

**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): October 8, 2026

Tenax Therapeutics, Inc.
(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction
of incorporation)

001-34600
(Commission
File Number)

26-2593535
(IRS Employer
Identification No.)

101 Glen Lennox Drive, Suite 300
Chapel Hill, North Carolina 27517
(Address of principal executive offices) (Zip Code)

919-855-2100
(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:

- ☐ 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(s)	Name of each exchange on which registered
Common Stock, \$0.0001 par value per share	TENX	The Nasdaq Stock Market LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (17 CFR 230.405) or Rule 12b-2 of the Securities Exchange Act of 1934 (17 CFR 240.12b-2).

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 8.01 Other Events.

As previously announced, Tenax Therapeutics, Inc. (the “Company”) is enriching its LEVEL-2 clinical trial based on key learnings from its recently completed Phase 3 LEVEL trial of TNX-103 in PH-HFpEF. The Company intends to amend LEVEL-2 enrollment criteria, as set forth in the attached Investor Presentation. To maximize the enrollment of these patients, whom LEVEL results suggest are those most likely to demonstrate improved exercise tolerance in the primary endpoint of LEVEL-2, the Company has temporarily paused enrollment in LEVEL-2. Enrollment may resume at each site as the amended protocol goes into effect there. The Company has requested a Type C meeting with the U.S. Food and Drug Administration to discuss the overall development of levosimendan. The Company’s corporate presentation, which it intends to use with investors and analysts, has been updated to address these matters and is attached hereto as Exhibit 99.1 and incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit 99.1 [Investor Presentation, dated October 8, 2026.](#)

Exhibit 104 Cover Page Interactive Data File (embedded within the Inline XBRL document).

SIGNATURES

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

Date: October 8, 2026

TENAX THERAPEUTICS, INC.

By: /s/ Christopher T. Giordano

Name: Christopher T. Giordano

Title: President and Chief Executive Officer



Corporate Presentation

October 2026

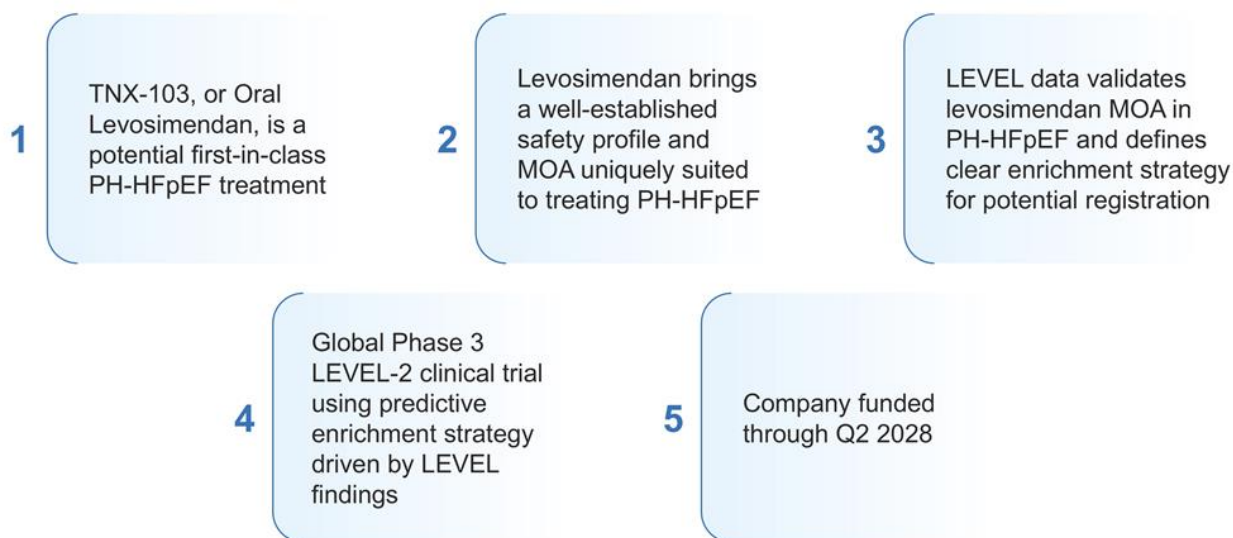
Forward-Looking Statements

Disclaimers

Except for historical information, all of the statements, expectations and assumptions contained in this presentation are forward-looking statements. These forward-looking statements include, but are not limited to, statements regarding our expectations about the design, enrollment, conduct, timing, and potential outcomes of the LEVEL-2 clinical trial; interpretations of clinical data from the LEVEL trial, including subgroup and post-hoc analyses, and the applicability of those data to the design and expected performance of LEVEL-2; our beliefs about the potential efficacy, safety, and regulatory path for oral levosimendan; our estimates of the potential market opportunity for our product candidates; our intellectual property position; our projected cash runway and ability to fund operations. Actual results might differ materially from those explicit or implicit in the forward-looking statements. Important factors that could cause actual results to differ materially include: risks of our clinical trials, including, but not limited to, the timing, delays, costs, design, location, initiation, enrollment, and results of such trials, including that the Phase 3 LEVEL trial did not meet its primary endpoint of change in 6-minute walk distance (6MWD) in the overall enrolled population; the risk that the Company's interpretation and characterization of clinical trial data, may not be shared by regulatory authorities, the medical and scientific communities, or investors, and that data from the LEVEL trial that the Company views as supportive of its LEVEL-2 trial design might not be predictive of LEVEL-2 outcomes; any delays in regulatory review and approval of product candidates in development; risks related to our business strategy, including the prioritization and development of product candidates; reliance on third parties, including Orion Corporation, our manufacturers and CROs; risks regarding the formulation, production, marketing, customer acceptance and clinical utility of our product candidates; the potential advantages of our product candidates; our competitive position; intellectual property risks; our ability to maintain our culture and recruit, integrate and retain qualified personnel and advisors, including on our Board of Directors; volatility and uncertainty in the global economy and financial markets in light of unexpected changes in tariffs and the possibility of pandemics, global financial and geopolitical uncertainties, including in the Middle East and the Russian invasion of and war against the country of Ukraine; risks associated with our cash needs; changes in legal, regulatory and legislative environments in the markets in which we operate and the impact of these changes on our ability to obtain regulatory approval for our products; and other risks and uncertainties set forth from time to time in our SEC filings. All forward-looking statements in this presentation speak only as of the date of this presentation and are based on the Company's current expectations and assumptions. Tenax Therapeutics assumes no obligation and does not intend to update these forward-looking statements except as required by law. This presentation shall not constitute an offer to sell or the solicitation of an offer to buy any securities of the Company.

Evidence-Driven Phase 3 Program

LEVEL DATA ENHANCES HELP TRIAL PROOF OF CONCEPT TO DE-RISK ONGOING PHASE 3; WELL-ESTABLISHED SAFETY PROFILE



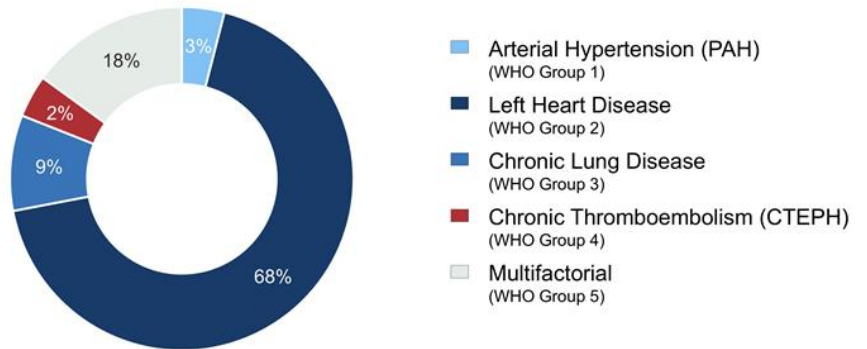
Pulmonary Hypertension in Heart Failure with Preserved Ejection Fraction (PH-HFpEF)

Group 2 Pulmonary Hypertension (Left Heart Disease)

PH-HFpEF is the most common form of PH

- Patients present with shortness of breath, leg edema, and poor exercise capacity
- A progressive, debilitating and often fatal disease
- No approved treatment is recommended by current guidelines

