TENAX THERAPEUTICS

Corporate Update

January 2018

Tenax Strategic Update

Specialty pharmaceutical company focused on search, development, and commercialization of drugs that address diseases with high unmet medical need

- Shift levosimendan development focus to pulmonary hypertension
  - WHO Group 2- pulmonary hypertension associated with heart failure with preserved ejection fraction (PH-HFpEF)
- Continue ongoing search for assets and collaborations that will build shareholder value

Shift Levosimendan Development Focus to Pulmonary Hypertension, WHO-Group 2

- **Leverage positive levosimendan clinical study data**
  - Positive levosimendan Phase 2 pulmonary hypertension study data
  - Positive levosimendan right heart failure data
- **Focus development in PH-HFpEF** –(Pulmonary Hypertension in patients with Heart Failure and Preserved Ejection Fraction)
  - High unmet medical need
  - Large patient population with no approved drugs
- **Capitalize on PH-HFpEF advisors expertise and advocacy**
  - Validate clinical development strategy with PH-HFpEF experts

PH-HFpEF Development Strategy Validated by World Recognized Experts in Pulmonary Hypertension and HFpEF

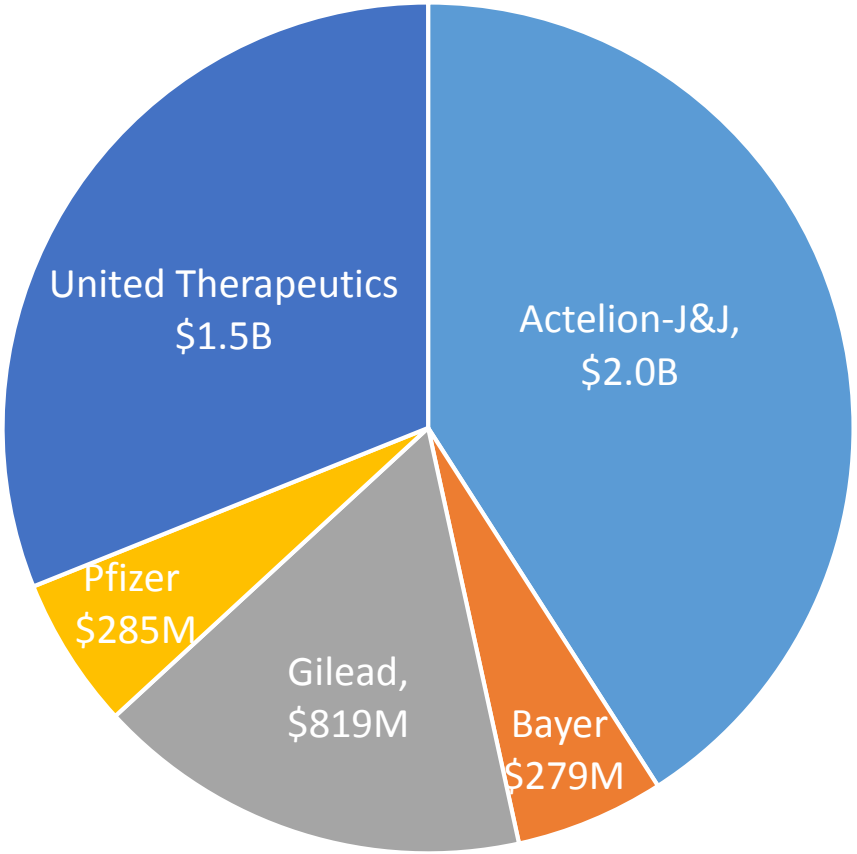
- Lead Scientific Advisor – Stuart Rich, MD

Stuart Rich, M.D.
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

Rationale for Development of Levosimendan in PH-HFpEF

- PH-HFpEF is an 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 >1,500,000
  - 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
- Efficient and timely Phase 2 trial is planned
- IV Levosimendan exclusivity as NCE

