and LV relaxation







↑ Vasodilation
Pulmonary & Systemic
↑ NO ↓ Endothelin-1

→ **↓ RV / LV* Afterload**

↑ LV Relaxation
↑ SERCA2 function

→ **Improved LV Diastolic Function**

↓ Fibrosis
Anti-Inflammatory
↑ MMPs ↓ TGFβ

→ **RV / LV and Pulmonary Artery Reverse Remodeling**

↑ Renal Blood Flow

→ **↑ Na^+ Excretion**
↓ RV / LV Preload

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

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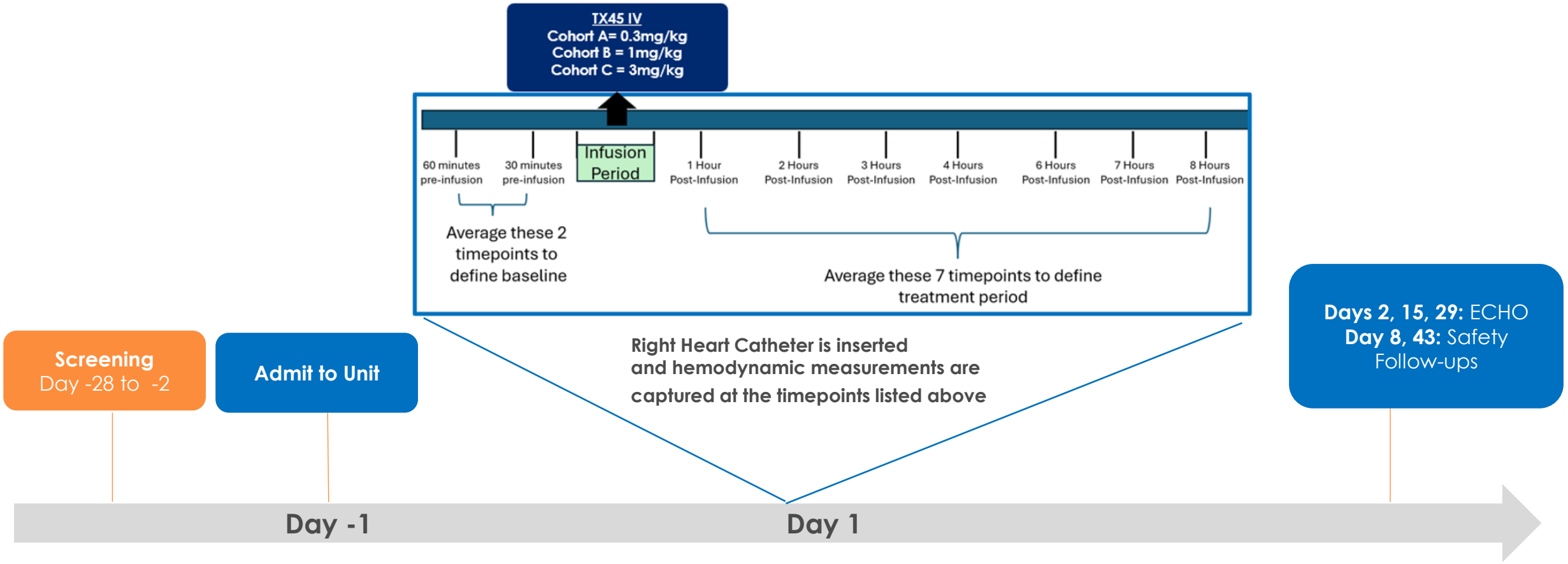
TX45 Background and Clinical Program Status

- TX45 is a human relaxin-2-Fc fusion protein with a potential best in class half-life of 2-3 weeks
- The Phase 1b hemodynamic clinical trial is ongoing:
  - **Part A** - Enrollment and dosing of PH-HFpEF subjects is completed (N=19)
    - Efficacy data is available for 16 of 19 subjects
      - Hemodynamic data on the last 3 subjects are in line with the findings on the first 16 [3]
      - Last 3 patients all have IpcPH, therefore the CpcPH cohort data is final
    - Safety data is available on 16 patients, 15 of whom have completed the full 43-day safety follow-up
  - **Part B** - Enrollment in PH-HFrEF[2] subjects is expected to initiate near term with data in 2H'25
- TX45 is currently enrolling in a Phase 2 trial for subjects with PH-HFpEF[1] enriched for CpcPH with results expected in 2026

[1] *PH-HFpEF = Pulmonary Hypertension due to Heart Failure with Preserved Ejection Fraction (LVEF ≥ 40%)*
[2] *PH-HFrEF = Pulmonary Hypertension due to Heart Failure with Reduced Ejection Fraction*
[3] *Based on data available to date*

Phase 1b (Part A) Trial Design, A Single Dose, Open-Label Acute Hemodynamic Trial in IpcPH and CpcPH Subjects



Hemodynamic data was prespecified to be pooled across all doses. After IV administration, all dose levels result in exposures which are in the predicted efficacious range during the 8-hour assessment period (i.e. above trough exposure of 2 ug/ml)

Key Hemodynamic Measures Assessed in Phase 1b Trial

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

Hemodynamic	Definition	Significance
PCWP *(Pulmonary Capillary Wedge Pressure)*	• Measure of left atrial pressure	• Key marker of left ventricular (LV) function
PVR *(Pulmonary Vascular Resistance)*	• Measure of resistance to blood flow in pulmonary vessels • PVR = (mPAP – PCWP)/CO	• Health of the pulmonary vessels
TPR *(Total Pulmonary Resistance)*	• Measure of right ventricular afterload • TPR = mPAP/CO	• Key marker of resistance, how hard must the right ventricle (RV) work
CO *(Cardiac Output)*	• Amount of blood heart pumps (volume/time) • CO = heart rate x stroke volume	• How well is the heart working (both RV and LV)
SV *(Stroke Volume)*	• Amount of blood ejected from ventricle per beat	• Effectiveness of the heart at pumping blood (both RV and LV)