Pulmonary Hypertension Global Prevalence

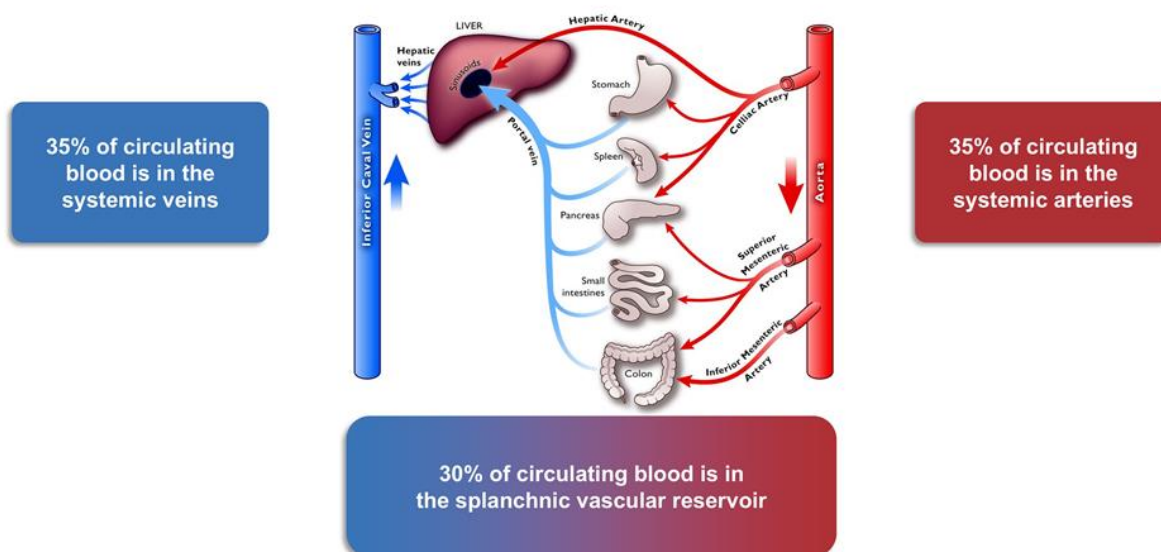


~50% of Group 2 patients have PH-HFpEF, a large patient population with significant unmet need

PH: pulmonary hypertension; PH-HFpEF: pulmonary hypertension in heart failure with preserved ejection fraction; WHO: World Health Organization.
Strange G, et al. *Heart (British Cardiac Society)* vol. 98,24 (2012): 1805-11.

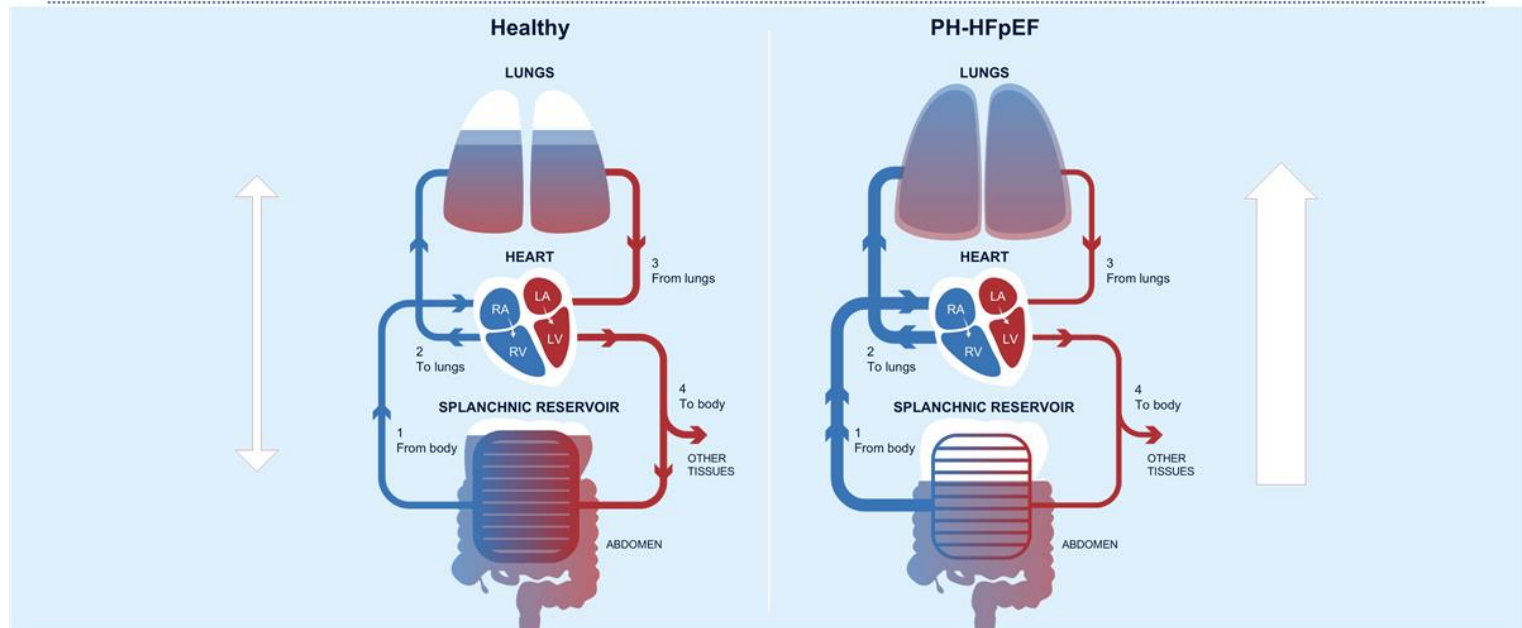
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The Fundamental Role of the Splanchnic Reservoir



Blood Volume Distribution

REDUCING BLOOD VOLUME TO LOWER VENOUS AND PULMONARY PRESSURE



7 LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle; PH-HFpEF, pulmonary hypertension in heart failure with preserved ejection fraction. Gelman S, et al. *J Am Soc Anesthesiol.* 2004;100(2):434-439.; Fudim M, et al. *Eur J Heart Fail.* 2021;23:1076-1084.; Yaku H, et al. *J Cardiol.* 2024;83:330-337.

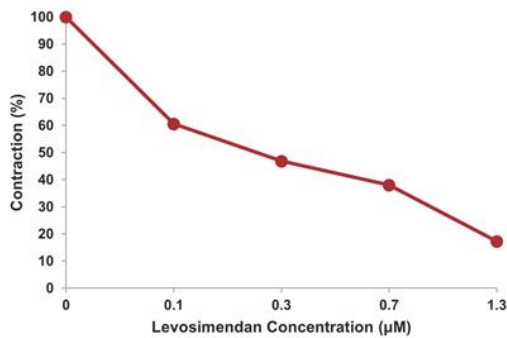
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Oral Levosimendan (TNX-103)

Levosimendan's MOA is Uniquely Suited to Treat PH-HFpEF

NOVEL, POTENTIAL FIRST-IN-CLASS K-ATP CHANNEL ACTIVATOR AND CALCIUM SENSITIZER

Dose-dependent dilation of human portal vein with levosimendan

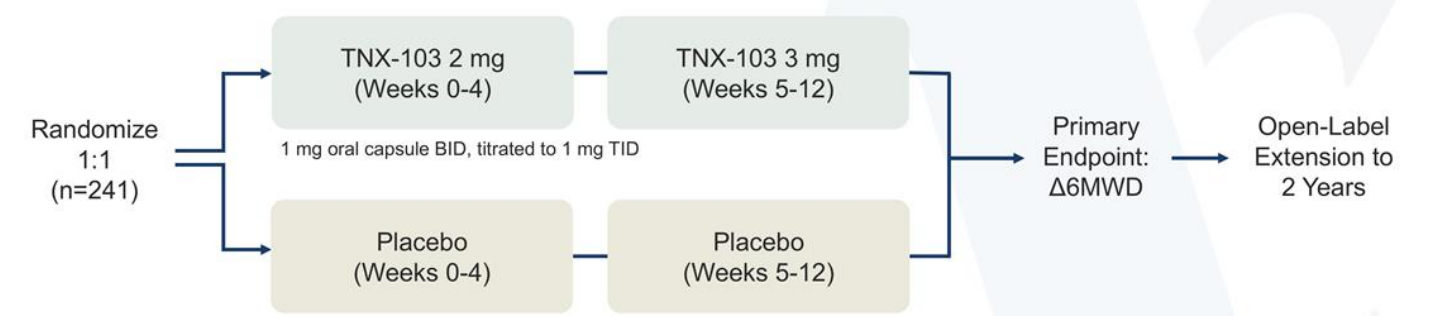


Vein Becomes Less Contracted as Concentration of Levosimendan Increases

- Human portal vein placed in tissue bath
- Vein is contracted with norepinephrine to mimic human physiology
- Levosimendan is then progressively added to tissue bath

Phase 3 LEVEL Trial Design

PHASE 3 REGISTRATIONAL TRIAL IN U.S. AND CANADA



Hemodynamic Inclusion Criteria

RHC with qualifying hemodynamics at rest:		Hemodynamics with passive leg raise		Hemodynamics with bicycle exercise
• PCWP ≥ 18 mmHg, and • mPAP ≥ 30 mmHg, and • RAP ≥ 8 mmHg	OR	• PCWP ≥ 20 mmHg, and • mPAP ≥ 32 mmHg, and • RAP ≥ 8 mmHg	OR	• PCWP ≥ 25 mmHg, and • mPAP ≥ 35 mmHg, and • RAP ≥ 10 mmHg

We Believe LEVEL Confirms the Biological Thesis

PRIMARY ENDPOINT MISSED ON PATIENT SELECTION, NOT ON DRUG EFFECT: LEVEL-2 IS DE-RISKED AS A RESULT

THE BIOLOGY IS CONFIRMED

Bi-ventricular disease, bi-ventricular effect

PH-HFpEF combines volume overload on both sides of the heart, with preload on the left ventricle and afterload and elevated PA pressure on the right. TNX-103 effect on both ventricles demonstrated across numerous echocardiographic parameters.