Global Pulmonary Hypertension Pharmaceutical Market > $5 Billion in 2016



Based on publicly reported sales from company annual reports

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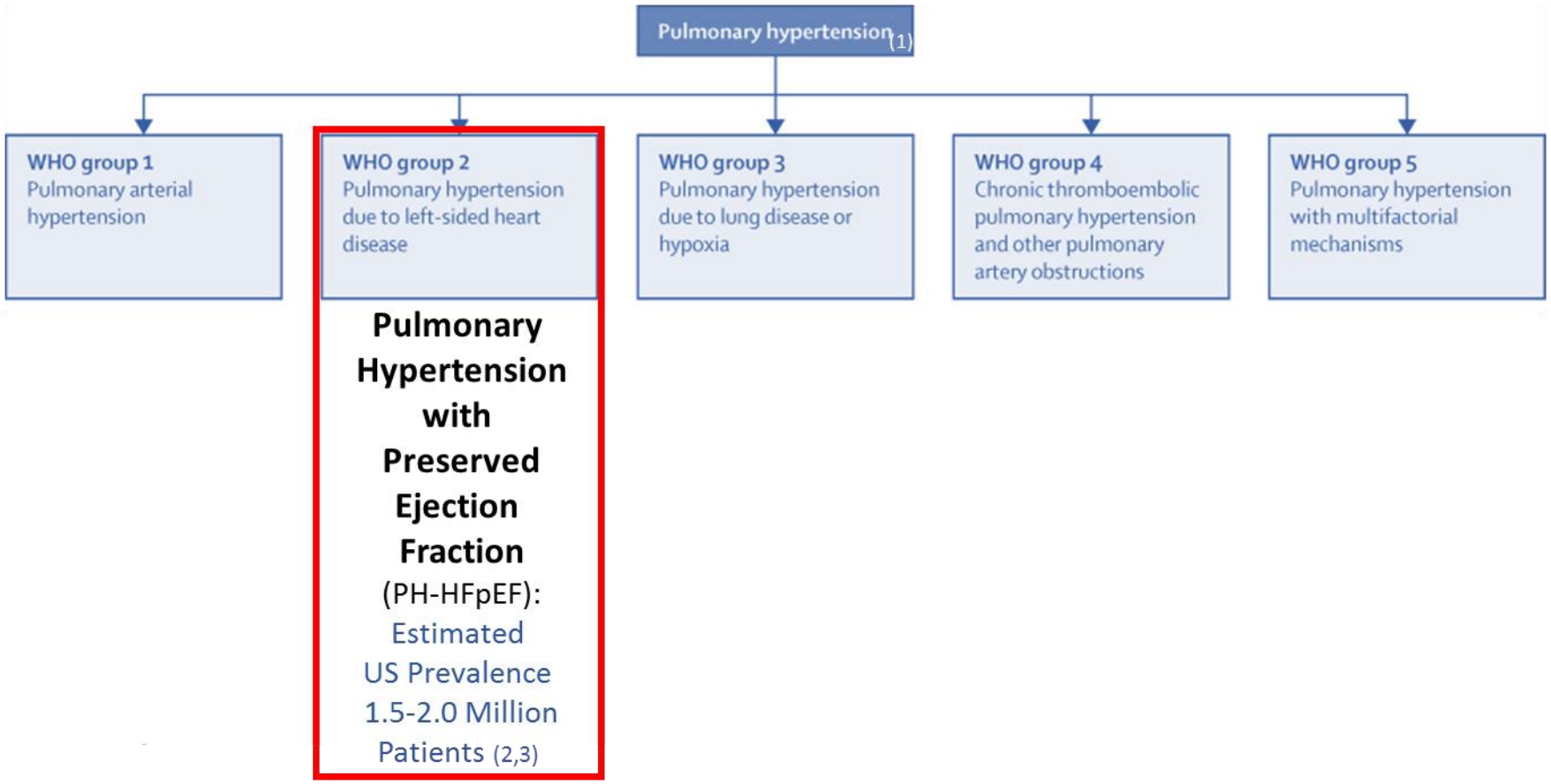
Pulmonary Hypertension WHO Classification Levosimendan Development Focused on Group 2



