



Corporate  
Presentation  
*January 2019*

**NASDAQ: TENX**

# Safe Harbor Statement

This presentation contains certain forward-looking statements by the Company that involve risks and uncertainties and reflect the Company's judgment as of the date of this release. The forward-looking statements are subject to a number of risks and uncertainties, including, but not limited to matters beyond the Company's control that could lead to delays in the clinical study, new product introductions and customer acceptance of these new products; matters beyond the Company's control that could impact the Company's continued compliance with Nasdaq listing requirements; the impact of management changes on the Company's business and unanticipated charges, costs and expenditures not currently contemplated that may occur as a result of management changes; and other risks and uncertainties as described in the Company's filings with the Securities and Exchange Commission, including in its annual report on Form 10-K filed on April 2, 2018, its quarterly report on Form 10-Q filed on November 14, 2018, as well as its other filings with the SEC. The Company disclaims any intent or obligation to update these forward-looking statements beyond the date of this release. Statements in this press release regarding management's future expectations, beliefs, goals, plans or prospects constitute forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995.

# Mission Statement



**Specialty pharmaceutical company focused on identifying and developing therapeutics that address diseases with high unmet medical need with an initial therapeutic focus on Cardio-Pulmonary diseases.**

# Investment Highlights

- **Levosimendan**

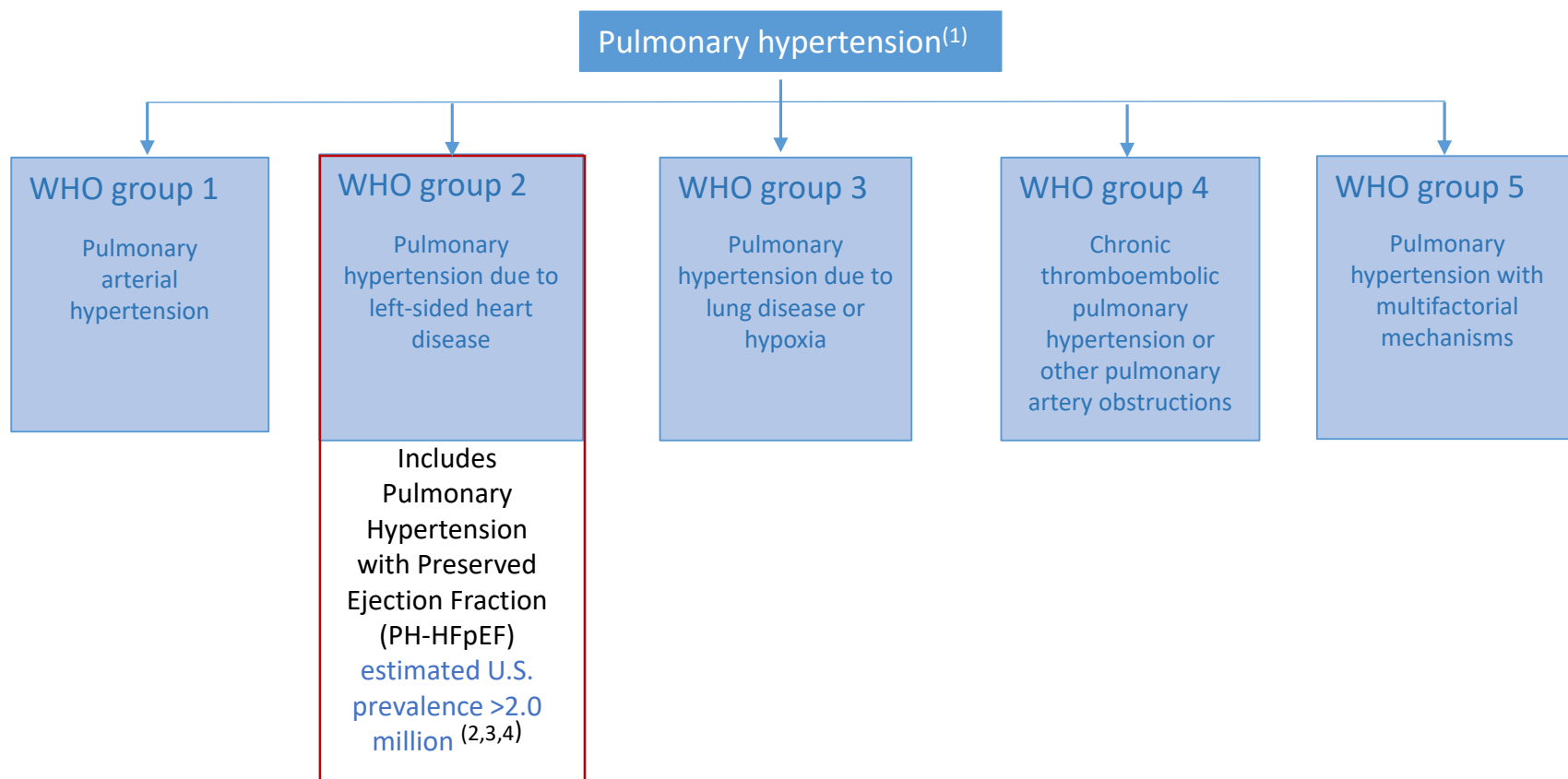
- Novel, first in class calcium sensitizer/K-ATP activator with unique triple mechanism of action
- Approved in over 60 countries acute decompensated heart failure
  - >1000 PubMed publication citations
- Hold US and Canada development and commercialization rights

