

TENAX THERAPEUTICS

Corporate Presentation

27 February 2024

Safe Harbor Statement

Disclaimer

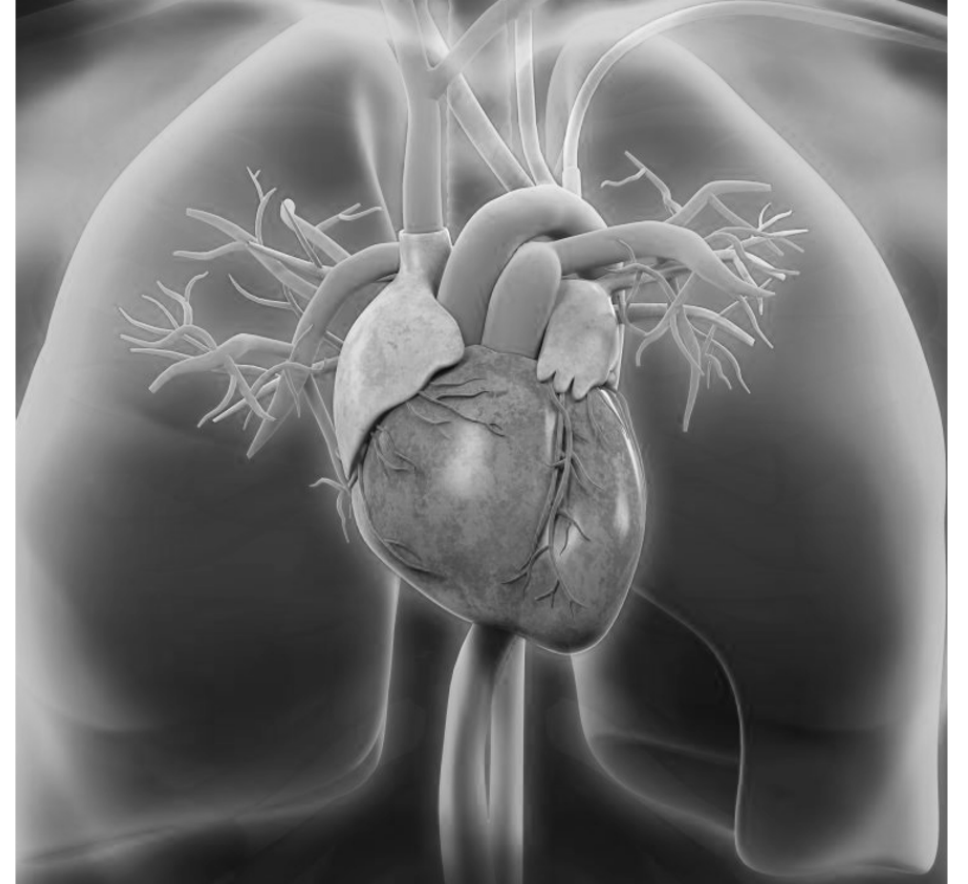
Except for historical information, all the statements, expectations and assumptions contained in this presentation are forward-looking statements. Actual results might differ materially from those explicit or implicit in the forward-looking statements. Important factors that could cause actual results to differ materially include: our ability to raise additional money to fund our operations for at least the next 12 months as a going concern; risks related to our business strategy, including the prioritization of product candidates; risks of our clinical trials, including, but not limited to, the timing, delays, costs, design, initiation, enrollment, and results of such trials; any delays in regulatory review and approval of product candidates in development; 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 estimates regarding the potential market opportunity for our product candidates; intellectual property risks; our competitive position; risks related to our continued listing on Nasdaq; our ability to maintain our culture and recruit, integrate and retain qualified personnel and advisors, including on our Scientific Advisory Boards and Board of Directors; volatility and uncertainty in the global economy and financial markets in light of the COVID-19 pandemic or similar health epidemics and geopolitical uncertainties such as in Ukraine; 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. Tenax Therapeutics assumes no obligation and does not intend to update these forward-looking statements except as required by law.

The Tenax Mission

A Phase 3, development-stage pharmaceutical company focused on identifying, developing, and commercializing products that address cardiovascular and pulmonary diseases with high unmet medical need.

Our current therapeutic focus is on pulmonary hypertension and the development of two products:

- TNX-103 for Treatment of PH-HFpEF (WHO Group 2 PH)
- TNX-201 for Treatment of PAH (WHO Group 1 PH)



Lead Product: TNX-103

- **TNX-103**
 - NCE, oral, small molecule (levosimendan)
 - Unique K-ATP mechanism relevant in pulmonary hypertension and HFpEF (PH-HFpEF)
 - Levosimendan is not available for oral administration anywhere in the world
- **Clinical - Positive Phase 2b data**
 - 6MWD +29 meters ($p=0.03$) and well-tolerated in PH-HFpEF patients*
 - First and only drug to show a benefit in PH-HFpEF
- **Regulatory**
 - Large safety database with >1.9M patient exposures via I.V. administration, for Acute HF
 - Positive FDA feedback on efficient Phase 3 development program (<500pts)
 - Potential for FDA Approval with a single trial ($p\leq 0.01$), or 2 trials ($p\leq 0.05$)
- **Manufacturing**
 - Produced at scale in FDA approved facility
 - ≥ 4 -year shelf life
- **IP**
 - U.S. patent protection to 2040+ via multiple method of use patents for treatment of PH-HFpEF
- **Commercial**
 - Large market (U.S. prevalence approaching 2M**) with no approved therapies

American Heart Association: Call to Action

PH-HFpEF Represents a Large Unmet Medical Need

AHA SCIENCE ADVISORY

Elucidating the Clinical Implications and Pathophysiology of Pulmonary Hypertension in Heart Failure With Preserved Ejection Fraction: A Call to Action: A Science Advisory From the American Heart Association

Evan L. Brittain, MD, MSc, FAHA, Chair; Thenappan Thenappan, MD, Vice Chair; Jessica H. Huston, MD; Vineet Agrawal, MD, PhD; Yen-Chun Lai, PhD; Debra Dixon, MD, MS; John J. Ryan, MD, FAHA; Eldrin F. Lewis, MD, MPH, FAHA; Margaret M. Redfield, MD; Sanjiv J. Shah, MD, FAHA; Bradley A. Maron, MD; on behalf of the American Heart Association Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation; Council on Arteriosclerosis, Thrombosis and Vascular Biology; Council on Lifestyle and Cardiometabolic Health; and Stroke Council

