TX45 Phase 1b (Part B) PH-HFrEF Data Release
Single Dose Hemodynamic Trial

October 2025

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Positive Results in TX45 Single Dose Study in PH-HFrEF Patients

Trial Goal

- Assess safety and tolerability of TX45 in patients with PH-HFrEF
- Observe trends in hemodynamic effects similar to Phase 1b (Part A) PH-HFpEF study (Topline data reported January 2025)

Results

- TX45 was observed to be well tolerated
- Improvements in left ventricular function and pulmonary hemodynamics in PH-HFrEF were consistent with effects demonstrated in PH-HFpEF

Outlook

- Phase 1b Part B data support further clinical investigation of TX45 in PH-HFrEF, pending data in APEX Phase 2, expanding potential market opportunity
- Ongoing APEX Phase 2 trial is evaluating chronic treatment in ~180 PH-HFpEF patients
  - Study enriched for CpcPH (PVR≥3), primary endpoint is in this patient population

PH-HFrEF *= pulmonary hypertension, heart failure with reduced ejection fraction*
PH-HFpEF *= pulmonary hypertension, heart failure with preserved ejection fraction*
PVR *= pulmonary vascular resistance*
CpcPH *= combined post- and pre-capillary pulmonary hypertension*

Rationale for Exploring TX45 in PH-HFrEF, Enriched for CpcPH

(Combined post- and pre-Capillary Pulmonary Hypertension)

Mechanism Appears Ideal to Address Disease Pathology	• Pulmonary and systemic vasodilator resulting in decreased right ventricle (RV) and left ventricle (LV) afterload • Cardiac relaxation during diastole to improve LV filling • Anti-fibrotic and reverse remodeling effects on pulmonary vasculature and LV
Clinically Demonstrated Effects on Hemodynamics and Echo[1]	• Phase 1b Part A in PH-HFpEF – Improvement in PCWP, PVR, mPAP, CO, and TPR – Echocardiographic improvements at Day 29
Unmet Need	• Like PH-HFpEF, PH-HFrEF patients have worse exercise capacity and mortality compared with those without PH, especially patients with CpcPH (PVR≥3) • No approved therapeutic options exist to treat PH-HFrEF
Potential Market Expansion	• PH-HFrEF in the U.S. is ~1.1M with ~300K CpcPH (PVR≥3)[2]

1. *Data shared in January 2025 and echo data in May 2025*
2. *Estimates based on company sponsored market analysis conducted by Health Advances*

***PCWP** = Pulmonary Capillary Wedge Pressure*
***PVR** = Pulmonary Vascular Resistance*
***mPAP** = mean Pulm. Artery Pressure*
***CO** = Cardiac Output*
***TPR** = Total pulmonary resistance*

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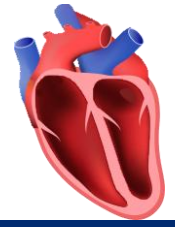
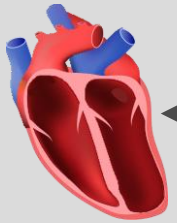
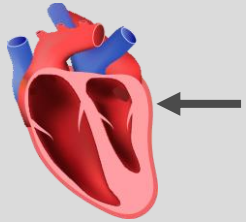
Different LV Pathology but Similar Pulmonary Vascular and RV Consequences







Characteristics	HFrEF (Heart Failure with Reduced Ejection Fraction)	HFpEF (Heart Failure with Preserved Ejection Fraction)
Ejection Fraction %	≤40%	>40%*
Common Causes	Myocardial infarction, cardiomyopathy	Hypertension, aging, diabetes, obesity
Left Ventricle State	Dilated, weak → pumping impairment during systole, sensitive to SVR	Less distensible, normal-sized or concentric hypertrophy → filling impairment in diastole
Driver of PH, RV failure	Elevated left heart filling pressures can lead to PH and RV failure	
Hemodynamic Changes	Increases in PCWP, mPAP, PVR; Decrease in CO	