- **Initiated Phase 2 trial for PH-HFpEF in Q4 2018**

- Significant unmet medical need with no approved therapies
- Positive preclinical and clinical data support moving forward in Pulmonary Hypertension
- 36 patient multi-center, double blind, placebo-controlled study
- Open-label lead in phase to identify responders ahead of randomization

# Pulmonary Hypertension WHO Classification

## Levosimendan Development Focused on Group 2

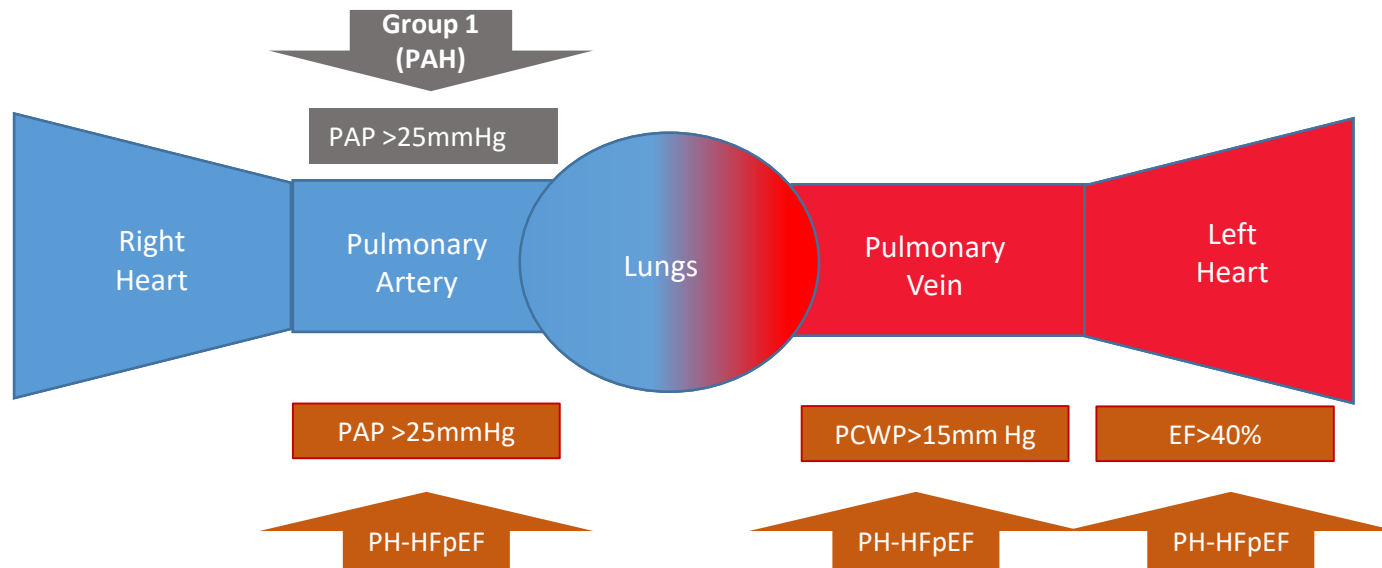


- 1) Hoepfer, Marius M., et al. "A global view of pulmonary hypertension." *The Lancet Respiratory Medicine* 4.4 (2016): 306-322
- 2) Dixon, Debra D., Amar Trivedi, and Sanjiv J. Shah. "Combined post-and pre-capillary pulmonary hypertension in heart failure with preserved ejection fraction." *Heart failure reviews* 21.3 (2016): 285-297.(Estimates 2.2M PH-HFpEFpatients)
- 3) 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 = ~50% of all US HFpEF patients)
- 4) Global Data epidemiological estimates