1) Hoeper, 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-HFpEFpatiients
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)

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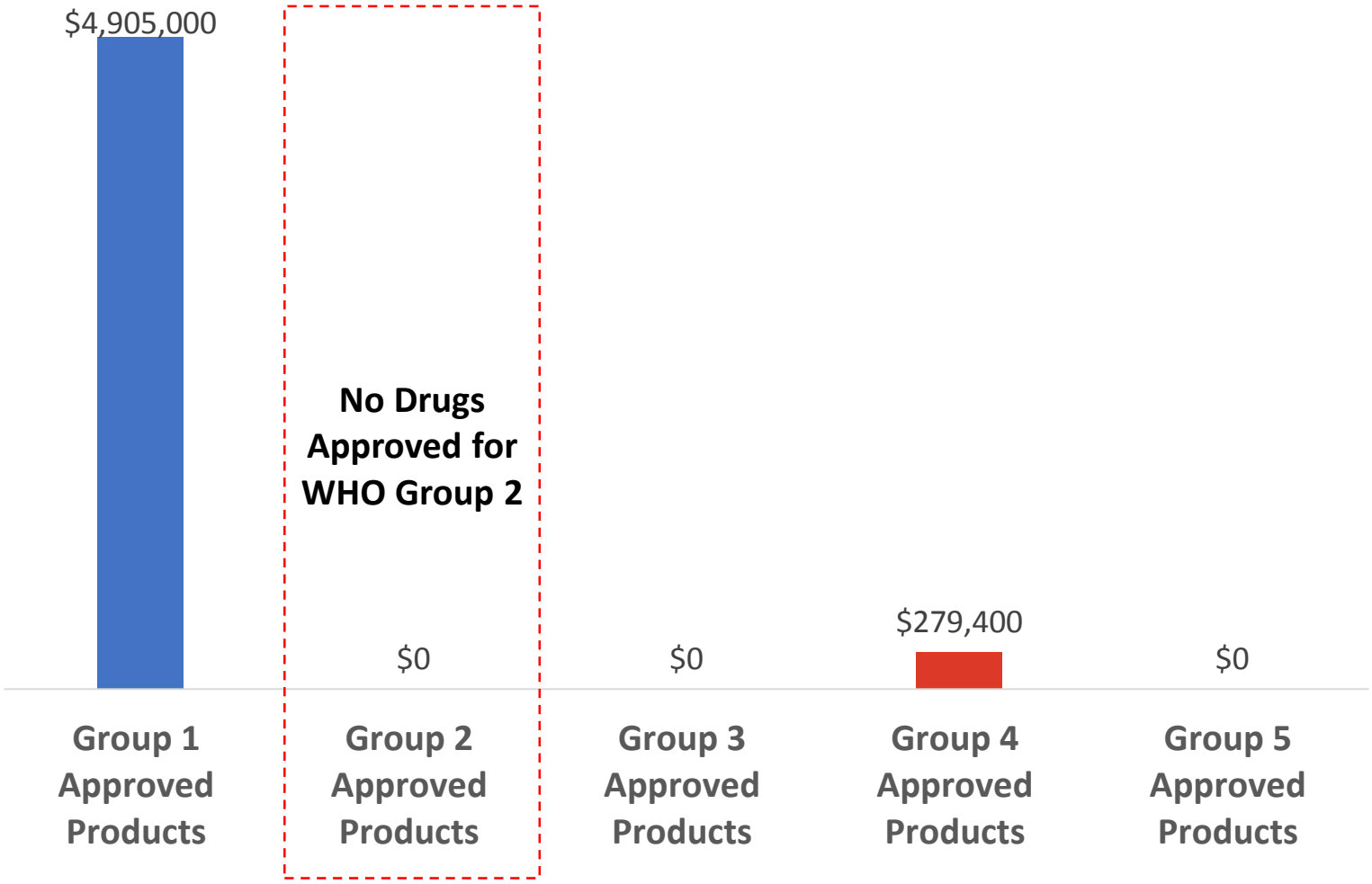
Global Pulmonary Hypertension Product Sales -2016 Allocated by WHO Group Approved Indication