Note: mPAP = mean Pulm. Artery Pressure = average pressure required to pump blood through the lungs

TX45 Phase 1b Trial Results Are Expected to Improve Probability of Success of TX45 in Phase 2 Clinical Trial

Phase 1b predefined hemodynamic target goals were:

- **~15-20% decrease in pulmonary capillary wedge pressure (PCWP) in overall patient population**
  - PCWP provides insight into left ventricular function and correlates with exercise capacity in HFpEF, HFrEF[1] and Group 2 pulmonary hypertension (CpcPH)[2]

- **~15-20% decrease in pulmonary vascular resistance (PVR) in patients with CpcPH[a]**
  - PVR is normal in IpcPH[b], so a floor effect is likely in this subgroup
  - In PAH, lowering of PVR is associated with improvement in 6MWD[3]
  - In Group 2 PH (CpcPH), lowering of PVR is correlated with increased 6MWD[2]

- **Reduction in total pulmonary resistance (TPR) in overall patient population**

- **No bar set for Cardiac Output as Cardiac Output is normal at rest in patients with HFpEF**

1.Wolsk E et al. Eur. J. Heart Fail. 2018
2.Zhang H et al. JACC: Cardiovascular Interventions. 2019
3.www.accessdata.fda.gov/drugsatfda_docs/nda/2017/209279Orig1s000MedR.pdf
a CpcPH = Combined Pre- and Post-Capillary Pulmonary Hypertension
b IpcPh = Isolated Post-Capillary Pulmonary Hypertension

Phase 1b (Part A) Demographics & Medical History

	All Subjects N = 16
Age (mean, SD)	64.3 (9.2)
Females [n (%)]	6 (37.5%)
BMI (mean, SD)	28.0 (3.2)
Creatinine (uMol/L; mean, SD)*	80.8 (18.7)
Comorbidities	
Hypertension [n (%)]	13 (81.3%)
Atrial fibrillation [n (%)]	10 (62.5%)
Diabetes mellitus [n (%)]	5 (31.3%)
Coronary artery disease [n (%)]	10 (62.5%)
NYHA Class [n (%)]	
NYHA Class II	9 (56.3%)
NYHA Class III	7 (46.8%)

Key Concomitant Medications	All Subjects N = 16
ACEi/ARB [n (%)]	8 (50.0 %)
MRA [n (%)]	13 (81.3 %)
SGLT2i [n (%)]	6 (37.5 %)
Loop Diuretic [n (%)]	11 (68.8 %)
Beta-blocker	12 (75.0 %)
Digoxin [n (%)]	5 (31.3 %)

*Creatinine normal range (uMol/L):
Males: 61.9-114.9
Females: 53.0 to 97.2

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Phase 1b (Part A) - Summary of Baseline Hemodynamics

Parameter	Baseline Value [mean, SD]
Heart Rate (bpm)	68.1 (10.9)
Systolic Blood Pressure (mm Hg)	128.8 (11.6)
Diastolic Blood Pressure (mm Hg)	78.5 (6.0)
Mean Pulmonary Artery Pressure (mm Hg)	26.6 (4.4)
Pulmonary Capillary Wedge Pressure (mm Hg)	16.7 (3.2)
Pulmonary Vascular Resistance (Woods Units)	2.45 (1.1)
Cardiac Output (L/min)	4.3 (1.0)
Stroke Volume mL	65 (18)
Total Pulmonary Resistance (Woods Units)	6.5 (1.6)

PVR < 2WU	2 WU ≤ PVR < 3WU	PVR ≥3 WU
7	4	5

If CpcPH is defined as PVR >3:
Total IpcPH = 11
Total CpcPH = 5

If CpcPH is defined as PVR >2:
Total IpcPH = 7
Total CpcPH = 9

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Phase 1b (Part A) - Primary Endpoint: TX45 Is Well Tolerated

Treatment-emergent adverse events (# of Subjects)

Preferred Term	Cohort A 0.3 mg/kg (n=3)	Cohort B 1 mg/kg (n=7)	Cohort C 3 mg/kg (n=6)	Total N=16
Fatigue*	0	0	4	4 (25%)
Nasopharyngitis	0	0	1	1 (6.3%)
Back pain	0	1	0	1 (6.3%)
Gout (worsening)	0	1	0	1 (6.3%)
Viral infection	0	0	1	1 (6.3%)
Procedural pain (catheter)	0	0	1	1 (6.3%)