# Disease Overview

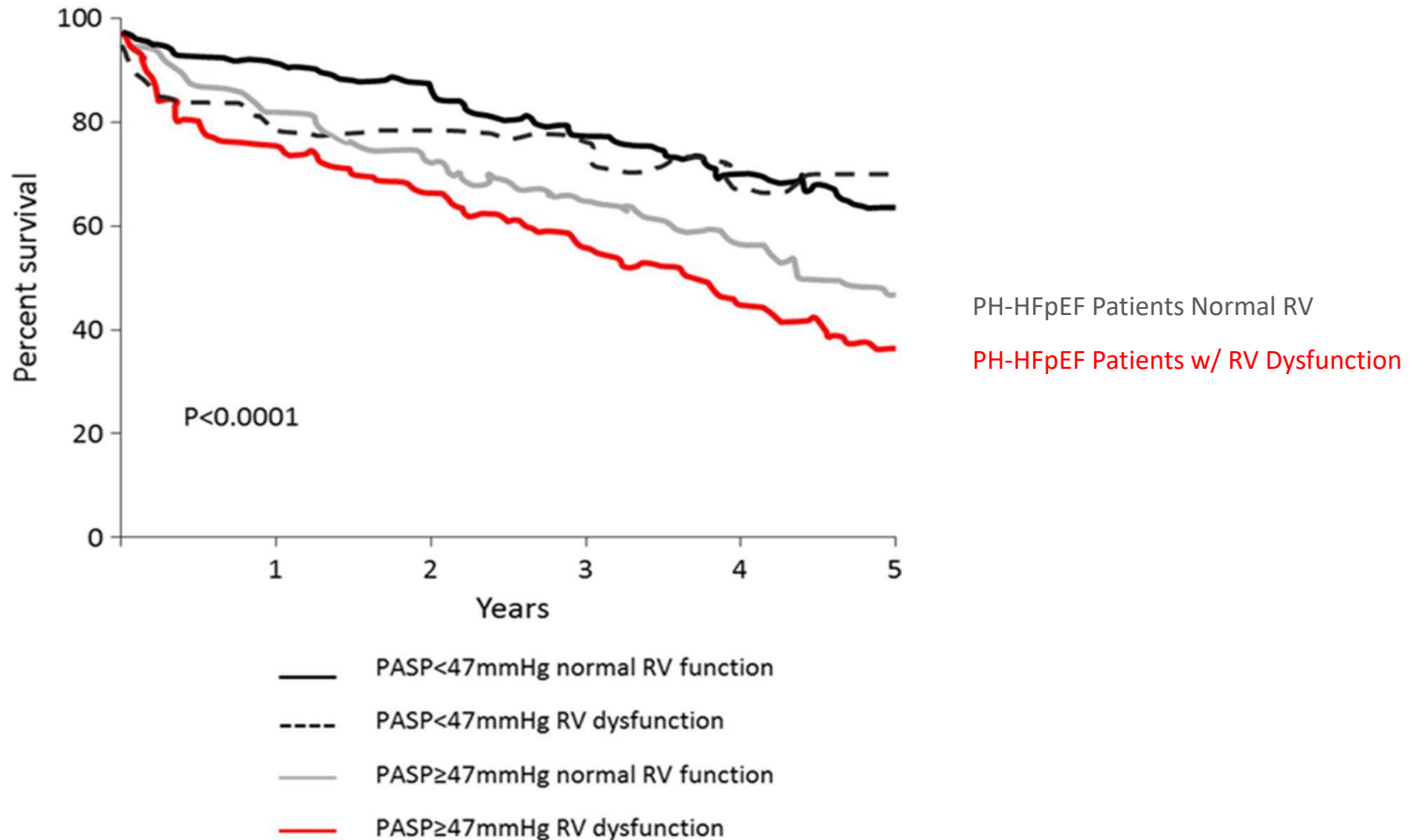
- **Pulmonary Hypertension associated with Heart Failure and preserved Ejection Fraction (PH-HFpEF)**

- Heart failure with impaired relaxation and stiffened myocardium, EF>40%
- Pulmonary capillary wedge pressure (PCWP) >15 mm Hg
- Pulmonary artery pressure (PAP) >25 mm Hg
- Sustained backward hemodynamic transmission leads to right ventricle dysfunction



# Poor PH-HFpEF Patients Outcomes

PH-HFpEF + Right Ventricle Dysfunction  
Associated with Highest Mortality



# Levosimendan

## Mechanism of Action

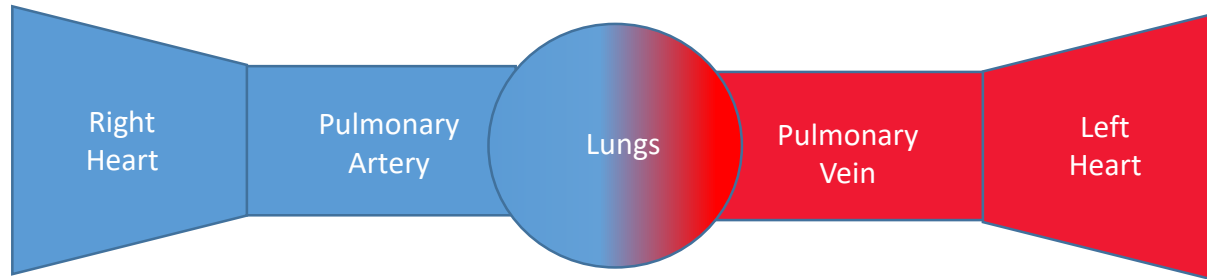
Molecular targets	Mechanisms of action	Pharmacological effects	Therapeutic effects
1. <u>Selective binding to the calcium-saturated form of cardiac troponin C</u>	Calcium sensitization	Positive inotropic Positive lusitropic	Increased ejection fraction Decreased left ventricular filling pressures
2. Opening of sarcolemma $K_{ATP}$ channels on <u>smooth-muscle</u> cells in vasculature	Hyperpolarization	Vasodilation in all vascular beds (also coronary and peripheral circulation)	Lowered pre- and after-load Anti-ischemic Better tissue perfusion Normalization of neurohormones
3. Opening of mitochondrial $K_{ATP}$ channels in <u>cardiomyocytes</u>	Protection of mitochondria in ischemia-reperfusion	Preconditioning, anti-stunning anti-apoptotic	Cardioprotection Anti-ischemic

Parissis, John T., et al. "Levosimendan: from basic science to clinical practice." *Heart failure reviews* 14.4 (2009): 265.