Preload down

Site-specific splanchnic venodilation cut cardiac wall stress 49% (NT-proBNP), by dramatically lowering filling pressures.

Pulmonary pressure down

RVSP fell 3.5 mmHg over 12 weeks in overall population, and 4.9 mmHg in the below-the-median population, in LEVEL (p-value 0.009).

THE MISS IS EXPLAINED

Design, not drug

The neutral primary result reflects a protocol design flaw, not an ineffective drug: too many patients walked too far at baseline to improve.

A clear gradient

Δ 6MWD rises as baseline walk falls. The most limited patients gained more than 26 M in 12 weeks, tracking HELP ($p = 0.0112$).

Not a chance finding

Baseline 6MWD, NT-proBNP and RVSP analyses converge on the same responder population.

LEVEL-2 IS DE-RISKED

Selection now defined

Enrichment is set by observed data, not assumption. LEVEL-2 population's baseline disease severity predicts a significant, clinically meaningful primary endpoint benefit.

Safety supports it

Treatment-emergent AEs were similar in patients above and below the median baseline walk.

More to come

Protocol design paper, primary publication and further analyses through 1H 2027.

Patient Demographics

BASELINE CHARACTERISTICS WERE BROADLY BALANCED ACROSS TREATMENT ARMS

Characteristic	TNX-103 (N=120)	Placebo (N=121)	Overall (N=241)
Age, years, mean (SD)	69.8 (9.7)	68.5 (10.1)	69.1 (9.9)
Female, n (%)	86 (71.7)	86 (71.1)	172 (71.4)
BMI, kg/m ² , mean (SD)	33.2 (5.8)	32.9 (6.6)	33.1 (6.2)
eGFR <60 mL/min/1.73 m ² , n (%)	33 (27.5)	44 (36.4)	77 (32.0)
SGLT2 inhibitor use, n (%)	80 (66.7)	93 (76.9)	173 (71.8)
GLP-1 receptor agonist use, n (%)	36 (30.0)	32 (26.4)	68 (28.2)
MRA use, n (%)	68 (56.7)	76 (62.8)	144 (59.8)
Diuretic use, n (%)	103 (85.8)	106 (87.6)	209 (86.7)
Baseline 6MWD, m, mean (SD)	316.5 (87.3)	322.5 (83.5)	319.5 (85.3)

Characteristic	TNX-103 (N=120)	Placebo (N=121)	Overall (N=241)
NYHA Functional Class II, n (%)	53 (44.2)	55 (45.5)	108 (44.8)
NYHA Functional Class III, n (%)	67 (55.8)	64 (52.9)	131 (54.4)
NYHA Functional Class IV, n (%)	0	2 (1.7)	2 (0.8)
Qualified at rest, n (%)	46 (38.3)	51 (42.1)	97 (40.2)
Qualified on provocation, n (%)	74 (61.7)	70 (57.9)	144 (59.8)
Slow acetylator, n (%)	66 (55.0)	54 (44.6)	120 (49.8)
Intermediate acetylator, n (%)	33 (27.5)	48 (39.7)	81 (33.6)
Rapid acetylator, n (%)	14 (11.7)	7 (5.8)	21 (8.7)
Acetylator status unknown, n (%)	7 (5.8)	12 (9.9)	19 (7.9)

Safety

TOLERABILITY DIFFERENCE BETWEEN ARMS; SERIOUS EVENTS AND CLINICAL WORSENING BALANCED

Adverse event summary	TNX-103 (N=120)	Placebo (N=121)
Any adverse event, n (%)	104 (86.7)	87 (71.9)
Treatment-related adverse event, n (%)	46 (38.3)	21 (17.4)
Leading to treatment discontinuation, n (%)	10 (8.3)	2 (1.7)
Leading to dose reduction, n (%)	18 (15.0)	5 (4.1)
Serious adverse event, n (%)	13 (10.8)	13 (10.7)
Adverse event of special interest, n (%)	11 (9.2)	7 (5.8)
Associated with adjudicated CWE, n (%)	3 (2.5)	3 (2.5)
Unplanned 24-hr CV hospitalization	0 (0)	3 (2.5)
Outpatient visit for IV diuretics	1 (0.8)	0 (0)
Death	2 (1.7)	0 (0)

- Higher rates of treatment-related AEs, dose reductions and discontinuations on drug, driven by headache, palpitations and hypotension
- Serious AEs and adjudicated clinical worsening events were balanced across arms
- No new-onset atrial fibrillation or ventricular tachycardia in patients without pre-existing evidence

Treatment Emergent Adverse Events

BALANCED BETWEEN TNX-103 AND PLACEBO IN THE $\geq$ AND $<$ MEDIAN BASELINE 6MWD SUBGROUPS

System Organ Class (SOC) Preferred Term (PT), n (%)	TNX-103			Placebo		
	Overall (N=120)	BL 6MWD < Median (N=62)*	BL 6MWD $\geq$ Median (N=58)*	Overall (N=121)	BL 6MWD < Median (N=57)*	BL 6MWD $\geq$ Median (N=64)*
Subjects with at least one TEAE	104(86.7%)	54(87.1%)	50(86.2%)	87(71.9%)	45(78.9%)	42(65.6%)
Headache	25(20.8%)	13(21.0%)	12(20.7%)	17(14.0%)	6(10.5%)	11(17.2%)
Palpitations	16(13.3%)	8(12.9%)	8(13.8%)	9(7.4%)	6(10.5%)	3(4.7%)
Dizziness	14(11.7%)	7(11.3%)	7(12.1%)	9(7.4%)	7(12.3%)	2(3.1%)
Diarrhoea	15(12.5%)	10(16.1%)	5(8.6%)	5(4.1%)	4(7.0%)	1(1.6%)
Dyspnoea	9(7.5%)	5(8.1%)	4(6.9%)	9(7.4%)	5(8.8%)	4(6.3%)
Oedema peripheral	12(10.0%)	8(12.9%)	4(6.9%)	6(5.0%)	3(5.3%)	3(4.7%)
Nausea	6(5.0%)	5(8.1%)	1(1.7%)	11(9.1%)	5(8.8%)	6(9.4%)
Fatigue	5(4.2%)	2(3.2%)	3(5.2%)	8(6.6%)	6(10.5%)	2(3.1%)

- Treatment Emergent Adverse Events, defined as AEs that appeared, or worsened, since the start of the trial
- TEAE types and rates are representative of a typical HFpEF population, and would not qualify as serious
- Trend observed: increased frequency of events related to levosimendan, all known to be associated with the therapy
- No difference appears in the frequency between groups whose baseline 6MWD was <333 M or ≥ 333 M

Primary and Key Secondary Endpoints

Primary Endpoint (Week 12)		TNX-103 (N=116)	Placebo (N=120)	Treatment difference
6MWD	LS mean	14.0 M (SE: 7.7 M)	10.4 M (SE: 7.6 M)	3.5 M (SE: 7.3; p = 0.63)
	Mean	17.7 M (SD: 40.2 M)	9.8 M (SD: 54.7 M)	8.0 M
Secondary Endpoints (Week 12)		TNX-103 (N=116)	Placebo (N=120)	Treatment difference
KCCQ-TSS, LS mean change		6.6 (SE: 2.4)	6.5 (SE: 2.3)	0.1 (SE: 2.2); NS
NYHA functional class improvement, n (%)		28 (24.1)	27 (22.5)	NS
Adjudicated clinical worsening, n (%)		3 (2.5)*	3 (2.5)*	NS