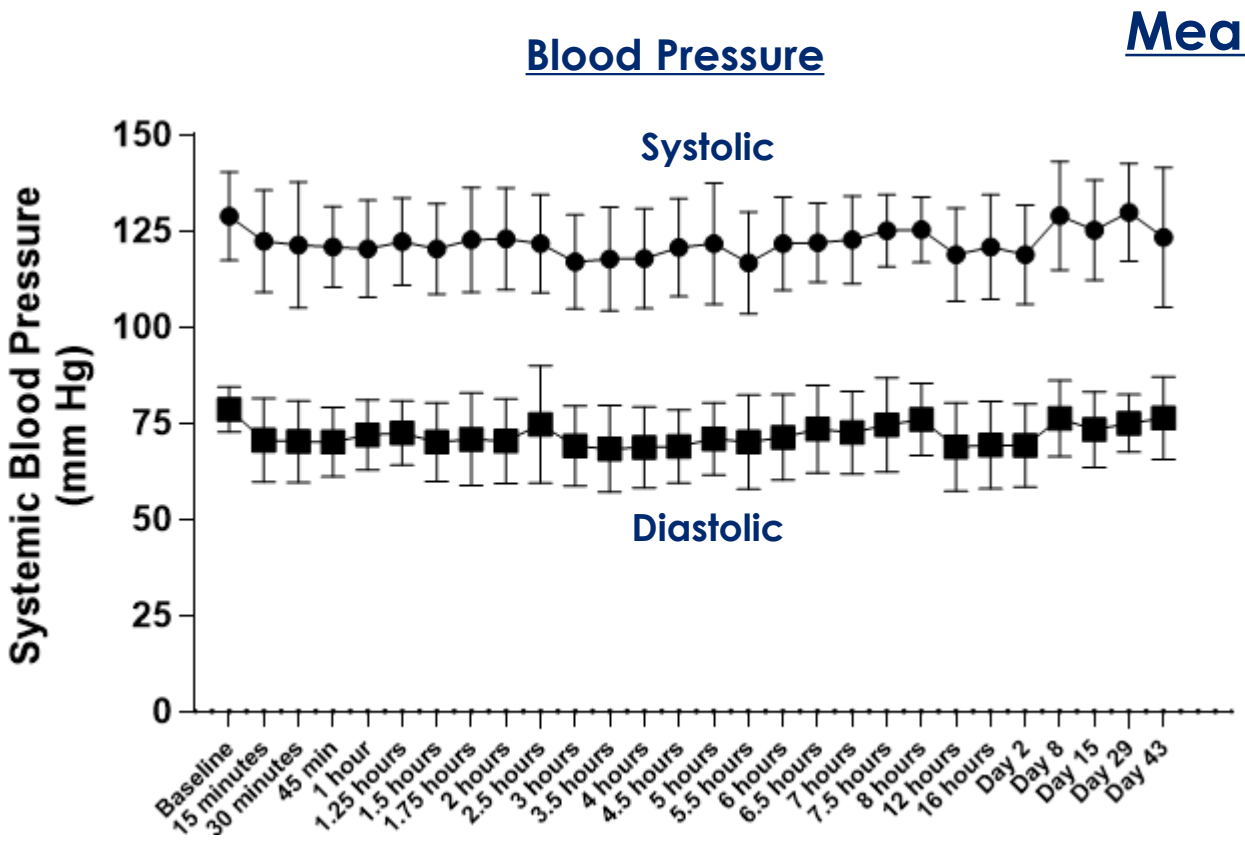
- There were 9 treatment-emergent adverse events (TEAEs) in 7 patients
- There were no serious or severe adverse events, discontinuations, infusion reactions or drug related adverse events
- There were no clinically significant changes in vital signs, physical exam or safety laboratory values
- *4 participants reported fatigue in the evening of D1; all reports of fatigue were brief (< 3 hours) and self-limited; there were no reports of fatigue after D1

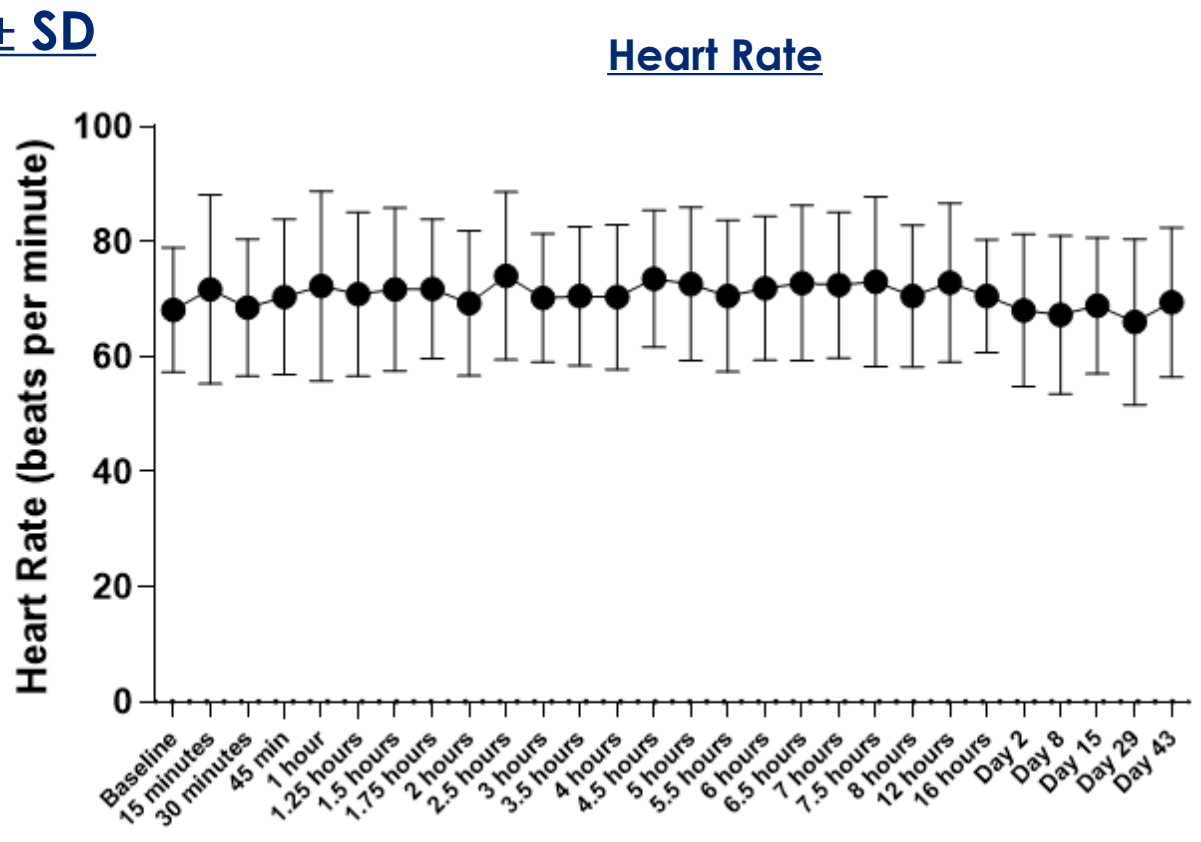
Phase 1b (Part A) Results - TX45 Achieved or Exceeded all Hemodynamic Target Goals