# Mechanistic Rationale for Levosimendan in PH-HFpEF – More than just a Vasodilator

## Cardio-Pulmonary System



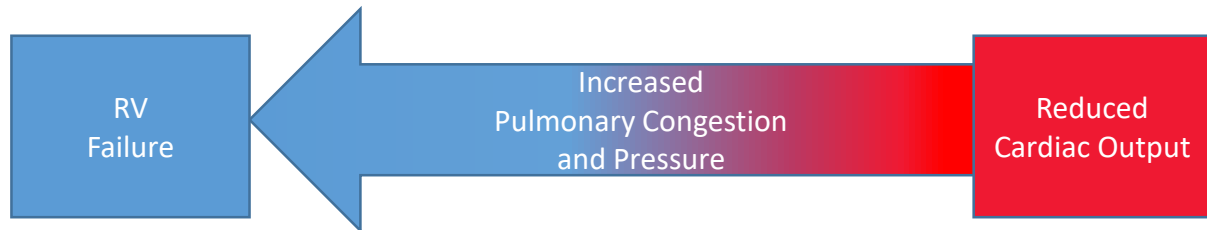
PH-HFpEF

PAP >25mmHg

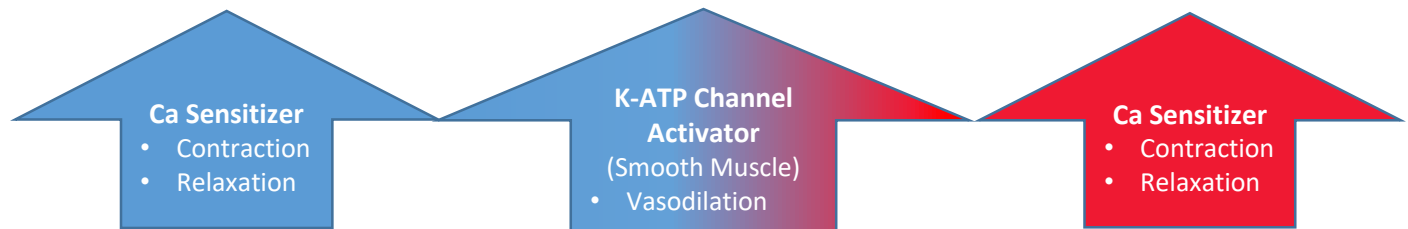
PCWP>15mm Hg

EF>40%

## Problem



## Levosimendan MOA



## Potential Benefits

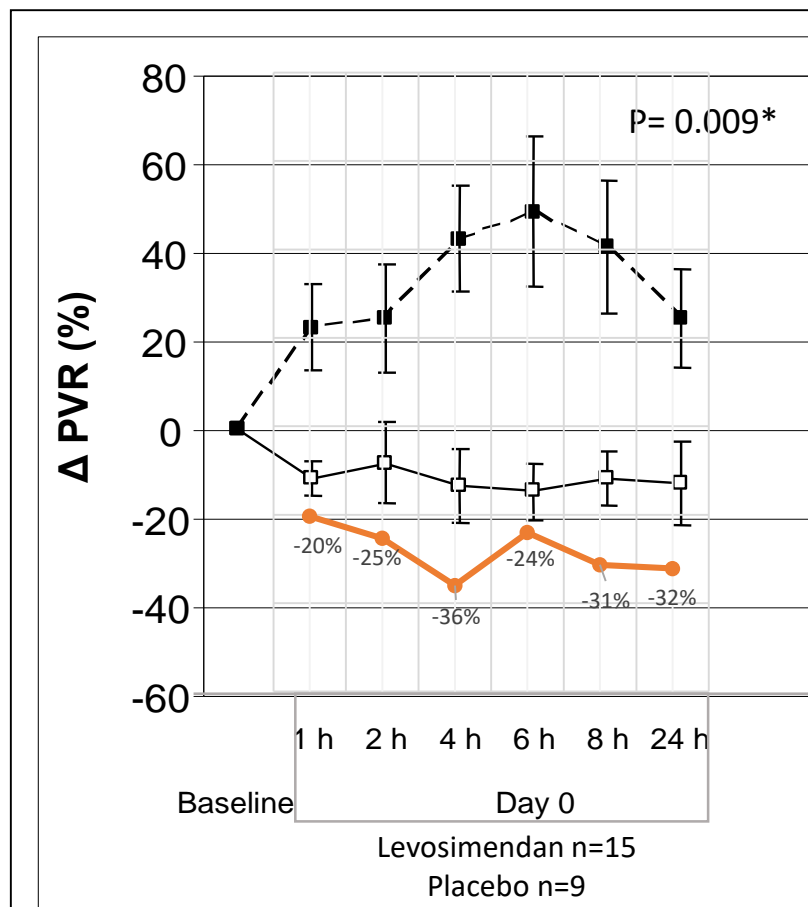
**Improved RV Function**

**Reduced Pulmonary Pressure**

**Improved LV Function**

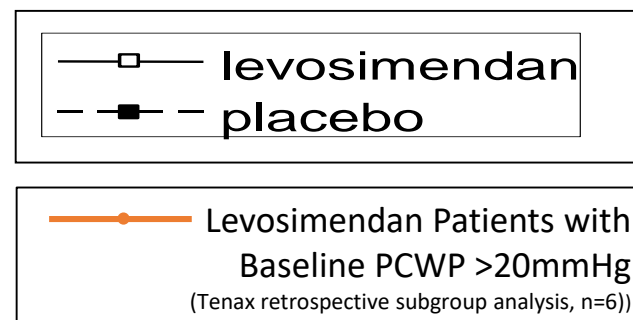
# Levosimendan in Pulmonary Hypertension