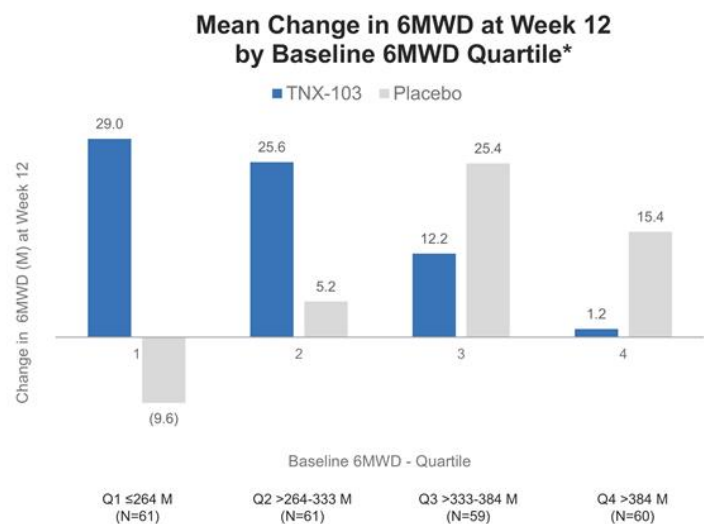
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*N=120 and N=121 for TNX-103 and placebo arms, respectively.
6MWD: 6-minute walk distance; LS: least squares; SE: standard error; SD: standard deviation; KCCQ-TSS: Kansas City Cardiomyopathy Questionnaire-Total Symptom Score; NYHA: New York Heart Association; NS: not significant p-value.



Mean Change in 6MWD by Baseline 6MWD Quartile

INVERSE LINEAR RELATIONSHIP BETWEEN BASELINE 6MWD AND TREATMENT EFFECT

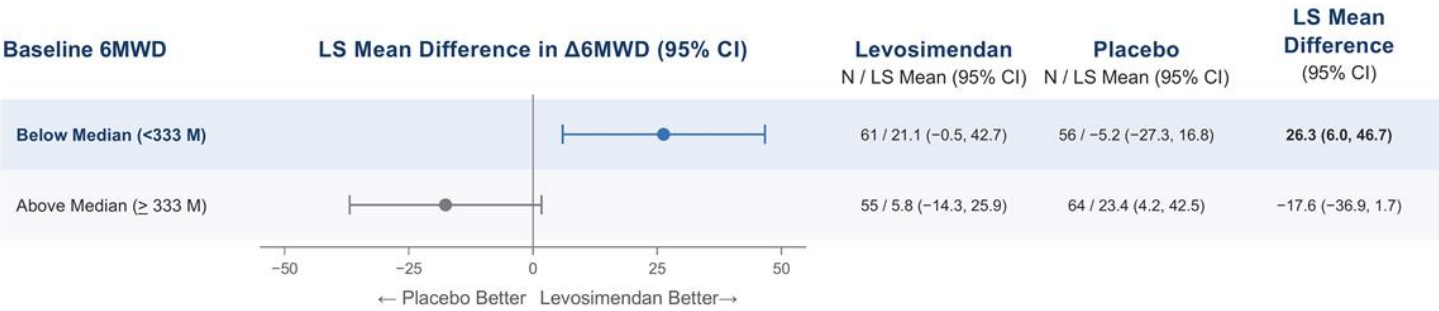


Levosimendan produced a large and clinically meaningful improvement in 6MWD in those patients who had a lower baseline walk distance (sicker) and room for improvement

Subgroup and quartile analyses show very clear evidence of treatment effect modification by baseline 6MWD: the treatment × baseline 6MWD interaction term in the primary analysis was significant in all 100 imputed datasets, with an average p-value of 0.006.

16 *Post-hoc analysis
6MWD: 6-minute walk distance; LS: least squares.

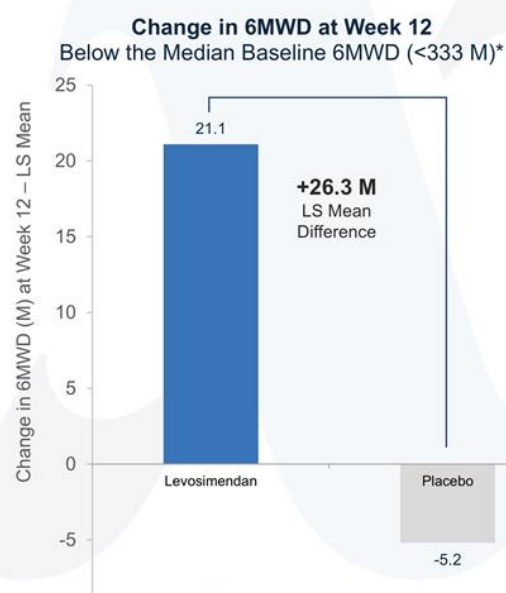
Drug Response Correlates with Baseline 6MWD



Patients with Greater Exercise Limitation Demonstrated Large Treatment Effect

Multi-variable analyses identified baseline 6MWD as the strongest predictor of improvement in 6MWD

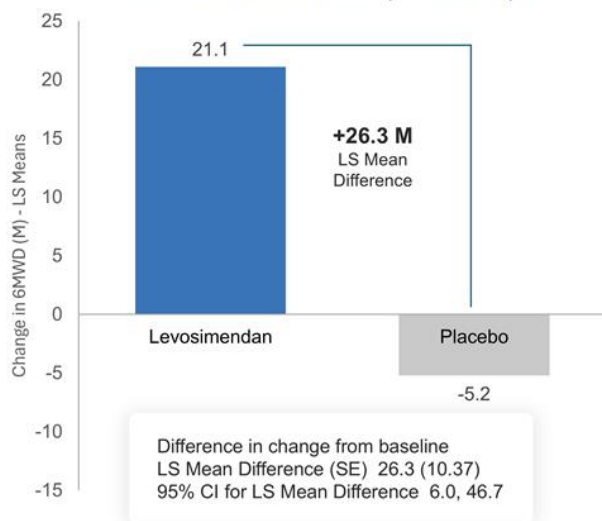
Treatment with TNX-103 resulted in a 26.3 M improvement compared to placebo in patients with a baseline 6MWD <333 M (95% CI: 6.0, 46.7; $p = 0.0112^{\#}$)