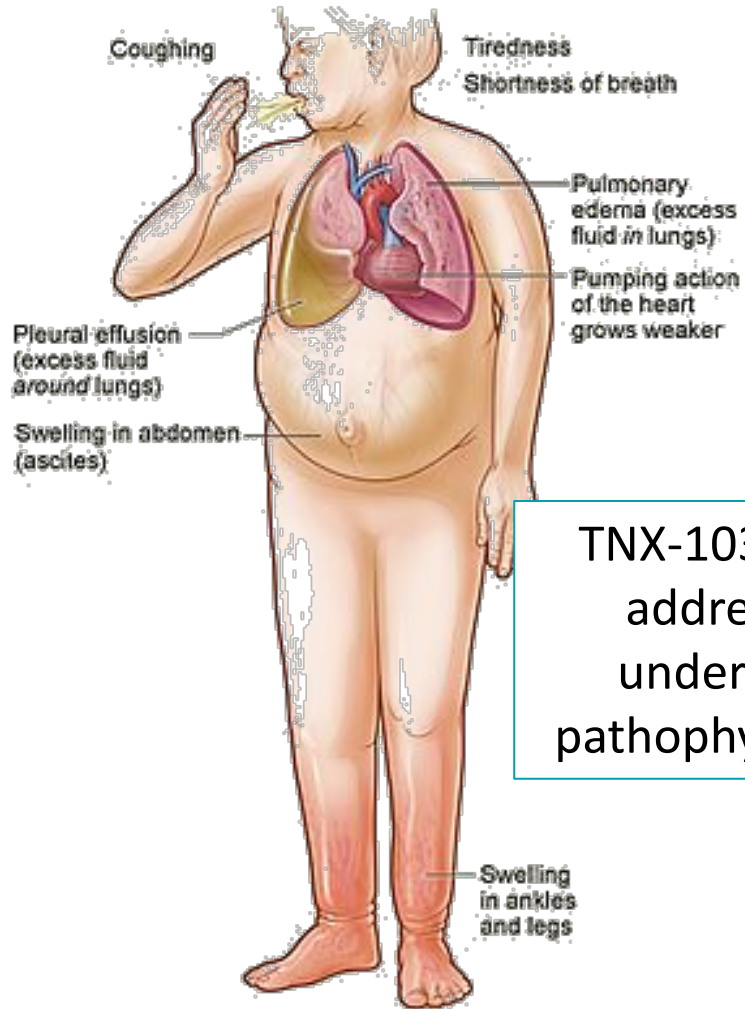
Circulation. 2022;146:e73–e88.

August 16, 2022

Heart failure (HF) with preserved ejection fraction (HFpEF) is one of the leading causes of pulmonary hypertension (PH) in the world.¹ The development of PH and particularly pulmonary vascular disease (which distinguishes functional pressure elevation from vascular dysfunction or remodeling) is among the strongest risk factors for adverse outcomes in HFpEF.² Despite this recognition, no evidence-based therapies exist for PH attributable to HFpEF (PH-HFpEF), in part because the pathophysiology is poorly understood. In this call to action, we encourage the scientific community to prioritize the study of PH-HFpEF, which has implications for collaboration, data sharing, and clinical trial design, among other considerations. The goal of this science advisory is to clarify key knowledge gaps in PH-HFpEF and to suggest scientific directions for addressing such gaps, which we synthesize in Table 1.

Overview: Pathophysiology of PH with HFpEF

The venous circulation has now been discovered to be the source of the problem



TNX-103 MOA addresses underlying pathophysiology

PH-HFpEF has recently been described to follow this course:

EXCESSIVE VENOUS RETURN/VOLUME



INCREASED CENTRAL VENOUS PRESSURE



INCREASED PULMONARY VENOUS PRESSURE



PULMONARY HYPERTENSION

TNX-103: Mechanism of Action in PH-HFpEF is Unique

01

TNX-103 (oral levosimendan) is a **unique K⁺ATP channel activator** and calcium sensitizer.* **No other drug** shares these properties

02

Strong vasodilatory effects on **venous beds****

Causes a **marked reduction** in central venous pressure (CVP)

Causes a **marked reduction** in pulmonary venous pressure (PCWP)

03

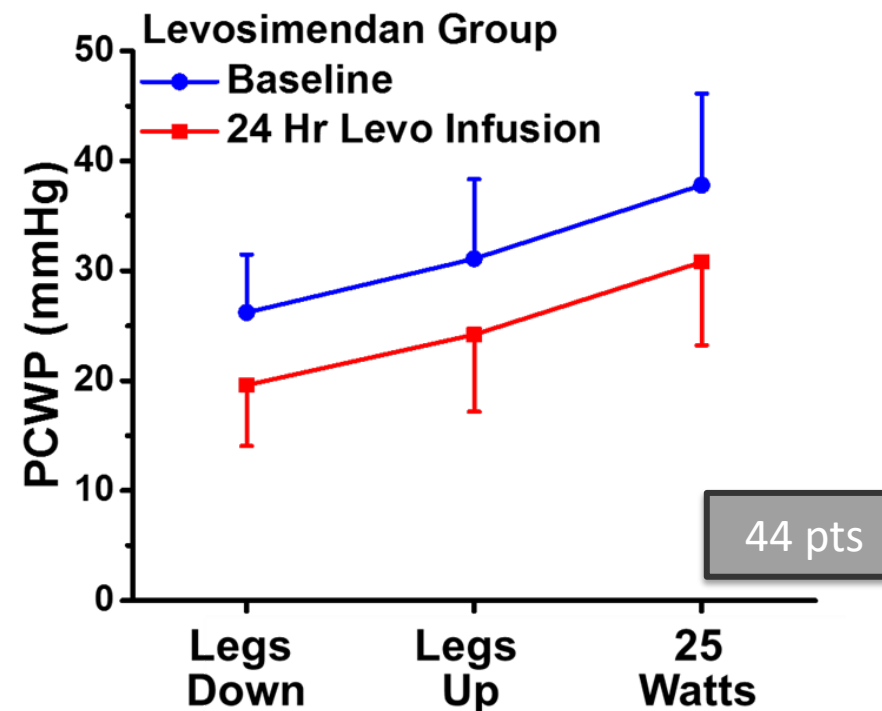
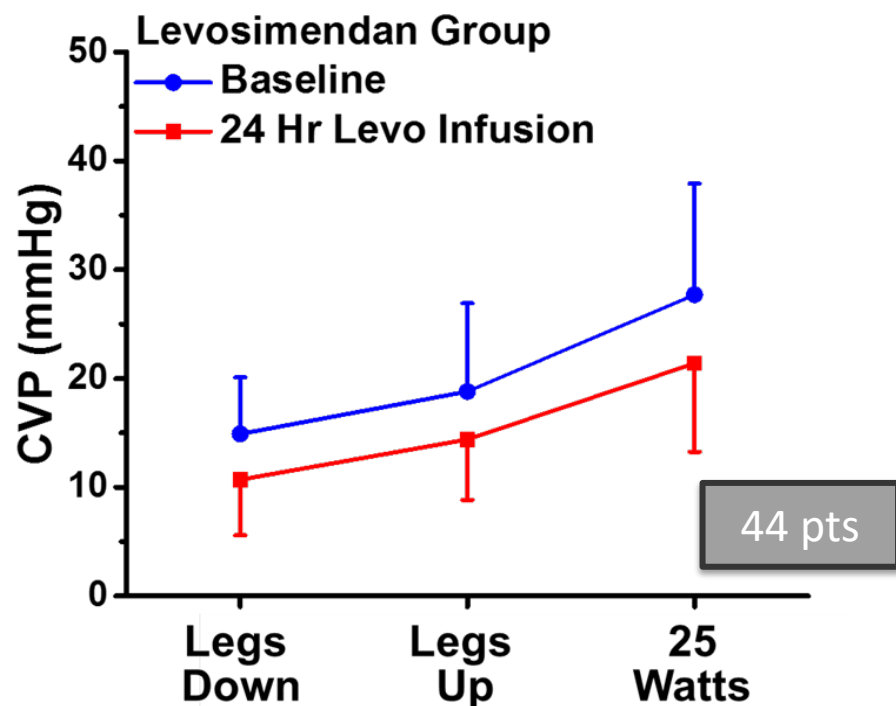
Recent clinical science has **confirmed** that reducing the **elevated CVP and PCWP are critical targets** for left heart failure***