Secondary Endpoints	Absolute CFB, Mean [95% CI]	Average % CFB, [95% CI]
Hemodynamics (Key 2º) (N = 16)		
Mean Δ PCWP in all participants	- 2.9 [-1.7 to -4.2] mm Hg	**-17.9% [-9.8% to -26.1%]**
Mean Δ PVR in CpcPH (PVR ≥ 2 WU) (n= 9)	- 1.06 [-0.78 to -1.34] Woods Units	**-32.0% [-28.1% to -35.9%]**
Mean Δ PVR in CpcPH (PVR ≥ 3 WU) (n= 5)	- 1.35 [-1.15 to -1.55] Woods Units	**-35.5% [-32.5% to -38.6%]**
Other Hemodynamic Effects		
Mean Δ Cardiac Output in all participants	+0.65 [0.34 to 0.96] L/min	**+17.4% [8.9% to 25.9%]**
Mean Δ Stroke Volume in all participants	+7 [2 to 12] mL	**+13.8% [5.3% to 22.3%]**
Mean Δ TPR in all participants	-1.79 [-1.24 to -2.34] Woods Units	**-26.3% [-20.1% to -32.5%]**
Mean Δ mPAP in all participants	-4.33 [-3.02 to -5.65] mmHg	**-15.9% [-11.2% to -20.6%]**

IV Administration of TX45 Resulted in a Transient, Asymptomatic Decrease in Blood Pressure

Mean ± SD





Transient, asymptomatic 5-12 mm Hg mean decrease in blood pressure was observed post- IV dosing of TX45 which resolved at subsequent visits

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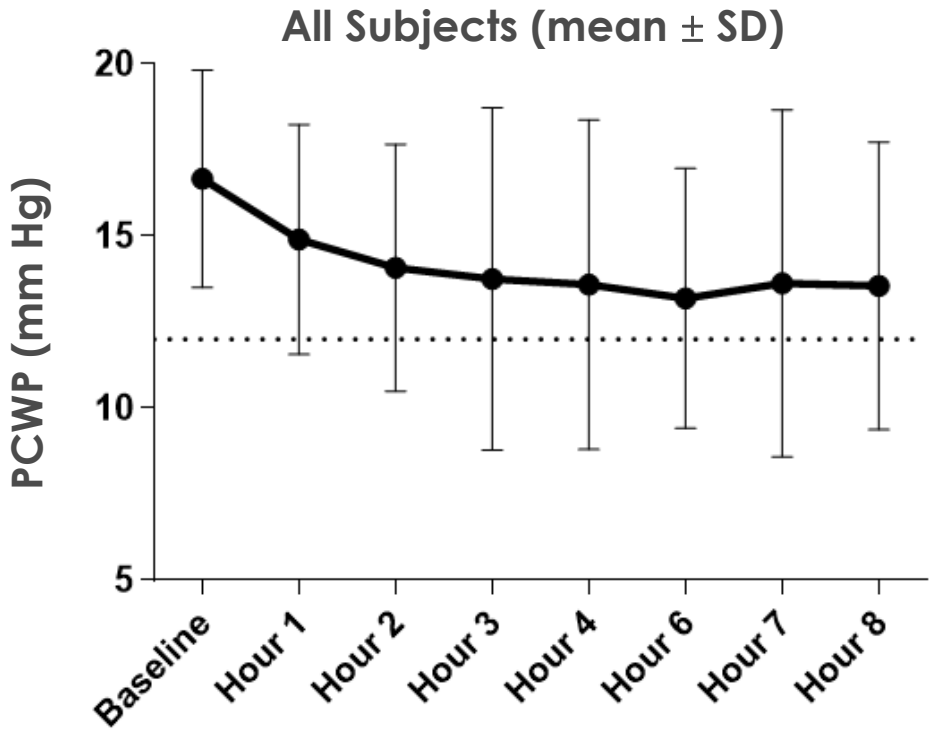
TX45 Decreases PCWP in PH-HFpEF

	Baseline (mm Hg) mean (SD)	Treatment Period (mm Hg) mean (SD)	Absolute CFB (mm Hg) mean (95% CI)	Average % CFB, (95% CI)
All subjects (N = 16)	16.7 (3.2)	13.7 (3.7)	-2.9, [-1.7 to -4.2]	**-17.9% [-9.8 to -26.1]**
Baseline PVR ≥ 2 WU (n = 9)	16.2 (2.7)	13.0 (3.5)	-3.2 [-2.0 to -4.4]	**-20.6% [-12.5 to -28.6]**
Baseline PVR ≥ 3 WU (n = 5)	16.0 (2.4)	13.3 (2.7)	-2.7 [-1.3 to -4.1]	**-17.1% [-7.8 to -26.4]**