LEVEL Patients with Baseline 6MWD <Median: Improvement Similar to HELP

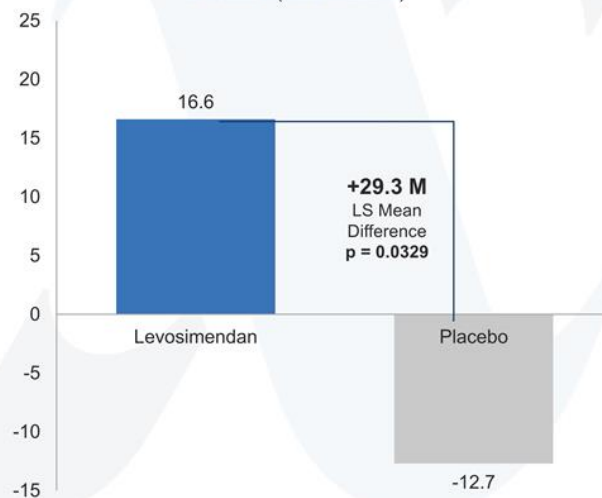
LEVEL Trial - Baseline <median 6MWD

Change in 6MWD at Week 12
Below the Median Baseline 6MWD (mean ~250 M)*

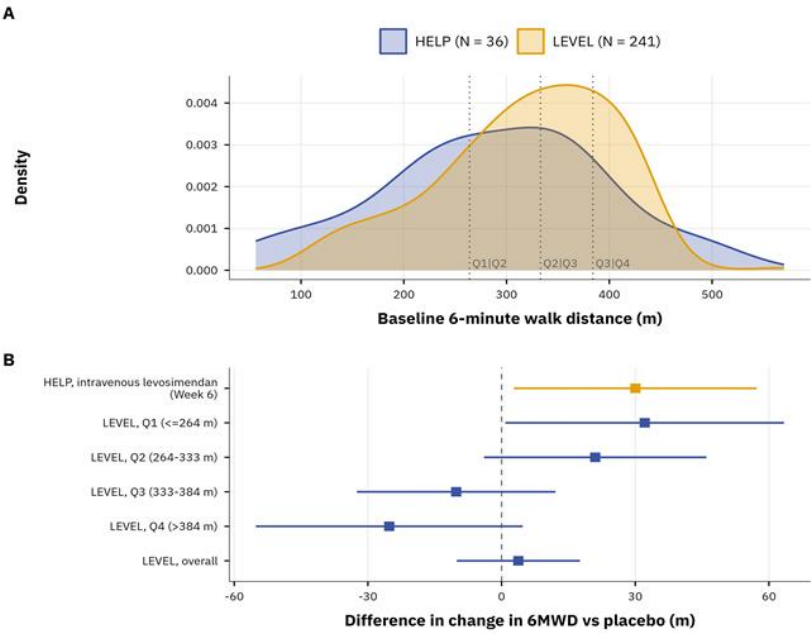


Phase 2 HELP Trial

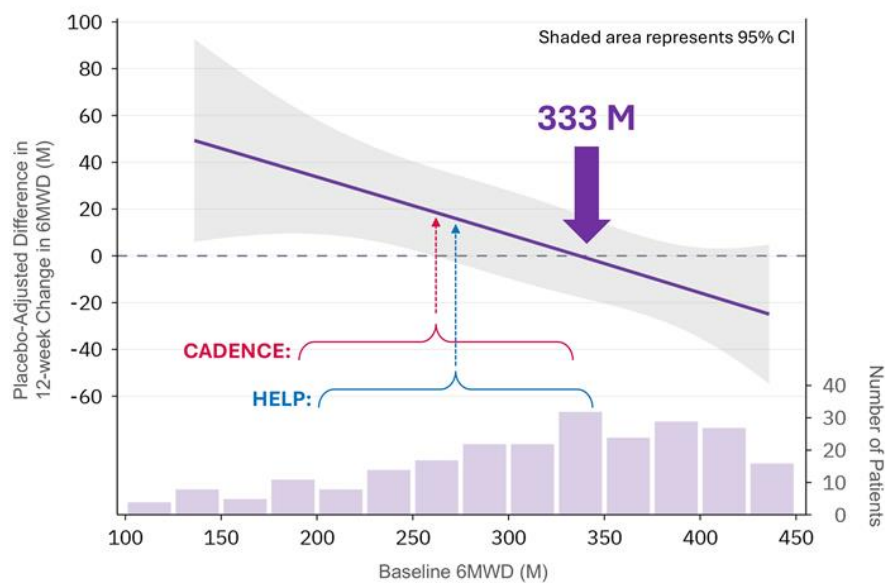
6MWD Change from Baseline
at Week 6 (mean ~282 M)



6MWD Treatment Effect: Comparison of LEVEL (12 Weeks) & HELP (6 Weeks)



Lower 6MWD, Greatest Benefit



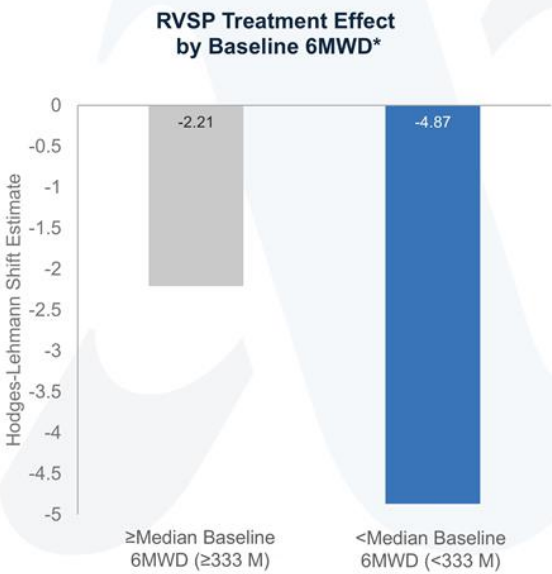
- Inverse linear relationship between baseline 6MWD and treatment effect
- In LEVEL, levosimendan-treated patients whose baseline 6MWD matched HELP and CADENCE (274-285 M) had a ~20 M placebo-adjusted improvement in 6MWD

RVSP Reduction Greatest in Patients with Baseline 6MWD <Median (<333 M)

LEVOSIMENDAN EFFECTIVELY LOWERS RVSP ACROSS THIS PULMONARY HYPERTENSION POPULATION

Physiologic improvement in RVSP aligns with 6MWD improvement in this cohort (Baseline 6MWD <333 M*)

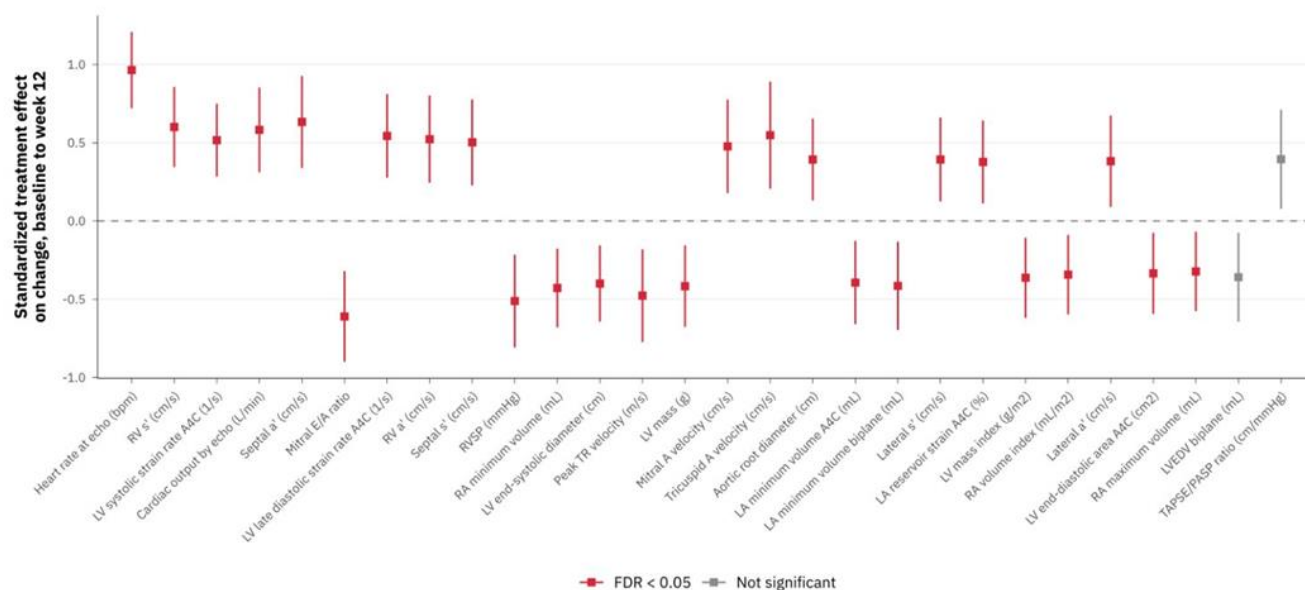
	≥Median Baseline	<Median Baseline
	-2.210 (1.5817)	-4.873 (1.8776)
95% CI	-5.370, 0.830	-8.410, -1.050
p-value	0.1322	0.0090



22 *Prespecified subgroup
6MWD: 6-minute walk distance; CI: confidence interval.

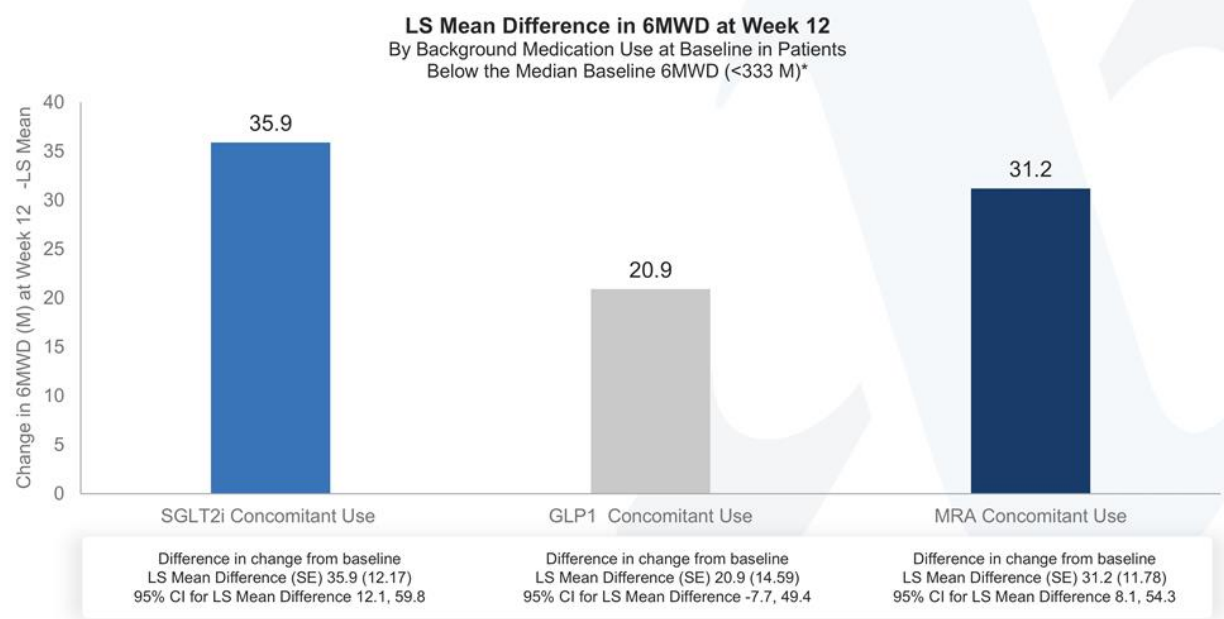
Echocardiographic Measures Point to RV & LV Functional Enhancement