* Rich, Stuart, Burkhoff, Daniel, Pollesello, Piero, Papp, Zoltan. "Levosimendan-induced ventilation is mediated by opening of potassium channels." *ESC Heart Failure*. 10.1002 (2021)

** Brener, Michael I., et al. "Changes in stressed blood volume with levosimendan in pulmonary hypertension from heart failure with preserved ejection fraction: insights regarding mechanism of action from the HELP trial." *Journal of Cardiac Failure* 27.9 (2021): 1023-1026

*** Fudim, Marat, et al. "Splanchnic Nerve Block for Chronic Heart Failure." *Heart Failure* 8.9 (2020): 742-752.

Levosimendan improves CVP and PCWP at rest and with exercise in PH-HFpEF Patients



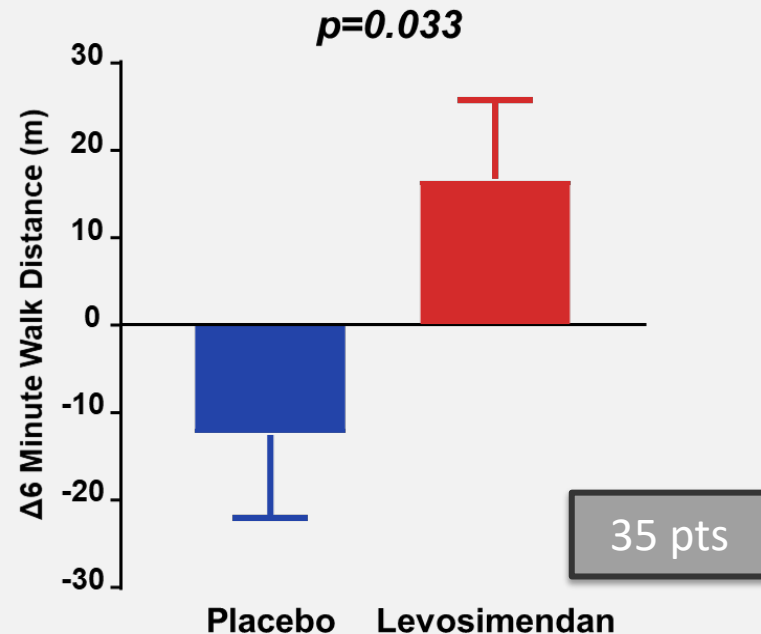
Burkhoff D, Rich S, et. al. Levosimendan Improves Hemodynamics and Exercise Tolerance in PH-HFpEF. JACC Heart Fail. 2021; 9:360-370



HELP Study: Six Minute Walk Distance

Levosimendan Improves Exercise Capacity in PH-HFpEF Patients after 6 Weeks

29 meter improvement in
6-minute walk distance



Dr Barry Borlaug, Mayo Clinic:

*“...this is the first medicine that has actually improved 6-minute walk distance in **any patient population with HFpEF...**”*



- 37 patients met hemodynamic criteria and were randomized; of these, 2 patients dropped out due to palpitations and COVID-19 infection. Both were in the placebo arm.
- Burkhoff D, Rich S, et. al. Levosimendan Improves Hemodynamics and Exercise Tolerance in PH-HFpEF. JACC Heart Fail. 2021; 9:360-370
- <https://www.medscape.com/viewarticle/938671> (Borlaug quote)

Patients in the Open Label Extension stage of HELP were transitioned from I.V. to Oral Levosimendan (TNX-103)

<i>Previous I.V. Infusion</i>	Week 0 (Office)	Week 2 (Home)	Week 4 (Home)	Week 6 (Office)
0.10 $\mu\text{g/kg/min}$	1mg QD (1mg total daily dose) Morning	1mg BID (2mg total daily dose) Every 12 hrs.	1mg TID (3mg total daily dose) Every 8 hrs.	Patient evaluated for further titration

6 Week Transition Period

Improvements in Efficacy Measures in 18 Patients Transitioned to TNX-103

“The transition to oral levosimendan was well tolerated without safety concerns over a 6-8-week period in patients with PH-HFpEF who had been receiving IV levosimendan for more than 18 months. Oral levosimendan was also associated with further improvements in 6MWD, BNP/NTProBNP, and KCCQ scores.”

(Thenappan, Borlaug, Burkhoff, et al.)

- **6MWD (exercise capacity)**
 - Improved *a further* 7 meters
- **BNP/NT-proBNP (measure of cardiac function)**
 - Improved by 23%
- **KCCQ (patient reported symptoms)**
 - Improved *further* in 6 of 7 different domains

18 pts

Thenappan, Thenappan, et al. "The Transition From Chronic Intravenous To Oral Levosimendan Is Safe And Effective In Patients With Pulmonary Hypertension With Heart Failure And Preserved Ejection Fraction." *Journal of Cardiac Failure* 29.4 (2023): 714-715.

Levosimendan Efficacy in PH-HFpEF Is Unprecedented

Unlike other drugs tested in this population, levosimendan targets underlying causes of PH-HFpEF.

- **Bosentan - (BADDHY Trial₁) – FAILED in PH-HFpEF**
 - “Six-minute walk distance (6MWD) did not change in the Bosentan group”
- **Macitentan - (MELODY Trial₂) – FAILED in PH-HFpEF**
 - “The mean treatment effect (6MWD) for macitentan versus placebo was negative 14.3 meters”
- **Riociguat - (DYNAMIC Trial₃) – FAILED in PH-HFpEF**
 - “The observed haemodynamic changes were not accompanied by significant improvements of NT-proBNP serum levels, WHO-FC, exercise capacity, or QoL.”

1) Koller, B., et al. "Pilot study of endothelin receptor blockade in heart failure with diastolic dysfunction and pulmonary hypertension (BADDHY-Trial)." *Heart, Lung and Circulation* 26.5 (2017): 433-441

2) Mascherbauer, Julia, et al. "Evaluation of the pharmacodynamic effects of riociguat in subjects with pulmonary hypertension and heart failure with preserved ejection fraction: study protocol for a randomized controlled trial." *Wiener Klinische Wochenschrift* 128 (2016): 882-889.

3) Vachiéry, Jean-Luc, et al. "Macitentan in pulmonary hypertension due to left ventricular dysfunction." *European Respiratory Journal* 51.2 (2018)

Recently Issued Method of Use Patents Cover Levosimendan in PH-HFpEF and Expire in December 2040

TNX-103 (Oral Use in PH-HFpEF)