Change in PVR (mean  $\pm$  SEM)  
during 24-hour infusion



**Multicenter, Randomized, Placebo Controlled, Pilot Study of Levosimendan in Pulmonary Hypertension Patients**

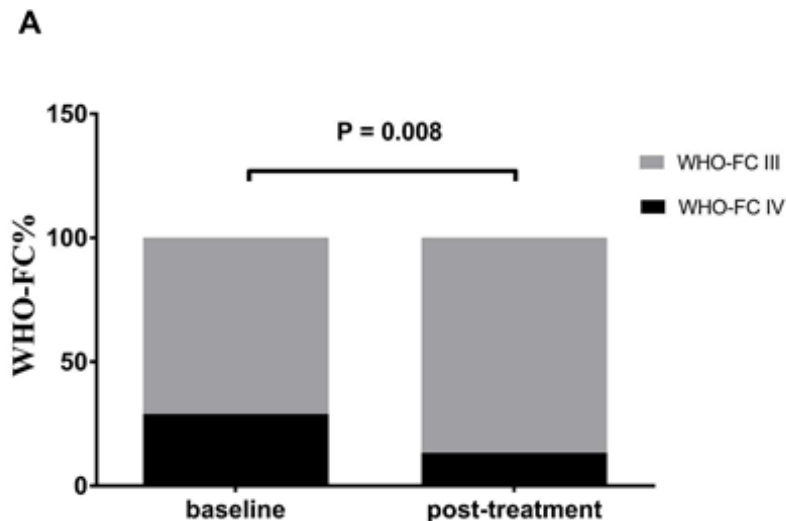
**\*Primary Endpoint: Change in PVR at end of initial 24-hour infusion**



# Levosimendan in Pulmonary Hypertension Patients with Right Heart Failure

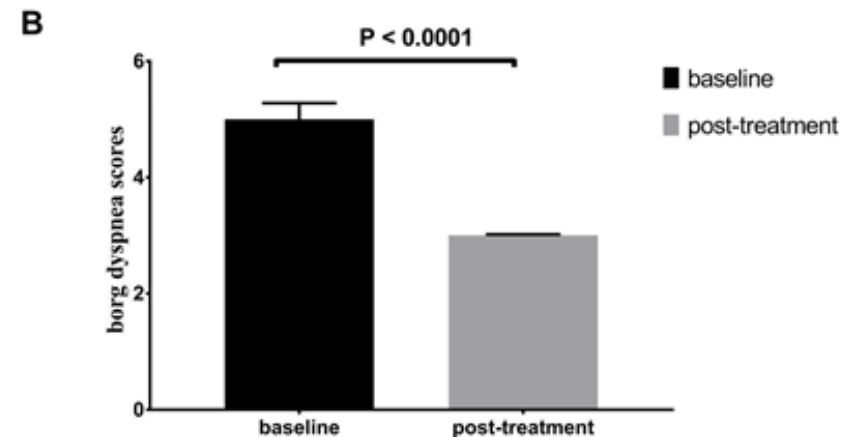
(Prospective Observational Study- September 2017)

Primary Endpoint: Change in WHO Functional Class



A. Change in WHO-FC after infusion of levosimendan from baseline to post-treatment. World Health Organization Function Class: WHO-FC.

Primary Endpoint: Change in Dyspnea Scores



B. Change in Borg dyspnoea scores from baseline to post-treatment

# Scientific Advisory Board

## PH-HFpEF Development Plan Guided by World Recognized Experts in Pulmonary Hypertension and HFpEF

### Stuart Rich, MD

- Professor of Medicine, Northwestern University Feinberg School of Medicine
- Director, Pulmonary Vascular Disease Program, Bluhm Cardiovascular Institute
- Previous FDA Cardio-Renal Advisory Committee Member
- Recognized Global Pulmonary Hypertension Expert

 **Northwestern Medicine**  
Feinberg School of Medicine

### Daniel Burkhoff, MD, PhD

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

 **Cardiovascular  
Research Foundation**



### Sanjiv Shah, MD, FAHA, FACC, FASE

- Professor of Medicine, Northwestern University Feinberg School of Medicine
- Director, T1 Center for Cardiovascular Therapeutics
- Director, Northwestern HFpEF Program, Division of Cardiology, Dept of Medicine, Northwestern University Feinberg School of Medicine