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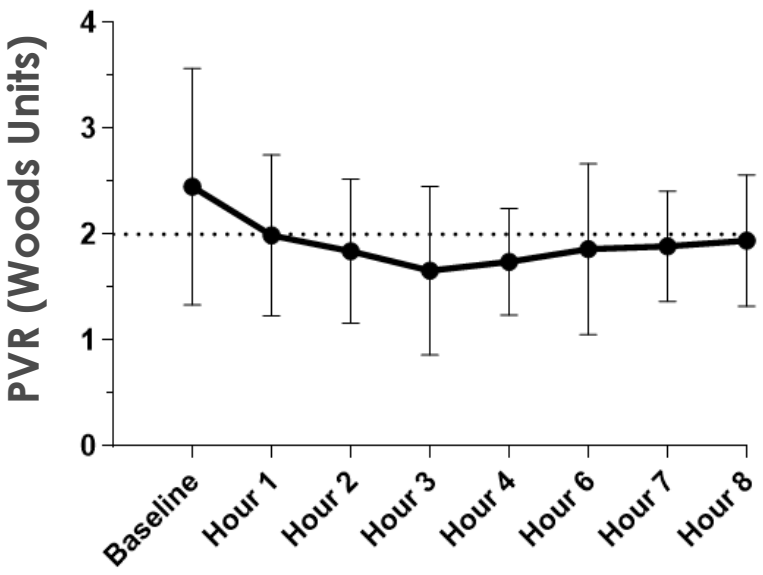
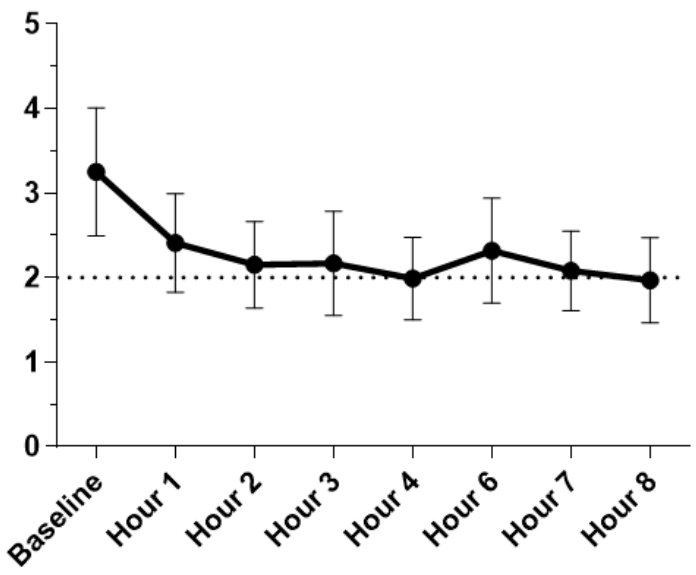
TX45 Decreases PVR in Patients with CpcPH

	Baseline (WU) mean (SD)	Treatment Period (WU) mean (SD)	Absolute CFB (WU) mean [95% CI]	Average % CFB mean [95% CI]
All subjects (N = 16) *	2.45 (1.12)	1.84 (0.57)	-0.61 [-0.22 to -0.99]	**-12.3% [-38.3 to +13.7]**
Baseline PVR ≥ 2 WU (n = 9)	3.25 (0.76)	2.19 (0.44)	-1.06 [-0.78 to -1.34]	**-32.0% [-28.1 to -35.9]**
Baseline PVR ≥ 3 WU (n = 5)	3.81 (0.46)	2.46 (0.34)	-1.35 [-1.15 to -1.55]	**-35.5% [-32.5 to -38.6]**

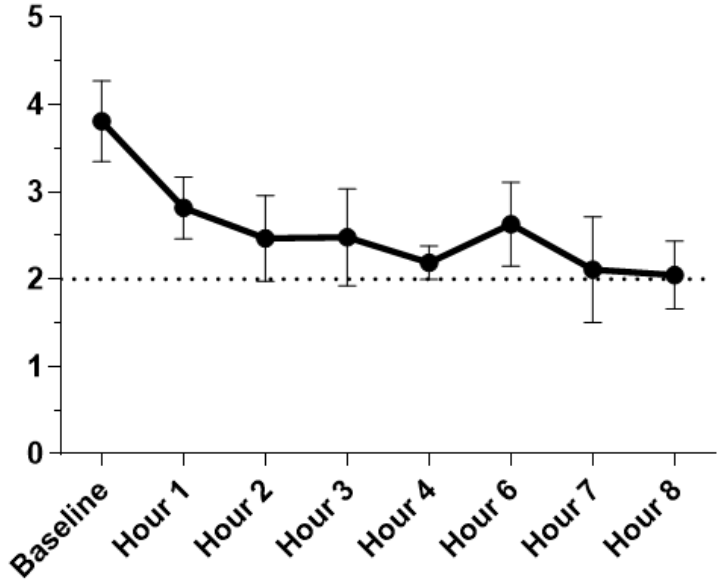
All Subjects (N = 16; mean ± SD)



Subjects with baseline PVR ≥ 2 WU (N = 9; mean ± SD)



Subjects with baseline PVR ≥ 3 WU (N = 5; mean ± SD)

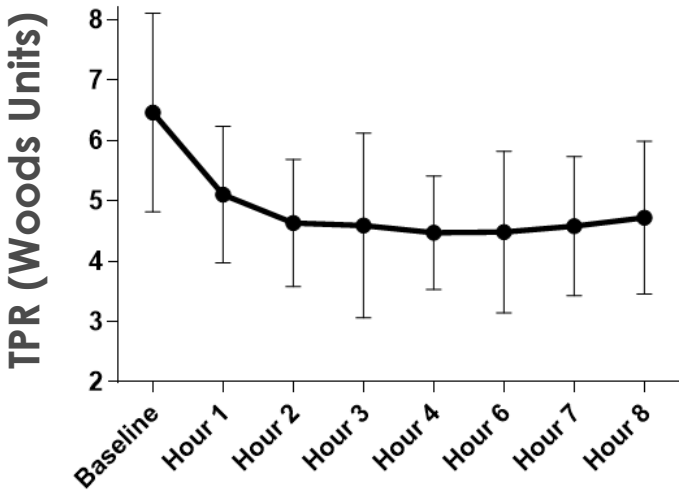


** All subjects include both IpcPH and CpcPH subjects*

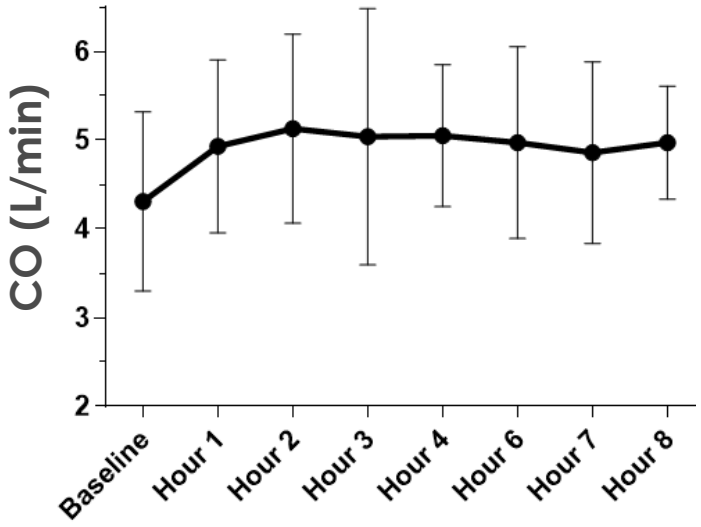
TX45 Improves Other Relevant Hemodynamics in PH-HFpEF