US011701355B2

(12) United States Patent Rich et al.	(10) Patent No.: US 11,701,355 B2 (45) Date of Patent: Jul. 18, 2023
(54) LEVOSIMENDAN FOR TREATING PULMONARY HYPERTENSION WITH HEART FAILURE WITH PRESERVED EJECTION FRACTION (PH-HFPEF)	<i>A61K 31/495</i> (2013.01); <i>A61K 31/502</i> (2013.01); <i>A61K 31/55</i> (2013.01); <i>A61K 31/7048</i> (2013.01); <i>A61K 38/2221</i> (2013.01); <i>A61K 38/2242</i> (2013.01); <i>A61K 45/06</i> (2013.01); <i>A61K 47/02</i> (2013.01); <i>A61K 47/10</i> (2013.01); <i>A61K 47/12</i> (2013.01); <i>A61K 47/26</i> (2013.01); <i>A61K 47/32</i> (2013.01); <i>A61K 47/40</i> (2013.01); <i>A61P 9/04</i> (2018.01); <i>A61P 9/12</i> (2018.01)
(71) Applicant: Tenax Therapeutics, Inc. , Morrisville, NC (US)	
(72) Inventors: Stuart Rich , Skokie, IL (US); Douglas Randall , Wake Forest, NC (US); Douglas Hay , Ottsville, PA (US)	
(73) Assignee: TENAX THERAPEUTICS, INC. , Morrisville, NC (US)	(58) Field of Classification Search CPC .. <i>A61K 2300/00</i> ; <i>A61K 31/216</i> ; <i>A61K 31/41</i> ; <i>A61K 31/495</i> ; <i>A61K 31/50</i> ; <i>A61K 31/502</i> ; <i>A61K 31/55</i> ; <i>A61K 31/7048</i> ; <i>A61K 38/2221</i> ; <i>A61K 38/2242</i> ; <i>A61K 45/06</i> ; <i>A61K 47/02</i> ; <i>A61K 47/10</i> ; <i>A61K 47/12</i> ; <i>A61K 47/26</i> ; <i>A61K 47/32</i> ; <i>A61K 47/40</i> ; <i>A61K 9/0019</i> ; <i>A61K 9/0053</i> ; <i>A61P 9/04</i> ; <i>A61P 9/12</i>
(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.	See application file for complete search history.
(21) Appl. No.: 18/057,116	
(22) Filed: Nov. 18, 2022	
(65) Prior Publication Data US 2023/0107461 A1 Apr. 6, 2023	(56) References Cited U.S. PATENT DOCUMENTS

Expires December 2040

TNX-101 (I.V. Use in PH-HFpEF)



US011607412B2

(12) United States Patent Rich et al.	(10) Patent No.: US 11,607,412 B2 (45) Date of Patent: Mar. 21, 2023
(54) LEVOSIMENDAN FOR TREATING PULMONARY HYPERTENSION WITH HEART FAILURE WITH PRESERVED EJECTION FRACTION (PH-HFPEF)	<i>31/7048</i> (2013.01); <i>A61K 38/2221</i> (2013.01); <i>A61K 38/2242</i> (2013.01); <i>A61K 45/06</i> (2013.01); <i>A61K 47/02</i> (2013.01); <i>A61K 47/10</i> (2013.01); <i>A61K 47/12</i> (2013.01); <i>A61K 47/26</i> (2013.01); <i>A61K 47/32</i> (2013.01); <i>A61K 47/40</i> (2013.01); <i>A61P 9/04</i> (2018.01); <i>A61P 9/12</i> (2018.01)
(71) Applicant: Tenax Therapeutics, Inc. , Morrisville, NC (US)	
(72) Inventors: Stuart Rich , Skokie, IL (US); Douglas Randall , Wake Forest, NC (US); Douglas Hay , Ottsville, PA (US)	(58) Field of Classification Search CPC <i>A61K 2300/00</i> ; <i>A61K 31/216</i> ; <i>A61K 31/41</i> ; <i>A61K 31/495</i> ; <i>A61K 31/50</i> ; <i>A61K 31/502</i> ; <i>A61K 31/55</i> ; <i>A61K 31/7048</i> ; <i>A61K 38/2221</i> ; <i>A61K 38/2242</i> ; <i>A61K 45/06</i> ; <i>A61K 47/02</i> ; <i>A61K 47/10</i> ; <i>A61K 47/12</i> ; <i>A61K 47/26</i> ; <i>A61K 47/32</i> ; <i>A61K 47/40</i> ; <i>A61K 9/0019</i> ; <i>A61K 9/0053</i> ; <i>A61P 9/04</i> ; <i>A61P 9/12</i>
(73) Assignee: TENAX THERAPEUTICS INC. , Morrisville, NC (US)	See application file for complete search history.
(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.	
(21) Appl. No.: 17/410,897	(56) References Cited U.S. PATENT DOCUMENTS
(22) Filed: Aug. 24, 2021	<i>6,730,673 B1</i> * <i>5/2004</i> Backstrom <i>A61K 47/12</i> <i>514/247</i>
(65) Prior Publication Data US 2021/0393625 A1 Dec. 23, 2021	<i>11,213,524 B2</i> <i>1/2022</i> Randall <i>2015/0374689 A1</i> <i>12/2015</i> Kelley et al. <i>2017/0182127 A1</i> <i>6/2017</i> Dschietzig <i>2018/0318210 A1</i> <i>11/2018</i> Weiland <i>2019/0091194 A1</i> <i>3/2019</i> Chin et al.
Related U.S. Application Data	

Expires December 2040

TNX-102 (including SC Use in PH-HFpEF)



US011213524B2


(12) United States Patent Randall et al.	(10) Patent No.: US 11,213,524 B2 (45) Date of Patent: Jan. 4, 2022
(54) PHARMACEUTICAL COMPOSITIONS FOR SUBCUTANEOUS ADMINISTRATION OF LEVOSIMENDAN	USPC <i>514/247</i> ; <i>544/224</i> See application file for complete search history.
(71) Applicant: Tenax Therapeutics, Inc. , Morrisville, NC (US)	(56) References Cited FOREIGN PATENT DOCUMENTS
(72) Inventors: Doug Randall , Wake Forest, NC (US); Douglas Hay , Ottsville, PA (US); Nancy J. M. Hecox , Durham, NC (US)	EP WO2017/077032 * <i>11/2017</i> <i>A61K 31/50</i> WO WO 2017/077032 <i>5/2017</i>
(73) Assignee: TENAX THERAPEUTICS, INC. , Morrisville, NC (US)	OTHER PUBLICATIONS International Preliminary Report on Patentability, dated Feb. 23, 2021 by the International Bureau on behalf of the International Searching Authority Under Rule 44 bis.1(a) in connection with the International Application No. PCT/US2019/047032, filed Aug. 19, 2019.
(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 87 days.	* cited by examiner
(21) Appl. No.: 16/544,098	<i>Primary Examiner</i> — Jeffrey H Murray (74) <i>Attorney, Agent, or Firm</i> — Gary J. Gershik
(22) Filed: Aug. 19, 2019	
(65) Prior Publication Data US 2020/0330463 A1 Oct. 22, 2020	(57) ABSTRACT <i>A composition containing levosimendan, one or more solu-</i>

Expires December 2039

USPTO – Notice of Allowance for Application # 17/122,921

Significantly Broadens IP Protection for Levosimendan Use in PH-HFpEF Patients

- Provides U.S. intellectual property **(IP) protection until December 2040**; may qualify for additional U.S. patent term extension (PTE) beyond 2040
- **Broadens IP protection** for **oral (TNX-103), I.V., and subcutaneous use** of levosimendan, and its active metabolites (**OR1896 and OR1855**), in PH-HFpEF
- Expressly provides IP protection for levosimendan at **all therapeutic doses** for use in PH-HFpEF
- Expressly provides IP protection for levosimendan in **combination with various cardiovascular drugs** for use in PH-HFpEF

	UNITED STATES PATENT AND TRADEMARK OFFICE		UNITED STATES DEPARTMENT OF COMMERCE United States Patent and Trademark Office Address: COMMISSIONER FOR PATENTS P.O. Box 1450 Alexandria, Virginia 22313-1450 www.uspto.gov	
NOTICE OF ALLOWANCE AND FEE(S) DUE				
23432	7590	02/08/2024	EXAMINER CORNET, JEAN P	
Gary J. Gershik; John P. White 405 LEXINGTON AVENUE NEW YORK, NY 10174			ART UNIT 1628	PAPER NUMBER
DATE MAILED: 02/08/2024				
APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/122,921	12/15/2020	Stuart Rich	91187-A/GJG/AWG/LMO	4817
TITLE OF INVENTION: LEVOSIMENDAN FOR TREATING PULMONARY HYPERTENSION WITH HEART FAILURE WITH PRESERVED EJECTION FRACTION (PH-HFpEF)				