 **Northwestern Medicine**  
Feinberg School of Medicine

# Levosimendan Phase 2 for PH-HFpEF

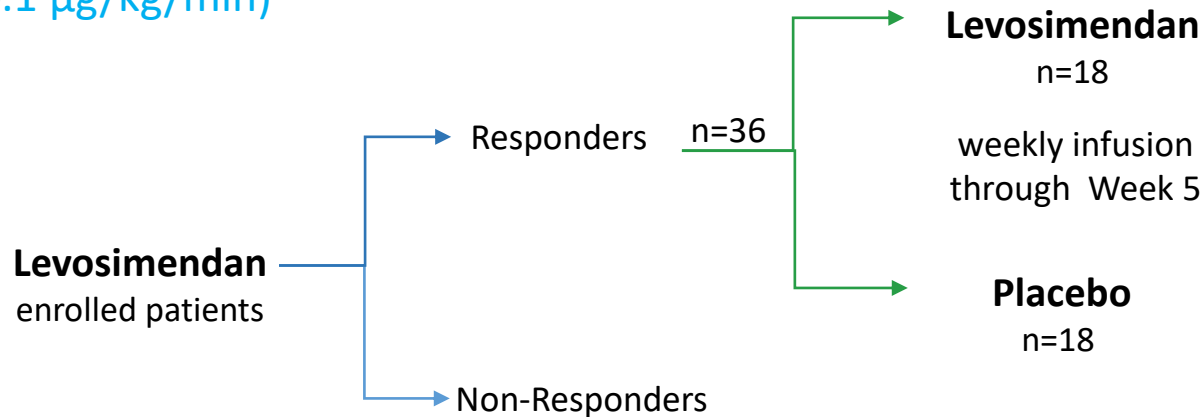
- **Multi-center, double-blind placebo-controlled study**
- **Enroll 36 evaluable patients at 12-15 sites**
  - PAP  $\geq 35$ , PCWP  $\geq 20$ , NYHA Class IIb/III, LVEF  $\geq 40\%$
- **Primary Endpoints:**
  - Change from baseline PCWP with bicycle exercise (25Watts) at Week 6
  - 80% power to detect a  $\geq 4.8$  mmHg change in PCWP from baseline
- **Secondary Endpoints:**
  - Change in Cardiac Index at rest and with exercise
  - Change in PVR effect at rest and with exercise
  - Change in PCWP when supine and legs elevated
  - Patient global assessment
  - Exercise duration via 6 minute walk test
  - Physician's assessment of functional class
  - Clinical events: death and hospitalizations