All Subjects (N = 16)	TPR (WU)	Cardiac Output (L/min)	mPAP (mm Hg)
Baseline (mean, SD)	6.46 (1.65)	4.31 (1.01)	26.6 (4.4)
Treatment Period (mean, SD)	4.68 (1.01)	4.96 (0.87)	22.3 (3.8)
Absolute CFB (mean, 95% CI)	-1.79 [-1.24 to -2.34]	+0.65 [0.34 to 0.96]	-4.3 (-3.0 to -5.7)
Average % CFB (mean, 95% CI)	**-26.3% [-20.1 to -32.5]**	**+17.4% [8.9 to 25.9]**	**-15.9% [-11.2 to -20.6]**

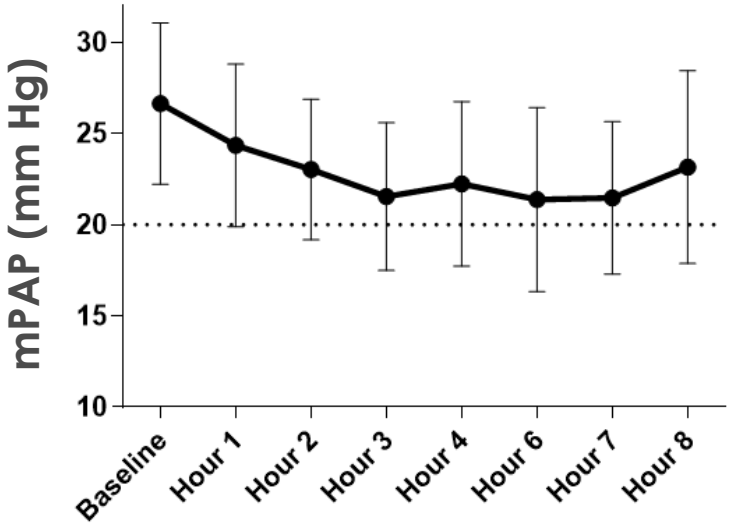
Total Pulmonary Resistance (N = 16; mean ± SD)



Cardiac Output (N = 16; mean ± SD)



Mean Pulmonary Artery Pressure (N = 16; mean ± SD)



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TX45 Decreases TPR and Increase CO in Both the Overall Population and CpcPH

Total Pulmonary Resistance

	Baseline (WU) mean (SD)	Treatment Period (WU) mean (SD)	Absolute CFB (WU) mean (95% CI)	Average % CFB, (95% CI)
All subjects (N = 16)	6.46 (1.65)	4.68 (1.01)	-1.79 [-1.24 to -2.34]	**-26.3% [-20.1 to -32.5]**
Baseline PVR ≥ 2 WU (n = 9)	7.34 (1.50)	4.97 (0.89)	-2.37 [-1.68 to -3.06]	**-31.5% [-25.2 to -37.9]**
Baseline PVR ≥ 3 WU (n = 5)	8.31 (1.11)	5.51 (0.77)	-2.80 [-1.89 to -3.71]	**-33.5% [-25.8 to -41.1]**

Cardiac Output

	Baseline (L/min) mean (SD)	Treatment Period (L/min) mean (SD)	Absolute CFB (L/min) mean (95% CI)	Average % CFB, (95% CI)
All subjects (N = 16)	4.31 (1.01)	4.96 (0.86)	+0.65 [0.34 to 0.96]	**+17.4% [8.9 to 25.9]**
Baseline PVR ≥ 2 WU (n = 9)	4.08 (1.19)	4.79 (0.93)	+0.70 [0.30 to 1.10]	**+20.5% [7.3 to 33.6]**
Baseline PVR ≥ 3 WU (n = 5)	3.62 (0.94)	4.46 (1.00)	+0.84 (0.35 to 1.32)	**+24.5% [7.4 to 41.5]**

Combined Decrease in PCWP and PVR Appears to Enhance Improvement in Exercise Capacity

- Decreasing **PCWP alone** is expected to improve exercise capacity
  - SGLT2 inhibitor dapagliflozin decreased resting PCWP 20%[1] and increased 6MWT by 20m in HFpEF[2]
- Decreasing **both PCWP and PVR** appears to further increase in exercise capacity
  - CpcPH patients undergoing pulmonary artery denervation surgery achieved a treatment-adjusted average decrease of 19% in PCWP and 32% in PVR, and increased 6MWT distance 69m[3]

[NOTE: This was a severe population of CpcPH patients (mean PVR>6 WU) and we expect impact on 6MWD will be clinically important but not as large as demonstrated in this study]

[1] Borlaug B et al. Circulation 2023
[2] Lewis GD et al. Circ. Heart Failure 2023
[3] Zhang H et al. JACC Cardiovasc. Interv. 2019