** Current definition of HFmrEF is 41% to 49% EF and HFpEF is EF≥50%*

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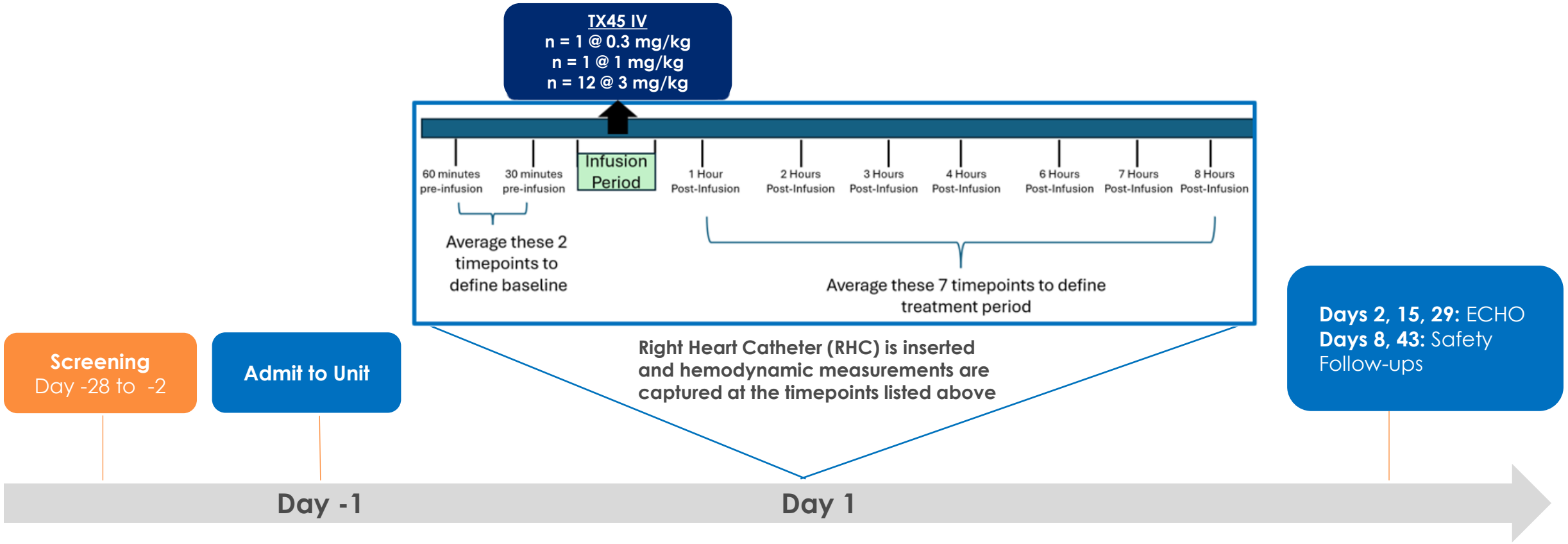
Phase 1b (Part B) Trial Design

A Single Dose, Open-Label, Acute Hemodynamic Trial in PH-HFrEF (n = 14)



- 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)
- Pure intention to treat (ITT) analysis performed: all data points included in the analysis

Key Hemodynamic Measures

Goal: Treatment for PH due to heart failure needs to **both** increase LV function and improve pulmonary vascular and right ventricular 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
SVR *(Systemic Vascular Resistance)*	• Measure of resistance to blood flow through the entire systemic circulation • SVR = (mAP – CVP)/CO	• Critical indicator of cardiovascular heath
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 Pulmonary Artery Pressure = average pressure required to pump blood through the lungs, mAP = mean Arterial Pressure, CO = Cardiac Output, CVP = central venous pressure

Baseline Characteristics and Concomitant Medications Consistent with HFrEF Population; Enriched for CpcPH

Baseline Characteristics	All Subjects
Age [mean (SD)]	66.9 (7.9)
Females [n (%)]	7 (50%)
LVEF (%); [mean (SD)]*	34.1 (6.6)
NT-proBNP (pg/mL); [mean (SD)]	3188 (2217)
BMI [mean (SD)]	30.1 (5.3)
Creatinine (uMol/L); [mean (SD)]**	98.6 (23.6)
Comorbidities:	
Hypertension [n (%)]	14 (100%)
Atrial fibrillation [n (%)]	10 (71.4%)
Diabetes mellitus [n (%)]	2 (14.3%)
Coronary artery disease [n (%)]	10 (71.4%)
NYHA Class [n (%)]:	
NYHA Class II	6 (42.9%)
NYHA Class III	8 (57.1%)

PVR < 2WU	2 WU ≤ PVR < 3WU	PVR ≥3 WU
n = 2	n = 5	n = 7

Key Concomitant Medications	All Subjects
ACEi/ARB/ARNi [n (%)]	14 (100%)
MRA [n (%)]	10 (71.4%)
SGLT2i [n (%)]	9 (64.3%)
Loop Diuretic [n (%)]	12 (85.7%)
Beta-blocker [n (%)]	11 (78.6%)
Digoxin [n (%)]	6 (42.9%)