Tenax's PH-HFpEF Scientific Advisors

World Recognized Experts in Pulmonary Hypertension and Heart Failure

Sanjiv Shah, MD

Professor of Medicine, Northwestern University Feinberg School of Medicine
Director, Northwestern HFpEF Program, Bluhm Cardiovascular Institute



Daniel Burkhoff, MD, PhD

Director Heart Failure, Hemodynamics and MCS Research at the Cardiovascular Research Foundation
Adjunct Associate Professor of Medicine, Columbia University



Barry Borlaug, MD

Professor of Medicine and Director, Circulatory Failure Research, Mayo Clinic
Chair for Research, Division of Circulatory Failure



Javed Butler, MD, MPH, MBA

President of the Baylor Scott and White Research Institute
Chair of Medicine, Chair of CV Research, Distinguished Professor of Medicine, Univ. of Mississippi



FDA Guidance: Phase 3 TNX-103 Development in PH-HFpEF

FDA meeting minutes record agreements on key details of potential Phase 3 program:

- *Two phase 3 trials ($p < 0.05$) with 6MWD as the primary endpoint would be sufficient*
or
- *Single phase 3 trial ($p < 0.01$) with 6MWD as the primary endpoint would be sufficient*
and
- *Safety database requirement: 300 patients followed for 6 months, and 100 patients followed for 12 months (ICH minimum requirement)*

Phase 3 Development Guided by Phase 2b Results

Leverage Phase2b (HELP) Study Results to Design Phase 3

Hemodynamic Entry Criteria

85% responder rate

6MWD, 29m, $p=0.03$

I.V.-to-Oral Transition: improvement
in BNP, KCCQ, 6MWD



Initial Phase 3 PH-HFpEF Study

Hemodynamic Entry Criteria

Primary Endpoint = 6MWD

~152 patients, 90% power, $p<0.05$



2nd Phase 3 PH-HFpEF Study

Results of Initial Phase 3 trial de-risks 2nd Phase 3 Trial

Provides additional data required for NDA filing
(FDA has confirmed minimum ICH requirement for safety database)



a PH-HFpEF study

LEVosimendan to Improve **E**xercise **L**imitation in Patients With PH-HFpEF

A Phase 3, Double-Blind, Randomized, Placebo-Controlled
Study of Levosimendan in Pulmonary Hypertension Patients
With Heart Failure With Preserved Left Ventricular Ejection Fraction (PH-HFpEF)

LEVEL Design & Study Objectives

By the Numbers

- **152** randomized patients
- ~50 investigator sites, U.S. & Canada
- Site initiation & enrollment: competitive
- Enrollment commenced Q1 2024

Double Blind Phase

- Randomized at a 1:1 ratio: 2mg/day (1 mg BID) Weeks 1-4; 3mg/day (1 mg TID) Weeks 5-12
- Onsite visits for Weeks 4, 8, 12
- Virtual Visit via phone call at Weeks 2, 13, 14
- 6 MWT (Day 1, Week 4, 8, 12) and any unscheduled visit

Primary Endpoint:

To evaluate the efficacy of levosimendan (TNX-103) compared with placebo in subjects with PH-HFpEF as measured by the change in 6MWD (Day 1 to Week 12)

Secondary Endpoints (all measured from Day 1 to Week 12):

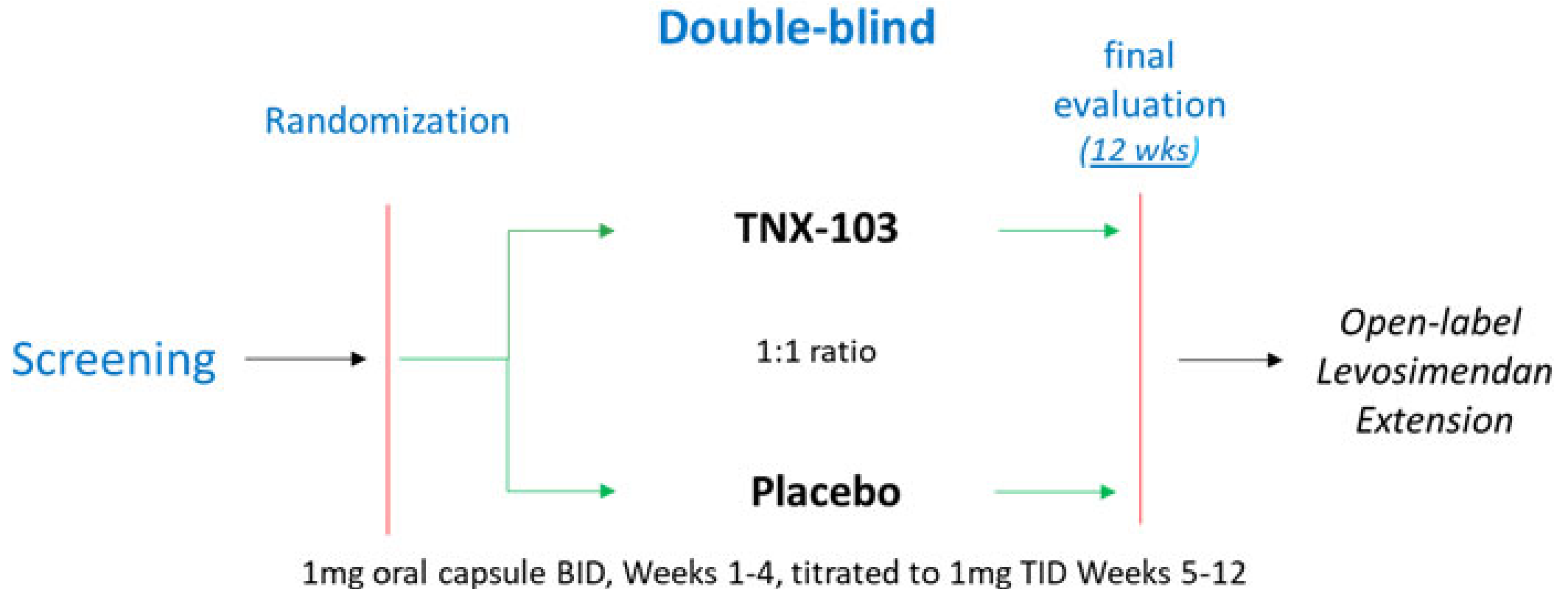
Change in KCCQ - Total Symptom Score (KCCQ-TSS)

Number of Clinical Worsening Events, e.g. death/hosp. due to PH/HF, ER visits requiring diuretics

Change in NT-proBNP





Improvement in NYHA Functional Class

Study Design



Primary Endpoint: change in 6MWD, >90% power to detect a 25-meter change (SD=45 meters) at alpha 0.05, N=152

The LEVEL Study: Projected Timelines

The LEVEL Study Phase 3 PH-HFpEF oral levosimendan	2023		2024		2025	
	H1	H2	H1	H2	H1	H2
Site Initiation Starts						
First Patient Enrolled						
Last Patient Enrolled						
Topline LEVEL Data						

PH-HFpEF Market Assumptions

- **PH-HFpEF Prevalence in the U.S.**
 - 6,700,000 Heart Failure patients in U.S. ⁽¹⁾
 - 2% Annual Growth Rate ⁽¹⁾
 - 54% is HFpEF, with HFpEF proportion increasing to 60% by 2040 ^(1,2,3,4)
 - 50% of HFpEF is PH-HFpEF ^(2,5,6)

1) Tsao, Connie W., et al. "Heart disease and stroke statistics—2023 update: a report from the American Heart Association." *Circulation* 147.8 (2023): e93-e621.