ECHOCARDIOGRAPHY CONDUCTED AT BASELINE AND WEEK 12



TNX-103 Benefited Patients on State-of-the-Art Therapy

PATIENTS WITH BASELINE 6MWD <MEDIAN (333 M) AND ON GLP-1s & GUIDELINE-DIRECTED MEDICAL THERAPY BENEFIT MOST



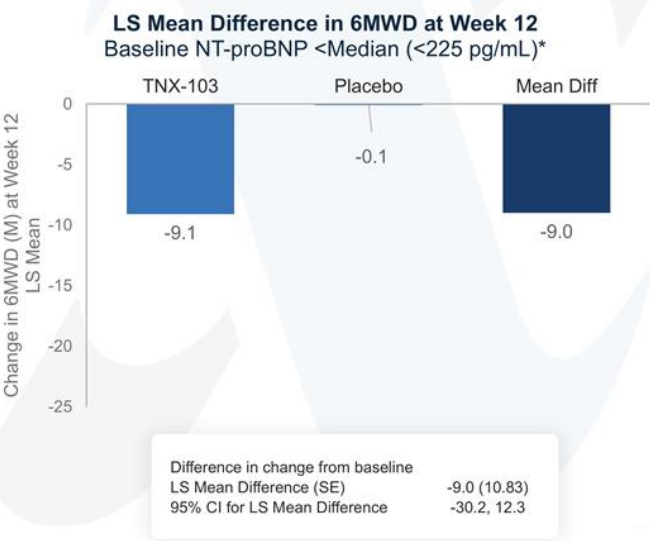
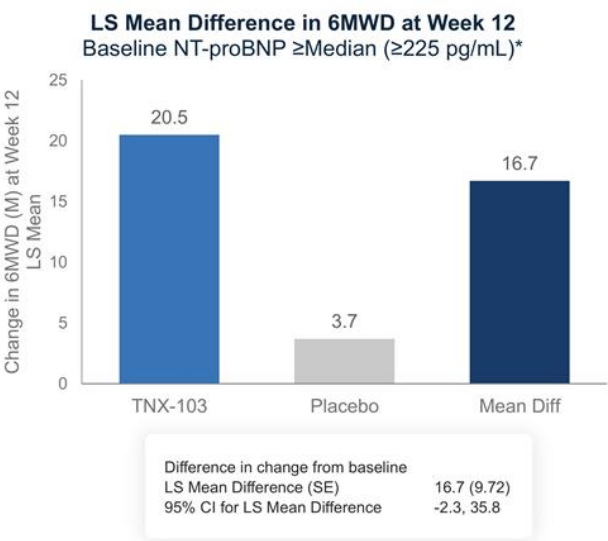
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*Prespecified subgroup

6MWD: 6-minute walk distance; LS: least squares; SE: standard error; CI: confidence interval.



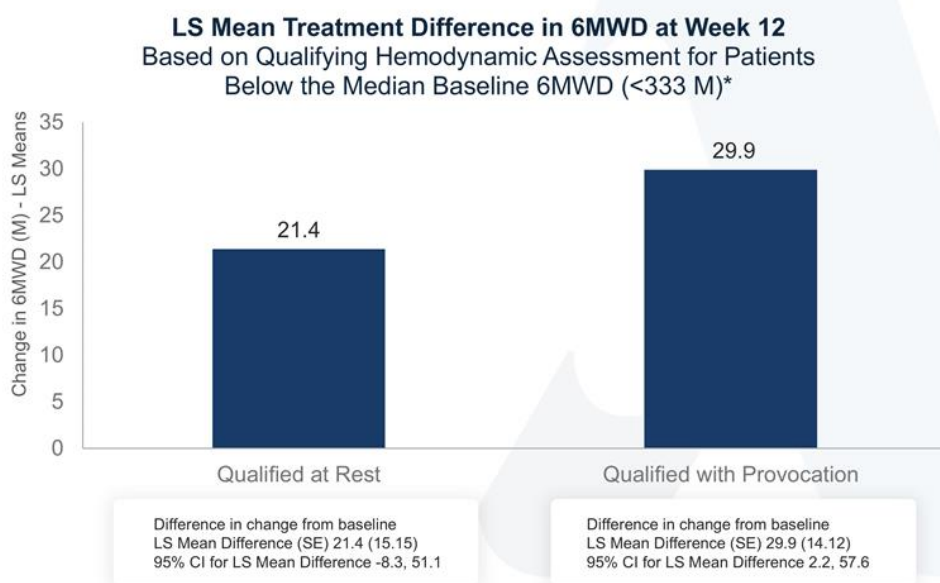
LEVEL Study 6MWD Change by Baseline NT-proBNP



25 *Post-hoc analysis
6MWD: 6-minute walk distance; NT-proBNP: N-terminal pro B-type natriuretic peptide; LS: least squares; SE: standard error; CI: confidence interval.

Δ 6MWD by Type of Qualifying RHC Hemodynamic Assessment

BY SUBGROUP WITH BASELINE 6MWD < MEDIAN (<333 M)



Strongest Δ 6MWD has been Observed in Lowest Baseline 6MWD Cohort

PAH STUDIES WITH BEST RESULTS IN LOWEST 6MWD COHORT

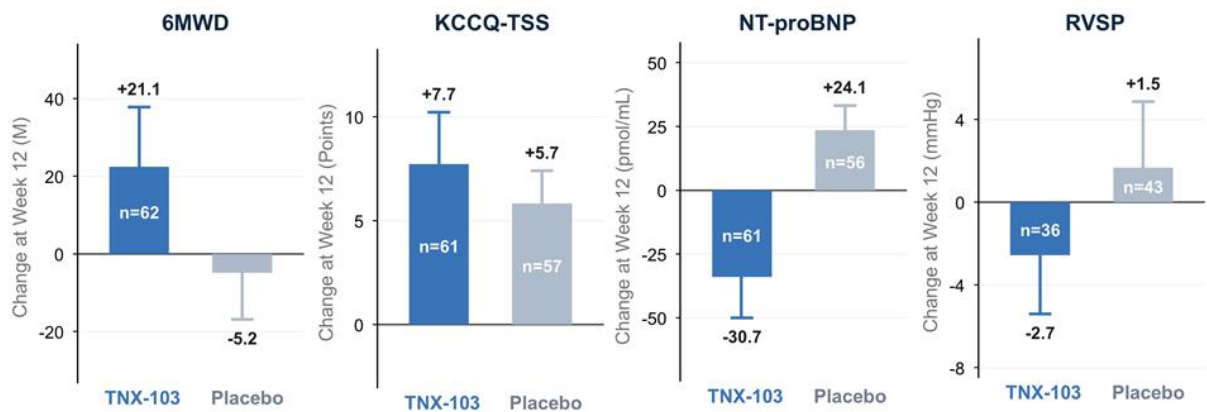
- **SERAPHIN Trial** (1) (macitentan) <300 M baseline cohort
- **SUPER-1 Trial** (2) (sildenafil) <325 M baseline cohort
- **PHIRST Trial** (3) (tadalafil) <325 M baseline cohort
- **TRIUMPH-1 trial** (4) (treprostinil) <350 M baseline cohort

PH/HFPEF STUDIES REPORTING POSITIVE 6MWD RESULTS

- **PRESERVED-HF** (5) (dapagliflozin) mean 244 M baseline
- **CADENCE** (6) (low dose sotatercept) median 259 M
- **HELP** (IV levosimendan) median 282 M

1. Souza, Rogério, et al. Association between six-minute walk distance and long-term outcomes in patients with pulmonary arterial hypertension: data from the randomized SERAPHIN trial. PLoS One 2018; 13.3: e0193226.
2. Galiè N, Ghofrani HA, Torbicki A, et al. Sildenafil citrate therapy for pulmonary arterial hypertension. N Engl J Med 2005; 353(20):2148–2157
3. Galiè N, Brundage BH, Ghofrani HA, et al. Tadalafil therapy for pulmonary arterial hypertension. Circulation 2009; 120(12):1068–1076
4. McLaughlin VV, Benza RL, Rubin LJ, et al. Addition of inhaled treprostinil to oral therapy for pulmonary arterial hypertension: a randomized controlled clinical trial. Journal of the American College of Cardiology 2010; 55(18):1915–1922
5. Nassif, Michael E., et al. The SGLT2 inhibitor dapagliflozin in heart failure with preserved ejection fraction: a multicenter randomized trial. Nature medicine 2021; 27.11: 1954-1960.
6. Gombert-Maitland, Mardi, et al. Sotatercept for combined post-and precapillary pulmonary hypertension associated with heart failure: results from the phase 2, randomized, placebo-controlled CADENCE study. Circulation 2026; 153.19: 1446-1459.