# Levosimendan Phase 2 for in PH-HFpEF Study Design

**Open-Label Lead-In**  
24 hours  
(0.1 µg/kg/min)

**Chronic Phase**  
5 weeks

**Week 6**  
Final Evaluation

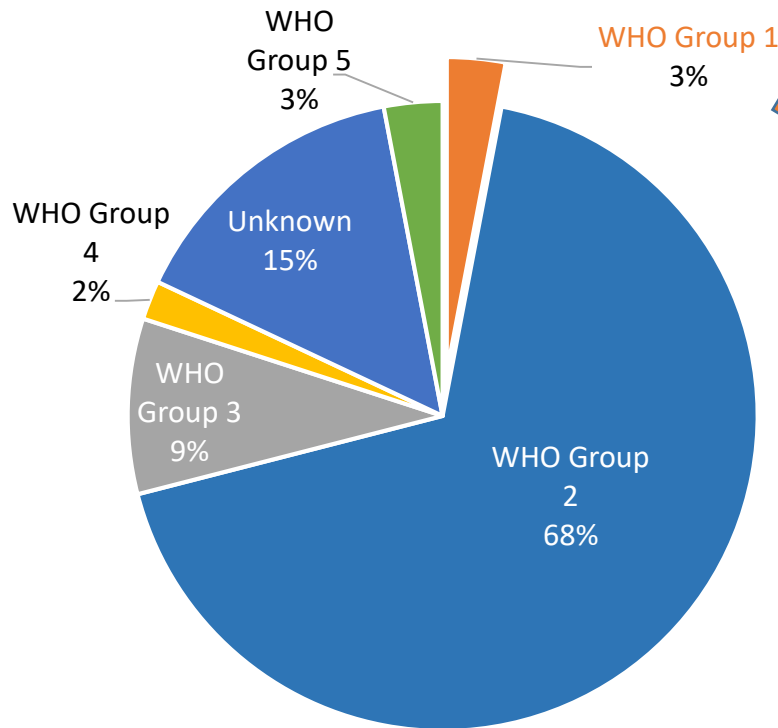


# Attractive Commercial Opportunity

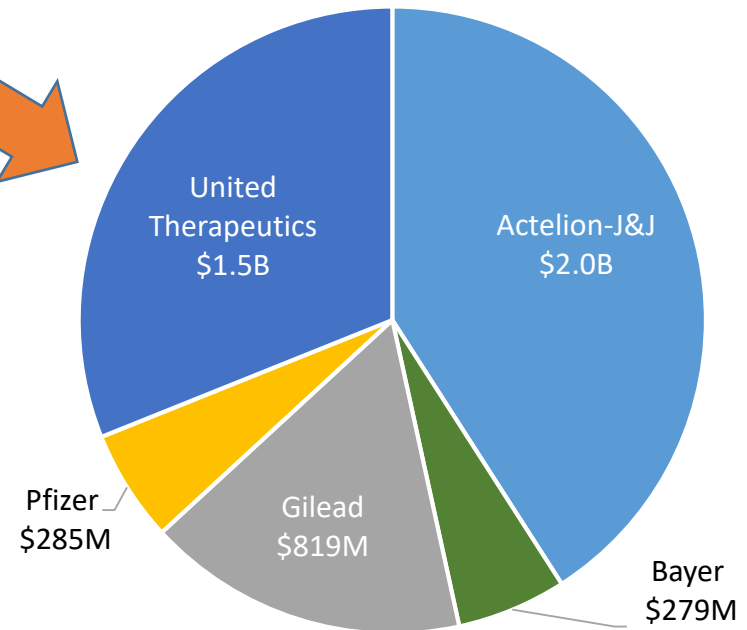
- **Large unmet medical need**
  - High mortality (up to 50% at 5 years)
  - Poor quality of life (poor exercise capacity)
  - No approved therapies
  - Large potential market
    - Estimated PH-HFpEF prevalence in the US >2,000,000
  - High value
    - Chronic therapy that addresses a large unmet medical need
- **IV levosimendan exclusivity as NCE**

# Pulmonary Hypertension Prevalence and Market Size

Estimated Prevalence by WHO Group



Pharmaceutical Sales >\$5 billion in 2016  
(primarily in Group 1)



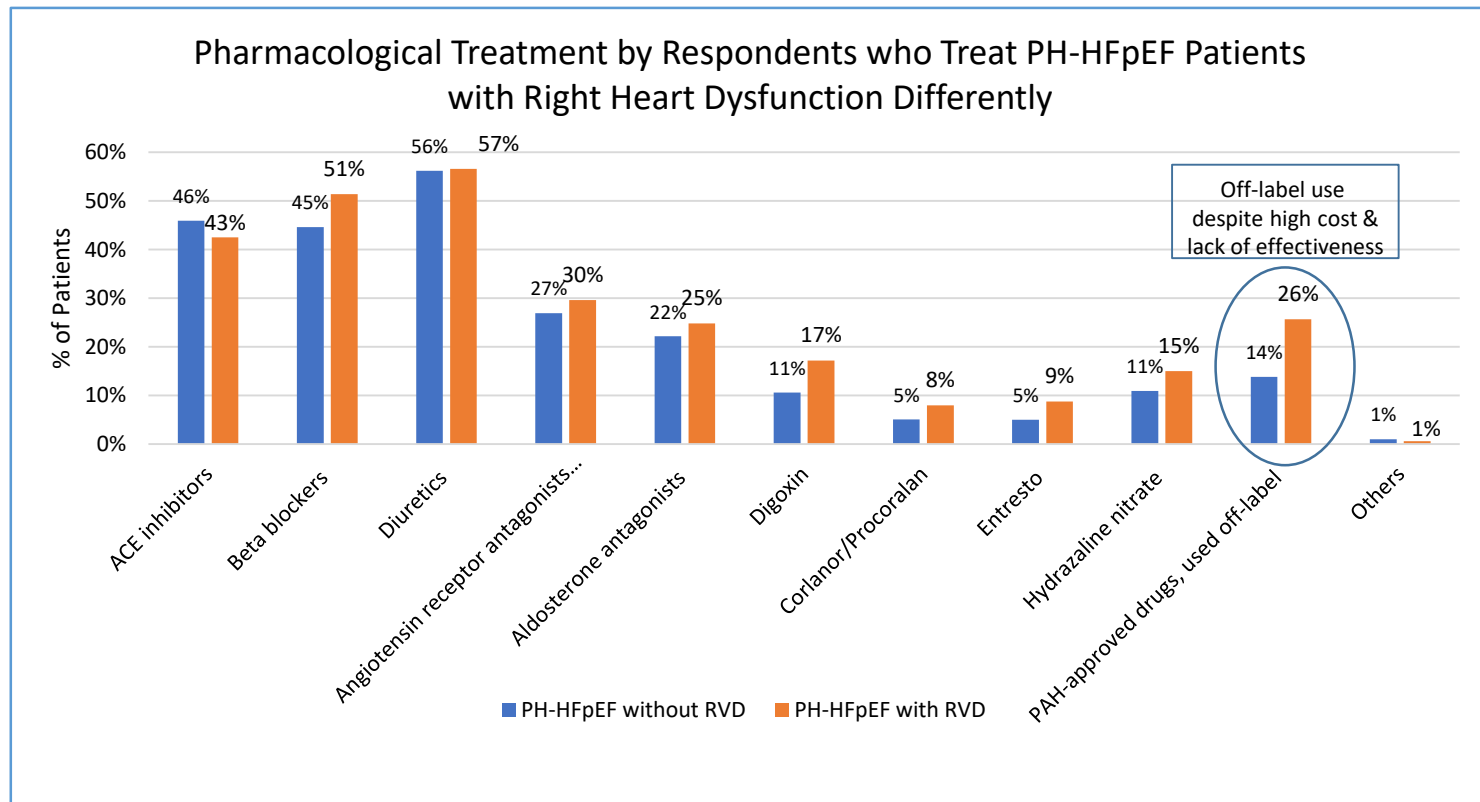
Source: Pulmonary Hypertension Association Strange G, et al. Heart. 2012;98(24):1805-11

Source: Company Annual Reports



# PH-HFpEF Pharmacologic Treatment in Right Heart Failure

55% of surveyed physicians indicate that they treat their PH-HFpEF patients with right heart dysfunction differently than those without it. Common treatments are those used to more broadly treat HF - diuretics, beta blockers, and ACE inhibitors



Q. Do you treat PH-HFpEF patients with right heart dysfunction pharmacologically DIFFERENTLY than you PH-HFpEF patients who do NOT have right heart dysfunction?