2) Lai, Yen-Chun, Longfei Wang, and Mark T. Gladwin. "Insights into the pulmonary vascular complications of heart failure with preserved ejection fraction." *The Journal of physiology* 597.4 (2019): 1143-1156.

3) Pfeffer, Marc A., Amil M. Shah, and Barry A. Borlaug. "Heart failure with preserved ejection fraction in perspective." *Circulation research* 124.11 (2019): 1598-1617.

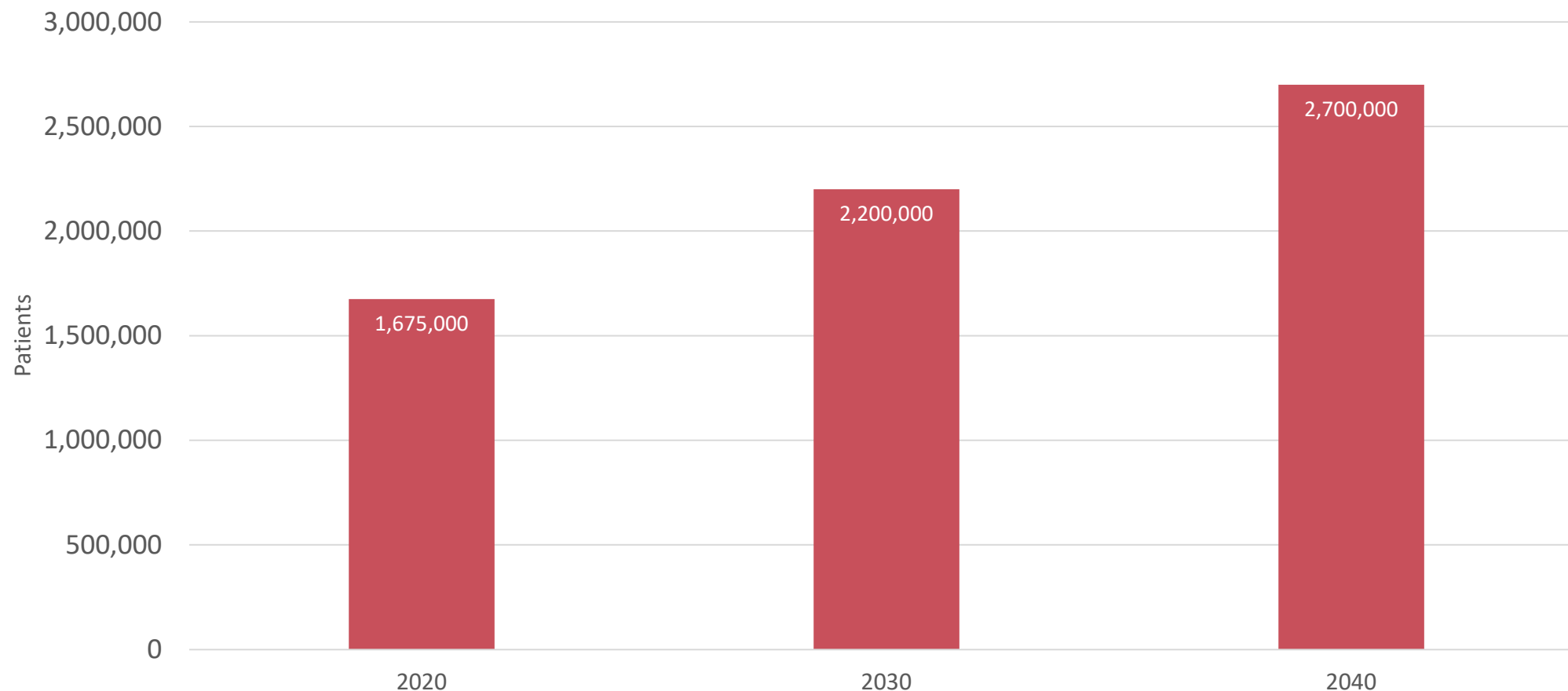
4) Steinberg, Benjamin A., et al. "Trends in patients hospitalized with heart failure and preserved left ventricular ejection fraction: prevalence, therapies, and outcomes." *Circulation* 126.1 (2012): 65-75.

5) Brittain, Evan L., et al. "Elucidating the Clinical Implications and Pathophysiology of Pulmonary Hypertension in Heart Failure With Preserved Ejection Fraction: A Call to Action." *Circulation* 146.7 (2022): e73-e88.

6) Guazzi, Marco. "Pulmonary hypertension in heart failure preserved ejection fraction: prevalence, pathophysiology, and clinical perspectives." *Circulation: Heart Failure* 7.2 (2014): 367-377.