Baseline 6MWD Below Median (<333 M) Subgroup



	6MWD	KCCQ-TSS	NT-proBNP	RVSP
Difference or Treatment Effect	+26.3 M	+2.0 points	0.53 ratio	-4.9 mmHg
95% CI	6.0, 46.7	-4.8, 8.7	0.42, 0.65	-8.4, -1.1
Nominal p-value	0.0112	0.5676	<0.0001	0.0090

6MWD: 6-minute walk distance; KCCQ-TSS: Kansas City Cardiomyopathy Questionnaire-Total Symptom Score;
NT-proBNP: N-terminal pro B-type natriuretic peptide;
RVSP: right ventricular systolic pressure; CI: confidence interval

We Believe Learnings from LEVEL will De-risk LEVEL-2

Strong treatment effect in patients with baseline 6MWD below the median (<333 M) is real:

- ❖ Prespecified subgroup finding supported by multivariable analysis
- ❖ No evidence that regression to the mean explains the finding
- ❖ RVSP reduction aligns with the improvement in 6MWD improvement
- ❖ Magnitude of improvement in 6MWD is consistent with Phase 2 HELP trial
- ❖ Treatment effect is additive to GLP-1s and guideline-directed medical therapy for HFpEF
- ❖ Other PAH and PH-HFpEF studies have observed the strongest responses in patients with lower baseline 6MWD

Confirming Biological Activity Using NT-proBNP

NT-proBNP FELL IN OVERALL POPULATION WITH SUBSTANTIAL REDUCTION OBSERVED IN FIRST VISIT AFTER RANDOMIZATION

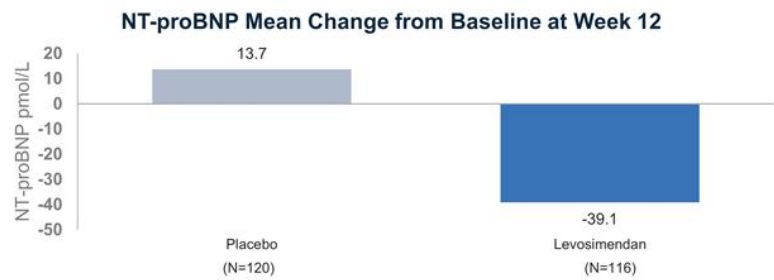
All Patients

- 49%

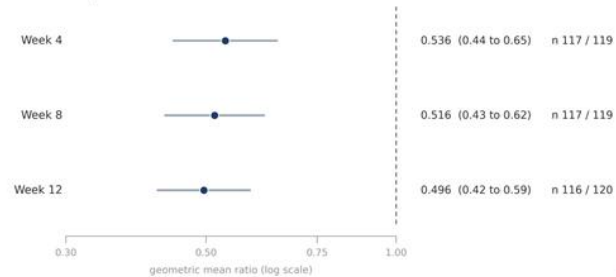
NT-proBNP vs. placebo at Week 12

Geometric LS mean ratio 0.51

(95% CI: 0.43, 0.60; p < 0.0001*)



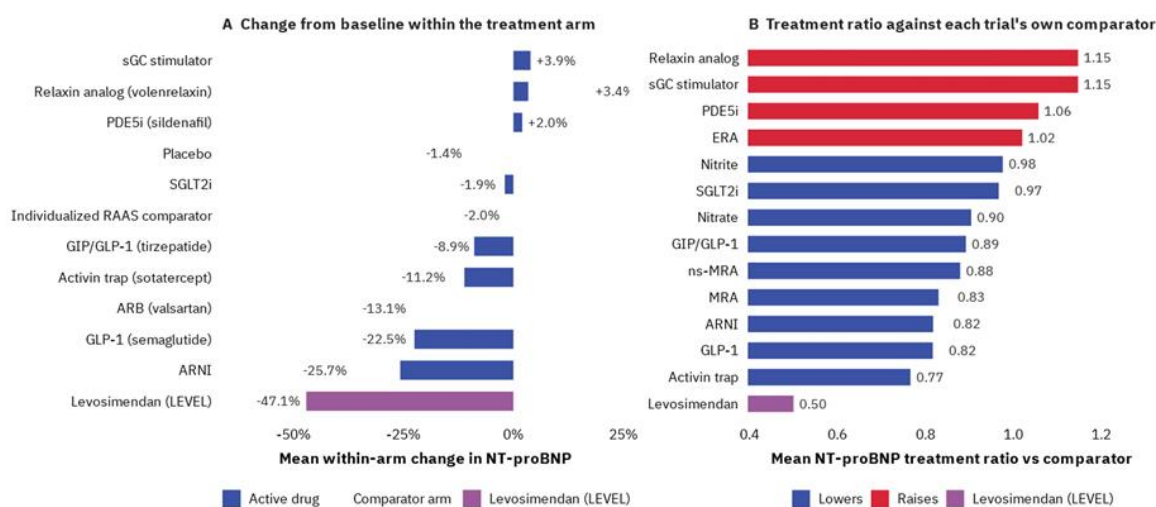
Substantial NT-proBNP reduction noted in first four weeks of TNX-103 treatment



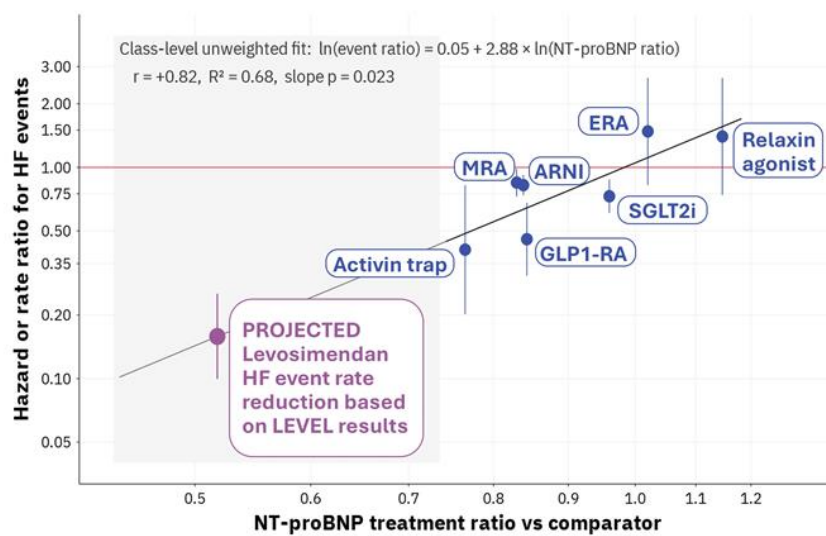
30 *nominal p-value.
NT-proBNP: N-terminal pro B-type natriuretic peptide; LS: least squares; CI: confidence interval.