Q. Of your diagnosed PH-HFpEF patients receiving pharmacological treatment, what percentages received the following drugs in 2017? Please provide your best estimates to the nearest whole number. If they were not treated with a particular therapy, please enter 0. Please note that the columns must equal at least 100 and will exceed 100% if multiple drugs are used.

# PH-HFpEF Unmet Need

Approved WHO Group 1 Drugs are **not Approved or Effective in Group 2 Patients**

Drug Class	Pulmonary Hypertension WHO Group 1 (PAH)	Pulmonary Hypertension WHO Group 2 (HFpEF)
PDE5 Inhibitors	FDA Approved	Efficacy not established (Hoendermis et al 2015-Negative)
Endothelin Receptor Antagonists	FDA Approved	Efficacy not established (MELODY Trial-Negative)
Soluble Guanylate Cyclase Stimulators	FDA Approved	Efficacy not established (DILATE Trial-Negative)
Prostacyclins (IV/SC/Inhaled/Oral)	FDA Approved	Efficacy not established (SOUTHPAW Trial - Ongoing)

# Management

**Anthony DiTonno**  
CEO

- 40 years of experience in increasing levels of responsibility at life sciences companies
- Aventis Medical Systems: CEO
- NeurogesX: President and Chief Executive Officer
- MBA from Drexel University; BA from St. Joseph University



**Michael Jebson**  
President, CFO

- >15 years of financial and accounting experience
- Grant Thornton, LLP: Auditor
- RTI International: Chief Ethics Officer, Senior Internal Auditor
- MS in Accounting from East Carolina University
- CPA licensed in North Carolina



**Doug Randall**  
EVP, Commercial Business and Operations

- >33 years of pharmaceutical executive experience
- Phyxius Pharma: Co-founder, CCO
- The Medicines Company: VP of Commercial Operations
- Sanofi-Aventis Pharmaceuticals: VP of US Diabetes Marketing
- Aventis: VP of Sales



**Doug Hay**  
EVP, Regulatory Affairs

- >29 years of pharmaceutical regulatory experience
- Phyxius Pharma: Co-founder, VP of Regulatory Affairs
- The Medicines Company, Shire Pharmaceuticals: Regulatory Affairs
- Bristol Myers Squibb: VP, Global Regulatory Sciences
- PhD from Northern Arizona University



# Board of Directors

**Ronald Blanck, DO**  
Chairman

- Martin, Blanck & Associates: Chairman
- Retired Surgeon General of the Army
- University of North Texas Health Science Center: President
- Walter Reed Medical Center: Commander

**UNT HEALTH**  
SCIENCE CENTER



**Chris Rallis**

- Pappas Capital: Executive-in-Residence
- ImmunoBiosciences: President and Chief Executive Officer
- Triangle Pharmaceuticals, Inc.: President, COO
- Aeolus Pharmaceuticals, Fennec Pharmaceuticals: Audit Committee Chairman



**Gerry Proehl**

- Dermata Therapeutics, LLC: Founder, President, CEO and Director
- Santarus, Inc.: President, Chief Executive Officer, Director
- HMR: Vice President of Global Marketing
- Sophiris Bio Inc., Ritter Pharmaceuticals, Inc., Kinetek Sports, Patara Pharma LLC, and MD Rejuvena, Inc: Director

**dermata**



**Jim Mitchum**

- NephroGenex Inc.: Director
- Heart to Heart International: CEO
- Americas for EUSA Pharma: President
- Enturia, Inc.: President, CEO
- Sanofi-Aventis Group and Aventis Pharma UK: President and CEO



**Gregory Pepin**

- Melixia SA: Senior Vice President
- Vatea Fund: Managing Director
- EOS Investment, Ltd.: Co-founder
- Independent Wealth Management, SA: Co-founder, analyst



# Summary:

## The Opportunity for Levosimendan in PH-HFpEF

- **Area of high unmet medical need**
  - High mortality (up to 50% at 5 years)
  - Poor quality of life (poor exercise capacity)
  - No approved therapies in PH-HFpEF
- **Commercially attractive market**
  - Large potential market - Estimated PH-HFpEF prevalence in the US >2,000,000
  - High value chronic therapy that addresses a large unmet need
- **Mechanistic rationale for Levosimendan in PH-HFpEF**
  - Including mechanisms directed at right heart failure
- **Existing preliminary positive Phase 2 clinical data in Pulmonary Hypertension**
- **Phase 2 trial is underway**
- **IV Levosimendan exclusivity as NCE**