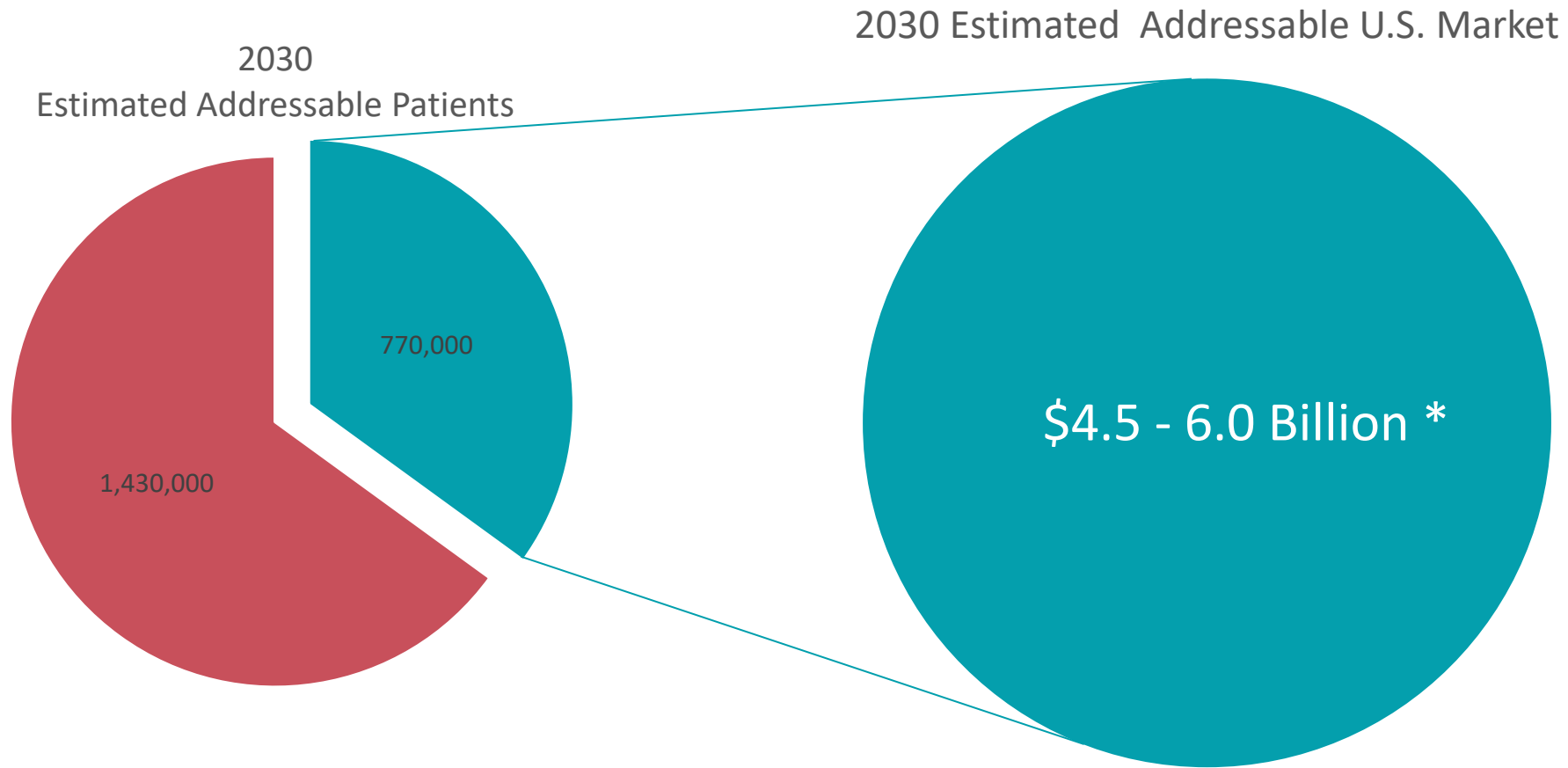
PH-HFpEF Market is Large and Growing

Estimated PH-HFpEF Prevalence in the U.S.



Prevalence estimates based on published epidemiology data referenced in prior slide

Estimated Total Addressable PH-HFpEF U.S. Market in 2030



*Assumes only 35% of patients are addressable and the estimated Annual Value = \$6-8K/patient (1)

1) Drugs.com. March 2023 Annual cost/patient branded for ANRI or SGLT2 inhibitors approved in HF. Assumes similar pricing for a PH-HFpEF drug

Multiple Levels of Derisking

Risk Considerations	Questions	De-risking Factors
Clinical Development	PH-HFpEF Efficacy Data (Ph2b)	Hemodynamic improvements 29M+ 6MWD , P=0.03
	Safety Database	>1,900,000 patient exposures (I.V.)
Regulatory	FDA Feedback	6MWD primary endpoint accepted
		ICH minimum safety database
		Single Study, $p \leq 0.01$ Two Studies, $p \leq 0.05$
Manufacturing	Facility Inspection	FDA inspected facility that produces other FDA approved products
	Production at Scale	1.5M capsules produced
	Shelf -life	≥ 4 years
	Clinical Supply	Produced and available
Commercial-IP	Market	Approaching 2.0M U.S. patient prevalence
	Competitors	No approved or effective therapies
	IP	Multiple granted patents to 2040+

Latest News



Tenax Therapeutics Announces USPTO Grants Notice of Allowance for U.S. Patent Application

Published: Feb 06, 2024

Once granted, this patent will:

- *provide U.S. intellectual property (IP) protection until December 2040, and may qualify for additional U.S. patent term extension (PTE) beyond 2040*
- *broaden IP protection for oral (TNX-103), IV, and subcutaneous use of levosimendan, and its active metabolites (OR1896 and OR1855), in PH-HFpEF*
- *expressly provide IP protection for levosimendan at all therapeutic doses for use in PH-HFpEF*

Tenax Therapeutics Announces Global License Amendment that Significantly Expands Rights to Levosimendan

Published: Feb 20, 2024

- *Amendment to existing exclusive license agreement with Orion Corporation expands Tenax's territory rights from North America, to the entire world*
- *Expanded rights position Tenax to engage potential global strategic pharmaceutical partners*
- *Improved net sales royalty rate structure, now ranging from high single-digit to low-teen percentages. Lowered maximum cost of goods*

New Value Proposition for Investors

Short-term and Long-term catalysts

- **Short-term**

- Site activation and patient enrollment updates
- Scientific presentations and investor/KOL events
- Potential expanded U.S. patent coverage
- European/International patent protection

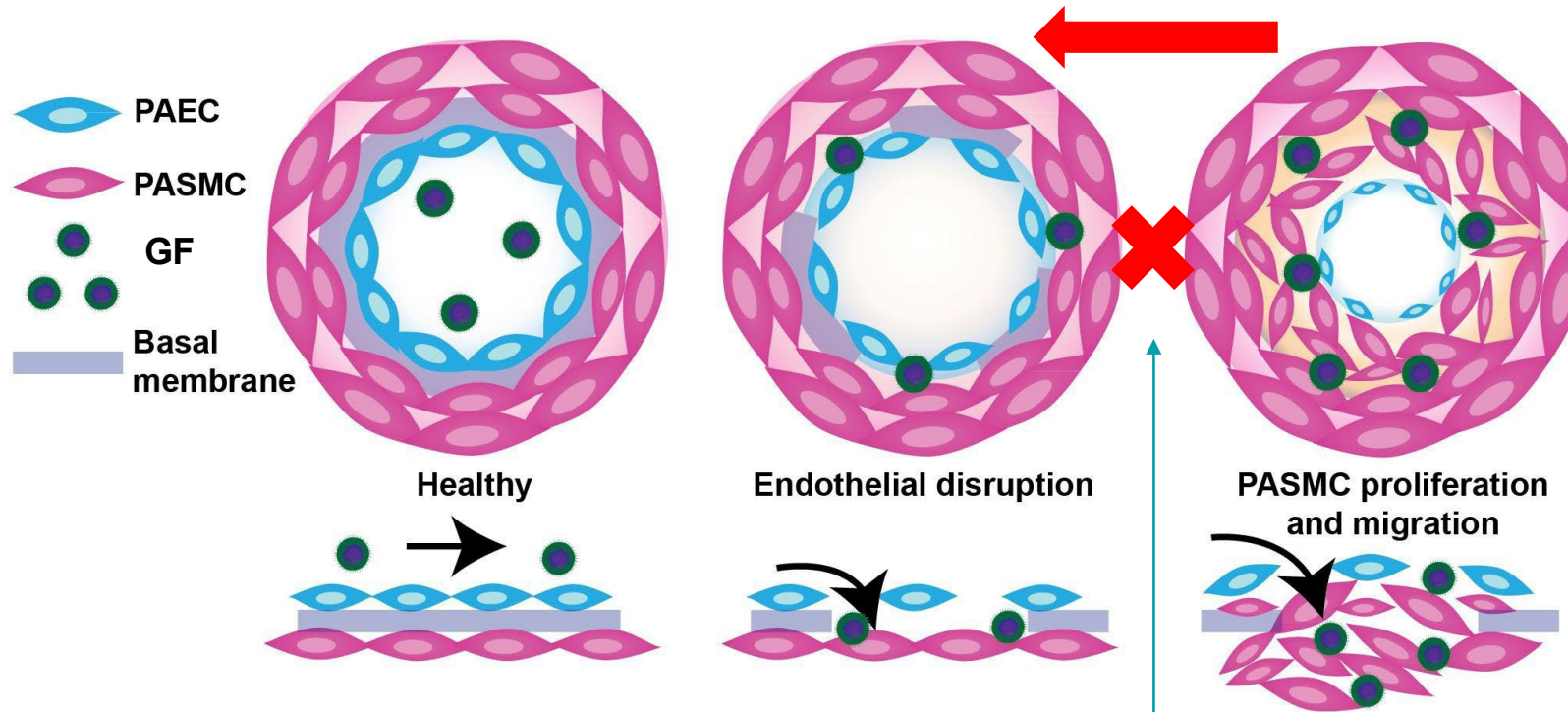
- **Long-term**

- Phase 3 LEVEL topline trial results
- Initiation of second Phase 3 trial
- Potential additional patent approvals
- Potential US Patent Term Extensions, beyond 2040