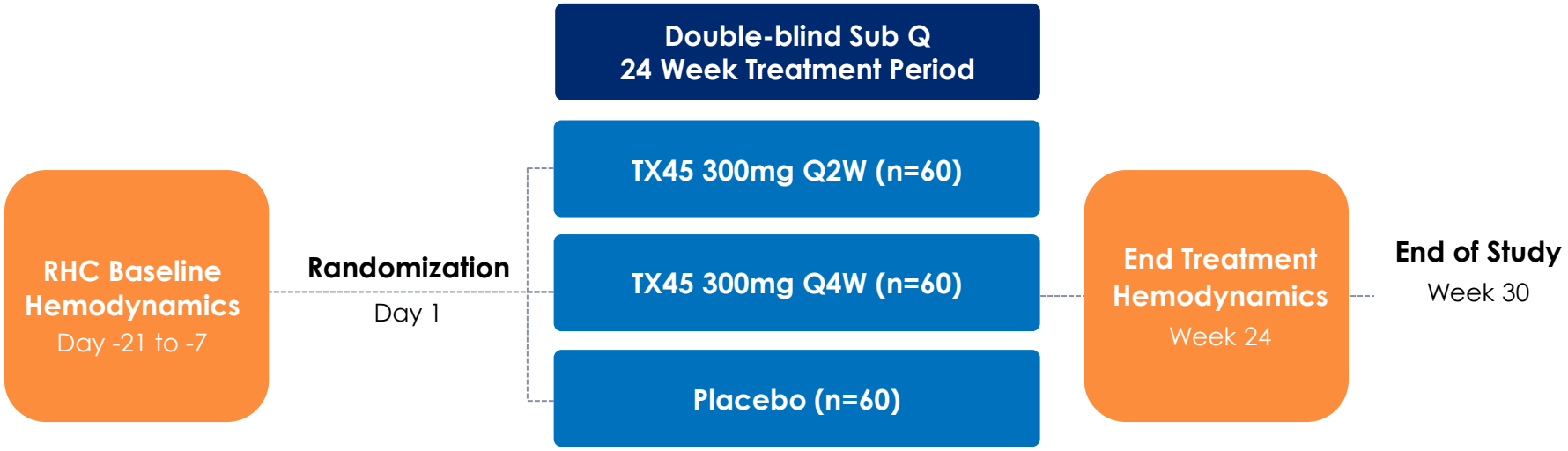
TX45 Phase 1b Interim Data in PH-HFpEF Met/Exceeded our Expectations, Increasing Probability of Phase 2 Success

- **TX45 was well-tolerated**
  - Transient asymptomatic decreases in BP were observed over the first 24 hours after an IV dose
- **TX45 observed to improve left heart function and pulmonary hemodynamics, which together should increase probability of success of Phase 2 Trial**
  - **Left Heart Function**: 17.9% decrease in PCWP and 17.4% increase in Cardiac Output in overall population
  - **Pulmonary Hemodynamics**: 32.0-35.5% decrease in PVR in CpcPH and 26.3% decrease in TPR in overall pop.
- **TX45 has a differentiated profile compared with PAH drugs which improved pulmonary hemodynamics without an improvement in left heart function and failed in PH-HFpEF**
- **These data support our focus on PH-HFpEF as the first indication for TX45, with enrichment in our Phase 2 trial for subjects with CpcPH where the benefit could be the greatest**

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



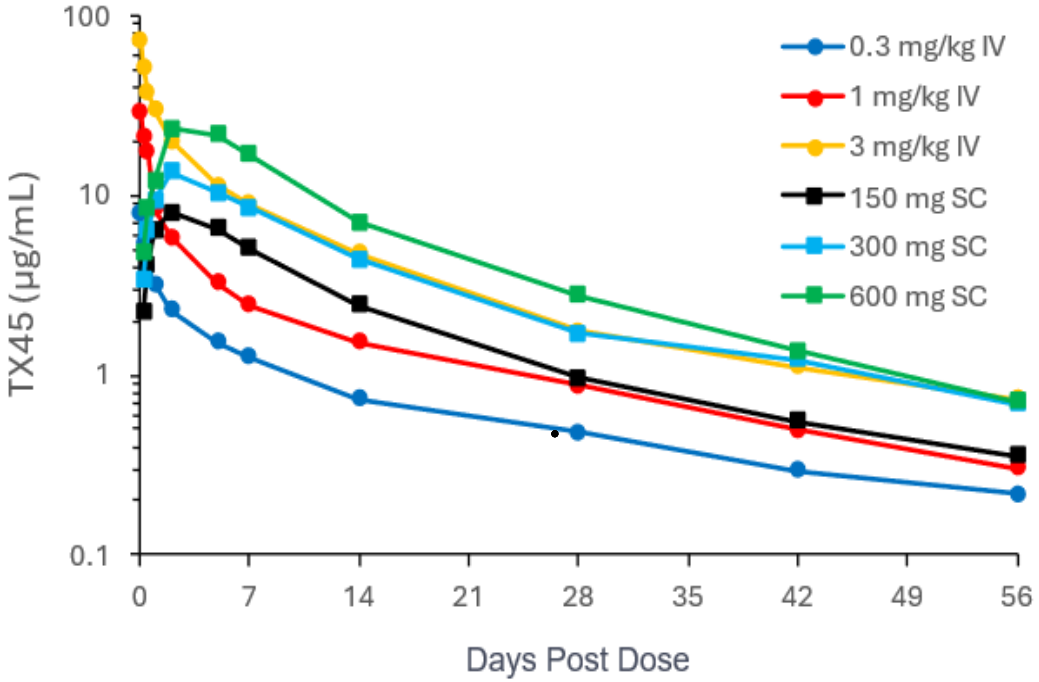
- **Primary Endpoint:**
  Change from baseline in PVR
- **Secondary Endpoints:**
  Change from baseline in PCWP, 6MWD, KCCQ*