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

Baseline Hemodynamics are Consistent with PH-HFrEF

Parameter	All Patients Baseline Value Mean (SD)	Generally Accepted Normal Ranges (At Rest)
Systolic Blood Pressure (mm Hg)	136 (14.1)	90-120
Diastolic Blood Pressure (mm Hg)	78 (11.3)	60-80
Pulmonary Capillary Wedge Pressure (mm Hg)	21.1 (5.2)	4-12
Pulmonary Vascular Resistance (Wood Units)	3.26 (1.46)	<2
Cardiac Output (L/min)	4.23 (1.53)	4-8
Stroke Volume (mL)	62.9 (23.9)	60-100
Total Pulmonary Resistance (Wood Units)	8.94 (3.31)	<3
Mean Pulmonary Artery Pressure (mm Hg)	34.1 (6.8)	12-16
Systemic Vascular Resistance (Wood Units)	22.4 (6.5)	10-15
Right Atrial Pressure (mm Hg)	10.3 (3.6)	2-8

TX45 was Well-Tolerated in PH-HFrEF After a Single Dose

- No serious or severe adverse events, discontinuations, infusion related reactions or drug related adverse events
- All TEAEs were mild/moderate and self-limited
- There were no clinically significant changes in vital signs, ECG or safety laboratory values
  - Transient asymptomatic drop of sBP (5-10 mm Hg) on day 1
- No signs or symptoms of congestion
- No TEAE of fatigue

Treatment-emergent adverse events (TEAE)				
Preferred Term	**0.3 mg/kg (n = 1)**	**1 mg/kg (n = 1)**	**3 mg/kg (n = 12)**	**Total (n = 14)**
Procedural back pain*	1	-	5	6 (42.9%)

** TEAE of procedural back pain due to Right Heart Catheterization*

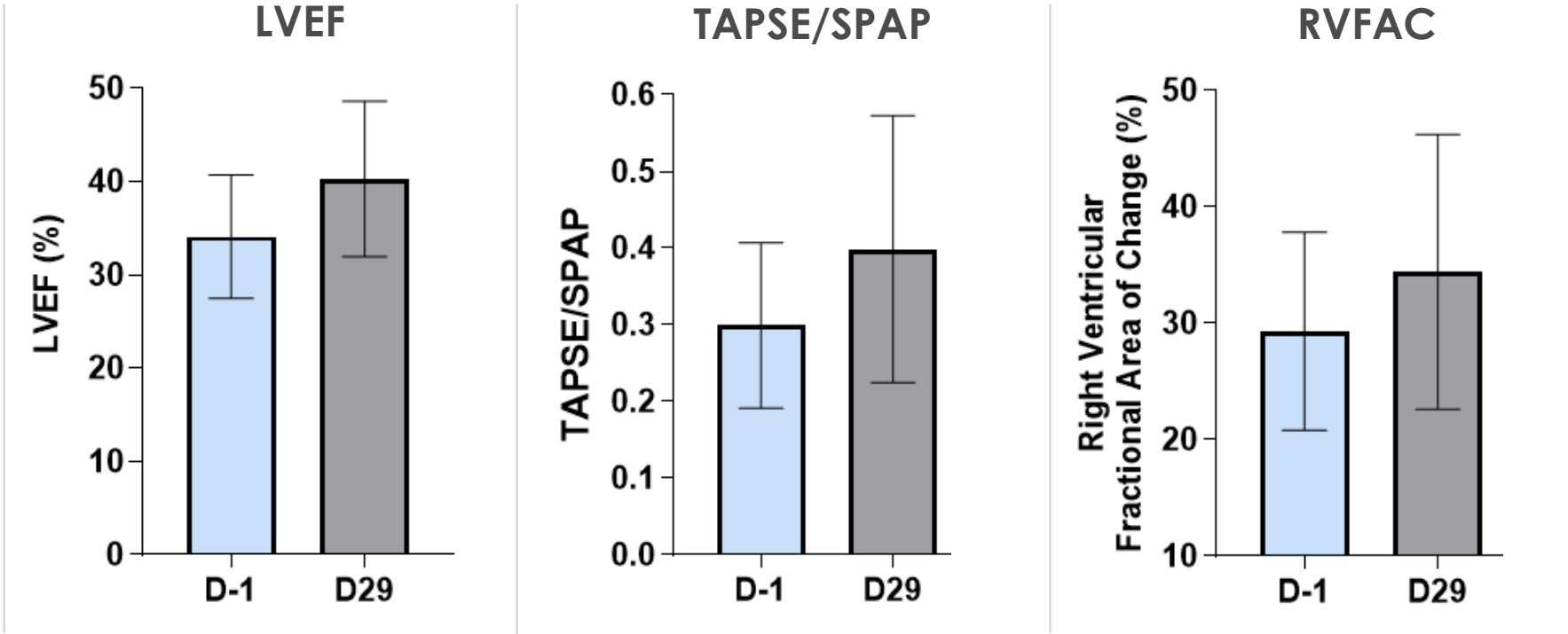
TX45 Improved Left Heart Function and Pulmonary Hemodynamics in PH-HFrEF Patients