LEVEL: Largest Reduction in NT-proBNP To Date in HFpEF



↓ NT-proBNP: Predicted Effect on ↓ HF Events



What LEVEL Tells Us

KEY LEARNINGS FROM THE FIRST PHASE 3 TRIAL

LEVEL did not meet its primary endpoint, but a strong treatment effect was seen across patients with higher disease burden

What we confirmed

- Oral levosimendan is safe and well-tolerated, with 1 mg BID/TID providing PK concentrations expected
- Targeting volume overload with K-ATP channel activation has direct effects on NT-proBNP and RVSP, two prespecified endpoints
- Treatment effect seen in HELP study validated
- Successful trial execution by sites and clinical development team



What we learned

- Drug effect is evident in patients with higher disease burden
- Study entry criteria allowed patients with moderate disease and little room to improve in 6MWD
- In patients with baseline 6MWD* < 333 m, treatment effect was **+26.3 m vs placebo** (95% CI: 6.0, 46.7; nominal p = 0.0112)
- In patients with baseline 6MWD* ≤ 300 m, or 300 m ≤ 6MWD ≤ 400 m & RAVI ≥ 25 mL/m², treatment effect was **+34 m vs placebo** (95% CI: 15, 53; nominal p = 0.001)
- In the overall population, NT-proBNP was reduced by 49% vs placebo (nominal p < 0.0001)

WHAT WE ARE DOING NOW

Amending LEVEL-2 to enrich on baseline 6MWD and RAVI

Building on LEVEL

A DATA-DRIVEN ENRICHMENT STRATEGY FOR LEVEL-2

- **Multivariable analyses** were used to identify a sub-population with strong treatment effects. 6MWD at baseline and Right Atrial Volume Index (RAVI) were the most robust and consistent predictors of treatment response
- **RAVI** reflects the size of the right atrium in relation to body surface area, and identifies those LEVEL patients with higher exercise capacity (walking 300m to 400m at baseline) most likely to benefit from treatment with levosimendan
- **Baseline 6MWD and RAVI requirements for LEVEL-2** are drawn from the LEVEL population with the strongest treatment effect
- **Tenax intends to Amend the LEVEL-2 protocol** to enrich the population for patients with high likelihood of demonstrating greater treatment effects resulting from their volume overload and demonstrated by more pronounced exercise impairment at baseline

Enriched LEVEL-2 entry criterion: $[100\text{m} \leq 6\text{MWD} \leq 300\text{m}]$ OR $[300\text{m} < 6\text{MWD} \leq 400\text{m AND RAVI} \geq 25 \text{ mL/m}^2]$

In LEVEL patients meeting these criteria:

- **> 34 meters vs placebo at Week 12** (95% CI: +15 M, +53 M; nominal $p = 0.001$)
- **> 50% of LEVEL patients meet these criteria**

Right Atrial Volume Index (RAVI) Identifies Patients with Strong Response to a Volume-Reduction Strategy

The primary driver of PH-HFpEF is excessive blood volume filling the heart and lungs

The established MOA of levosimendan in patients with PH-HFpEF is dilation of the veins of the splanchnic circulation, thereby reducing this excessive volume

- The excess blood entering the heart initially enters the right atrium, where the effect of this excess can be measured during a right heart catheterization (RHC) as right atrial pressure (RAP)
- LEVEL and LEVEL-2 participation requires an RAP of at least 8 mmHg on entry. Normal resting RA pressure is 5 mmHg, and the upper limit of normal is 8 mmHg
- Right atrial volume index (RAVI) is an echo measure of RA size. Normal RAVI is 25 for men and 21 for women, with an upper limit of normal of 30 for both
- Analysis of LEVEL data demonstrates:
 - a baseline 6MWD ≤ 300 m predicts a strong response to levosimendan
 - a baseline 6MWD of $>300 - 400$ m **and** a RAVI ≥ 25 mL/m² predict a strong response to levosimendan

LEVEL results enable the identification of patients most likely to have a robust response to levosimendan as those with qualifying hemodynamics, and a baseline 6MWD ≤ 300 meters, or a 6MWD of $>300 - \leq 400$ meters with a RAVI ≥ 25 mL/m²

LEVEL-2 Update: Protocol Amendment Implementation

TEMPORARY ENROLLMENT PAUSE; FDA INTERACTIONS

Effective execution of the Amended LEVEL-2 protocol requires a temporary pause in enrollment

- **Timely:** pause in screening and randomization instituted upon confirmation of enrichment strategy, to maximize enrollment of patients with these enrichment factors. LEVEL analyses demonstrate these patients stand to benefit most from treatment with levosimendan: those who demonstrated higher disease burden at baseline according to the most robust factors predicting improvement in exercise tolerance. Echocardiography collected at screening will be centrally reviewed to confirm eligibility
- **Temporary:** pause in enrollment will be limited to the time required to institute this Amendment. It is estimated less than 5% of LEVEL-2 patients to be included in the primary efficacy analysis will have been enrolled without meeting the stricter criteria in the Amended protocol
- **Not safety-related:** temporary pause in enrollment does not affect the ongoing treatment of patients enrolled in Q1-Q3 2026, who remain blinded for one year, and then can continue in LEVEL-SET. The enrollment pause is not related to a concern about safety, nor was it made in response to any request from a regulatory authority

FDA interactions

- Topline LEVEL results were shared with FDA in mid-August
- Tenax has since requested a Type C meeting to discuss the overall development of levosimendan in PH-HFpEF
- Publication of the LEVEL-2 protocol design paper is expected in Q1 2027
- **Further updates on levosimendan development are expected in Q1 2027**

IP Portfolio Protects Global Rights to Levosimendan Use in PH-HFpEF

- ❖ US patents for oral (TNX-103), IV, expanded dose and combination use through 2040
- ❖ Global protection pending across potential markets
- ❖ All patents have continuation applications pending

United States:

US 11,213,524, issued January 4, 2022, **expires November 14, 2039** (SC Formulation/Use)

US 11,607,412, issued March 21, 2023, **expires December 15, 2040** (IV Use)

US 11,701,355, issued July 18, 2023, **expires December 15, 2040** (Oral Use)

US 11,969,424, issued April 30, 2024, **expires December 15, 2040** (Expanded dose & CV drug combo use)

US 12,616,694, issued May 5, 2026, **expires October 15, 2041** (SC Use)

All patents have continuation applications pending

Europe

EP 4076398 B1 issued February 18, 2026, **expires December 15, 2040**

Japan/Canada/New Zealand/Australia/Thailand/Malaysia/Singapore:

Regional stage applications filed (PCT/US2020/065166)

Canadian Patent Application No. 3,161,960 – Allowed

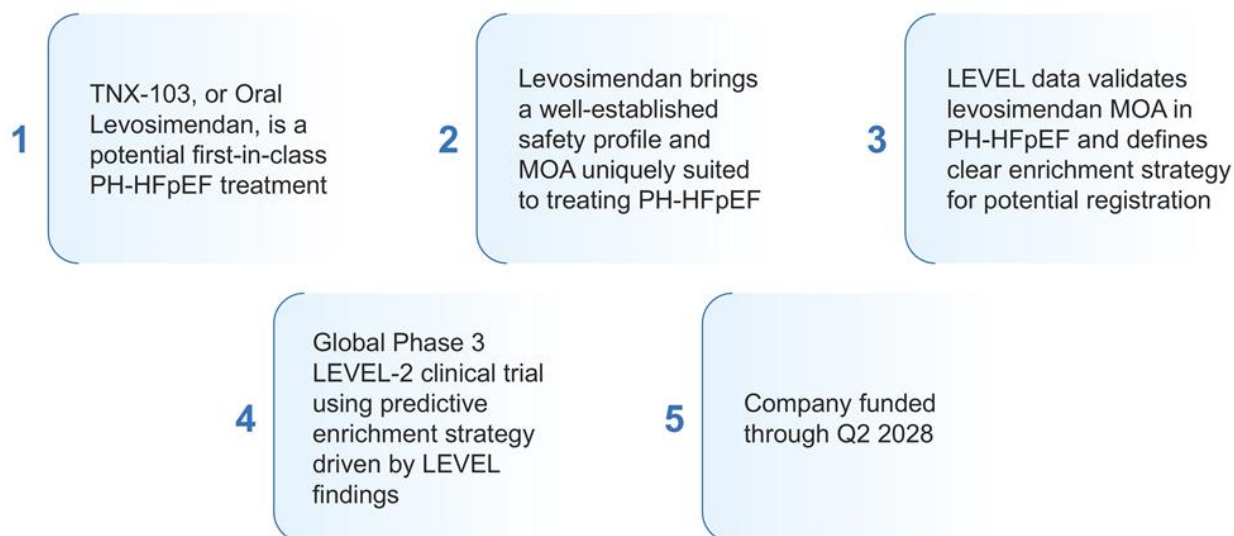
Other PCT Applications:

PCT/US2022/080708, filed November 30, 2022 (Combination use of levosimendan and SGLT-2 in HF)

PCT/US2022/082561, filed December 29, 2022 (Oral Levosimendan use in PH-HFpEF)

Evidence-Driven Phase 3 Program

LEVEL DATA ENHANCES HELP TRIAL PROOF OF CONCEPT TO DE-RISK ONGOING PHASE 3; WELL-ESTABLISHED SAFETY PROFILE





Developing a
therapy uniquely
suited for PH-HFpEF