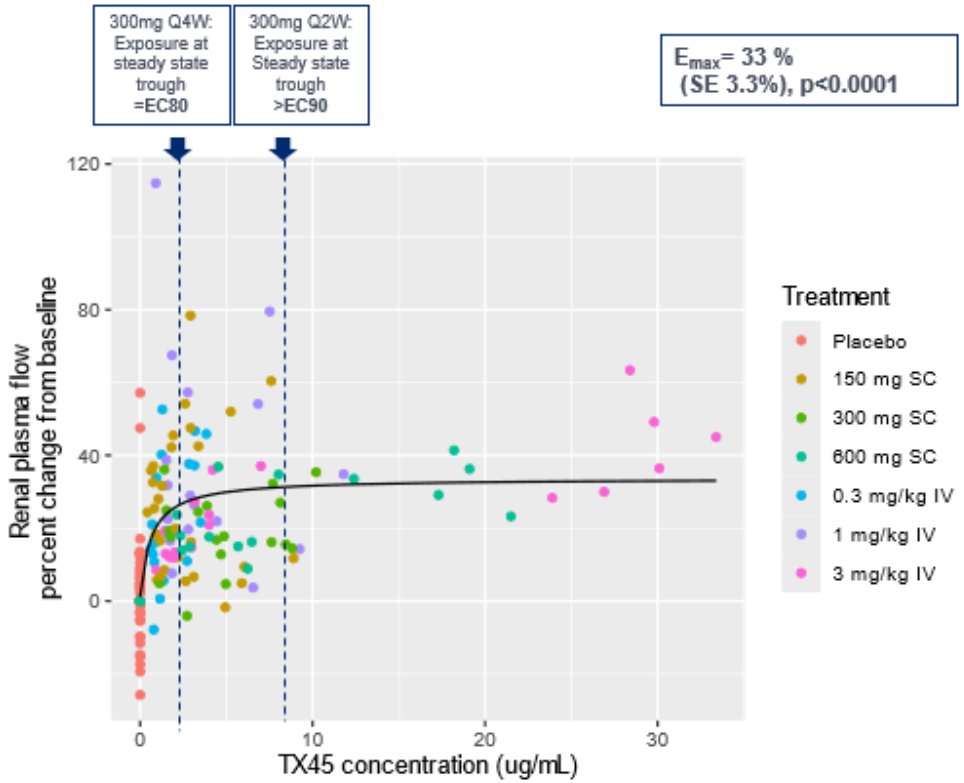
** Kansas City cardiomyopathy questionnaire*

Phase 1a Trial In Healthy Volunteers (IV) Enabled Sub-Q Dose Selection for Phase 2 Trial

- Phase 2 doses provide maximal to near-maximal agonism of RXFP1 throughout the dosing interval
  - Near maximal agonism at trough provided for maximal effect in preclinical models

- 3 mg/kg exposure over two to four weeks is similar to 300 mg Sub-Q





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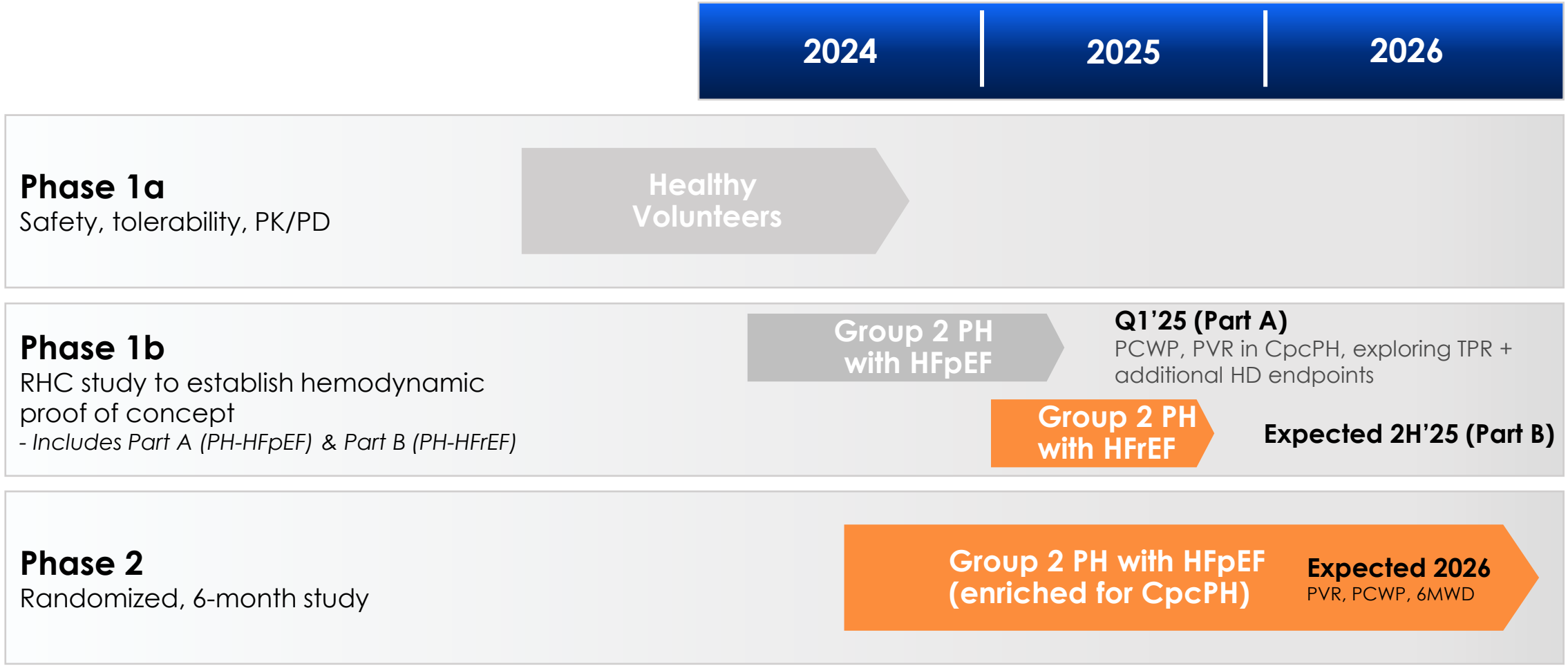
TX45 Development Program Clinical Readouts in 2025-2026



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

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