TNX-201 (imatinib)
Development Program
for Pulmonary Arterial Hypertension
(WHO Group 1)



Imatinib Targets the Pathophysiology of PAH



PAEC = pulmonary artery endothelial cell

PASMC = pulmonary artery smooth muscle cell

GF = growth factors BCR-Abl, PDGFR, c-Kit

**imatinib blocks
and reverses**

Proof of Concept IMPRES STUDY

Imatinib is Proven Effective in Treating PAH

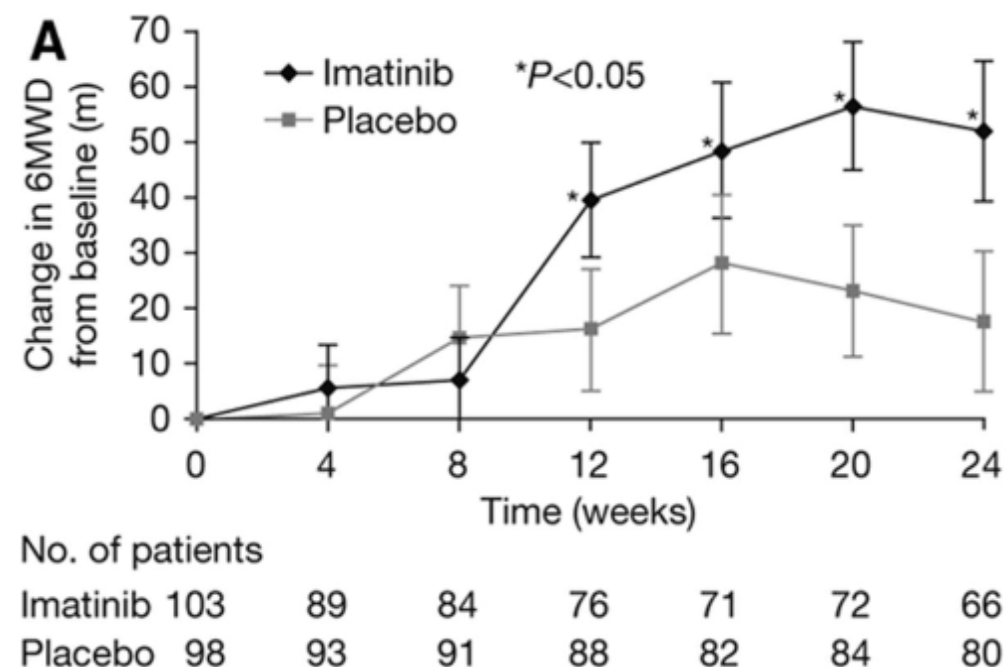
Phase 3 Clinical Trial:

Imatinib Mesylate as Add-On Therapy for Pulmonary Arterial Hypertension: Results of the Randomized IMPRES Study

Results: After 24 weeks, the mean placebo-corrected treatment effect on 6-minute walk distance was 32 meters (95% confidence interval, 12–52; **P=0.002**)

Conclusions: Imatinib improved exercise capacity and hemodynamics in patients with advanced PAH, but **frequent dropout events prevented approval.**

The primary endpoint was change in 6-minute walk distance



Circulation. 2013;127:1128-1138.

Key Learnings from IMPRES Study Informed Phase 3 IMPROVE

IMPROVE

01

Efficacy was established in PAH

PAH



02

Adequate dose is critical (400mg) to achieve clinical efficacy

>400 mg



03

Avoid excessive dropouts, mostly related to early-onset side effects

Open-label
Lead-in



04

Gastrointestinal side effects are most the common, novel formulation to reduce

Modified
Formulation



Execution Led by a Highly Experienced Team

Management Team

Chris Giordano – President & CEO, Board Director

Previous President of IQVIA Biotech
20+ years of clinical trial expertise

Stuart Rich, MD - CMO, Board Director

Globally recognized expert in Pulmonary Hypertension
40+ Years clinical experience in PH and HF
Former FDA Cardio Renal Advisory Panel Member

Doug Hay, PhD - EVP, Regulatory

Experienced senior pharmaceutical regulatory expert
35+ years regulatory experience, including founder

Doug Randall - EVP, Business Development and Operations

Experienced BD and Commercial expert
40+ years BD commercial roles, including founder

Board of Directors

Gerry Proehl - Chairman

President, CEO and Chairman, Dermata Therapeutics
Previously CEO, Santarus

June Almenoff , MD

CMO, Redhill Biopharma
Previously President and CMO, Furiex Pharmaceuticals

Declan Doogan, MD

CMO, Juvenescence
Previously Head of Global Drug Development, Pfizer
Previously Chairman/Co-Founder, Biohaven Pharmaceuticals

Michael Davidson, MD

CEO, New Amsterdam Pharma
Previously CSO, Corvidia Therapeutics

Robyn Hunter

CFO, Sotio Biotech Business
Previously CFO, Fortress Biotech

Tenax Investment Opportunity

- **Therapeutic Focus - Pulmonary Hypertension**
 - PH-HFpEF (approaching 2.0M U.S. patients, no approved therapies)
 - PAH (orphan)
- **Pipeline - Two Phase 3-Ready Products**
 - TNX-103: Levosimendan oral (First in class oral KATP Activator/Ca⁺⁺ Sensitizer) for PH-HFpEF
 - TNX-201: Imatinib (Modified Release/Modified Dose) for PAH
- **Positive Phase 2 & Phase 3 Data**
 - HELP Study – Levosimendan in PH-HFpEF
 - IMPRES Study – Imatinib in PAH
- **Efficient Clinical Development Pathway**
 - Small Phase 3 trials required (FDA confirmed)
- **Significant Exclusivity**
 - Levosimendan
 - 3 U.S. method of use & 1 formulation patent granted, covering oral, I.V., subcutaneous
 - Imatinib - orphan exclusivity
- **Large Commercial Potential**
 - TNX-103: \$4.5-\$6.0B market in 2030
 - TNX-201: >\$5B market, currently

Abbreviations and Acronyms

6MWD	result of the 6MWT, a measurement in meters
6MWT	6-minute walk test, an assessment of exercise tolerance, specifically the distance one can walk in 6 min.
CVP	Central Venous Pressure
HF	Heart Failure
HFpEF	Heart Failure with preserved Ejection Fraction
K-ATP	ATP-sensitive potassium channels, which control the vascular tone (state of constriction and dilation) of the blood vessels
KCCQ	Kansas City Cardiomyopathy Questionnaire, a scale commonly used in assessing HF
KCCQ-TSS	KCCQ - Total Symptoms Score; a subscore of the KCCQ
PAH	Pulmonary Arterial Hypertension (Group 1 in WHO's PH classification system)
PCWP	Pulmonary Capillary Wedge Pressure
PH	Pulmonary Hypertension
PH-HFpEF	Pulmonary Hypertension in the setting of heart failure with preserved ejection fraction, the most common form of Group 2 PH in WHO's PH classification system
PVR	Pulmonary Vascular Resistance
WHO	World Health Organization, which established a PH classification including 5 categories, or "groups"