Hemodynamic Endpoints	CFB* Mean [95% CI]	% CFB* Mean [95% CI]
Key Hemodynamic Endpoints (n = 14)		
Δ PCWP in all participants	**-6.4 [-8.6 to -4.2] mm Hg**	**-29.2% [-36.0% to -22.4%]**
Δ PVR in CpcPH (PVR ≥ 3 WU) (n = 7)	-1.10 [-2.79 to +0.59] WU	-19.7% [-45.2% to +5.8%]
Δ PVR in CpcPH (PVR ≥ 2 WU) (n = 12)	-0.61 [-1.72 to +0.50] WU	-10.3% [-36.6% to +15.9%]**
Other Hemodynamic Effects (n = 14)		
Δ CO (cardiac output)	**+0.65 [+0.25 to +1.05] L/min**	**+17.3% [+5.2% to +29.3%]**
Δ SV (stroke volume)	**+6.8 [+0.6 to +13.0] mL**	**+13.4% [+0.9% to +25.9%]**
Δ TPR (total pulmonary resistance)	**-2.82 [-4.00 to -1.64] WU**	**-29.2% [-37.1% to -21.3%]**
Δ mPAP (mean pulmonary artery pressure)	**-6.5 [-8.7 to -4.2] mm Hg**	**-19.3% [-24.8% to -13.8%]**
Δ SVR (systemic vascular resistance)	**-3.2 [-5.7 to -0.7] WU**	**-12.9% [-20.8% to -5.0%]**
Δ RAP (right atrial pressure)	**-3.1 [-4.3 to -1.9] mm Hg**	**-29.2% [-39.1% to -19.4%]**

WU = Wood Unit
***Green** CFB endpoints signify 95% confidence interval does not cross zero*
** CFB = Change from Baseline = (Average of Hours 1-8) – Baseline*
*** In the PVR ≥2 WU group, there was one outlier that drove a difference between the mean (-10.3%) and the median (-18.3%); mean and median values were similar for other hemodynamic assessments*

Echo Results at Day 29 Demonstrated Sustained Improvement in Markers of LV and RV Function, and Pulmonary Hemodynamics

Data Presented as Mean ± SD for All Subjects (n = 14)



CFB Mean [95% CI]	+6.2 [+2.7 to +9.7]	+0.10 [+0.03 to +0.17]	+5.1 [-0.11 to +10.3]
% CFB Mean [95% CI]	+19.4% [+9.0% to +29.8%]	+36.3% [+11.3% to +61.2%]	+20.3% [+3.2% to +37.3%]

CFB = change from baseline, CI = confidence interval
Green CFB endpoints signify 95% confidence interval does not cross zero
LV / RV = left ventricle / right ventricle
LVEF = left ventricular ejection fraction
TAPSE/SPAP = tricuspid annular plane systolic excursion/systolic pulmonary arterial pressure, an inversely correlated surrogate for PVR
RVFAC = right ventricular fractional area of change; a measure of right heart function

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Summary: TX45 Improves Cardiac and Pulmonary Hemodynamics in PH-HFrEF and PH-HFpEF Patients

- TX45 was well-tolerated in both patient populations
- TX45 demonstrated hemodynamic improvements in both left heart function and in the pulmonary vasculature in PH-HFrEF, consistent with effects in PH-HFpEF
  - Acute improvement in left ventricular hemodynamics and pulmonary vascular / RV hemodynamics (PCWP, CO, PVR, TPR, mPAP)
  - Echocardiographic improvements at Day 29 (LVEF, TAPSE/SPAP, RVFAC)
  - The magnitude of the reduction in PCWP and PVR, demonstrated in our HFpEF and HFrEF cohorts, have been associated with meaningful changes in 6MWD in previous studies[1-3]
  - Right ventricular afterload, as assessed by TPR, was reduced. Reduced RV afterload has been associated with improved mortality and outcomes in cohort studies of patients with Group 2 PH[4]
- Results support future expansion of TX45's addressable Group 2 PH patient population to PH-HFrEF, pending results of ongoing APEX Phase 2 clinical trial

1. *Lewis GD et al. Circ. Heart Failure 2023*
2. *Lewis GD et al. Circulation 2007*
3. *Zhang H et al. JACC Cardiovasc. Interv. 2019*
4. *Tampakakis,, Circ Heart Failure, 2018*