Excludes potential off-label uses

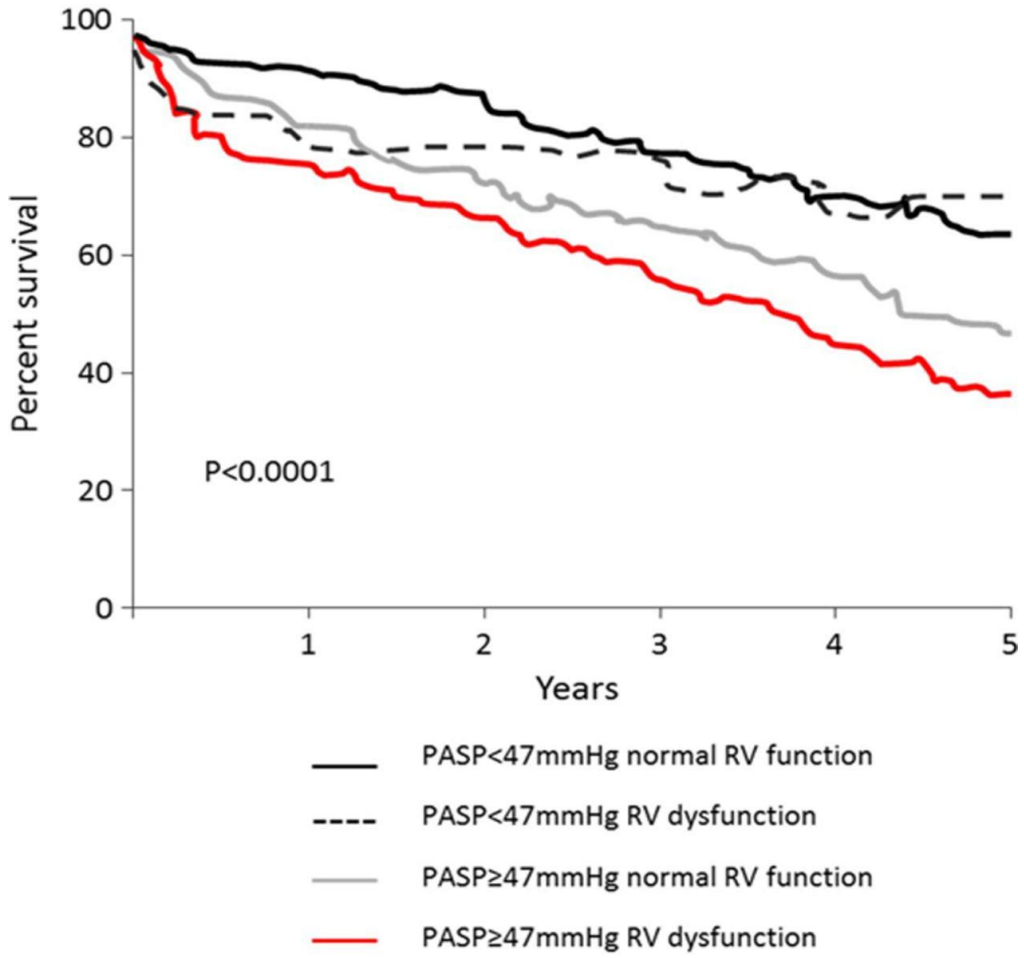
PH-HFpEF Unmet Need

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**
Endothelin Receptor Antagonists	**FDA Approved**	**Efficacy not established**
Soluble Guanylate Cyclase Stimulators	**FDA Approved**	**Efficacy not established**
Prostacyclins (IV/SC/Inhaled/Oral)	**FDA Approved**	**Efficacy not established**

PH-HFpEF Patients have Poor Outcomes

PH-HFpEF + RV Dysfunction is Associated with Highest Mortality



PH-HFpEF Patients Normal RV

PH-HFpEF Patients w/ RV Dysfunction

Mohammed, Selma F., et al. "Right ventricular systolic function in subjects with HFpEF: a community based study." (2011): A17407-A17407.

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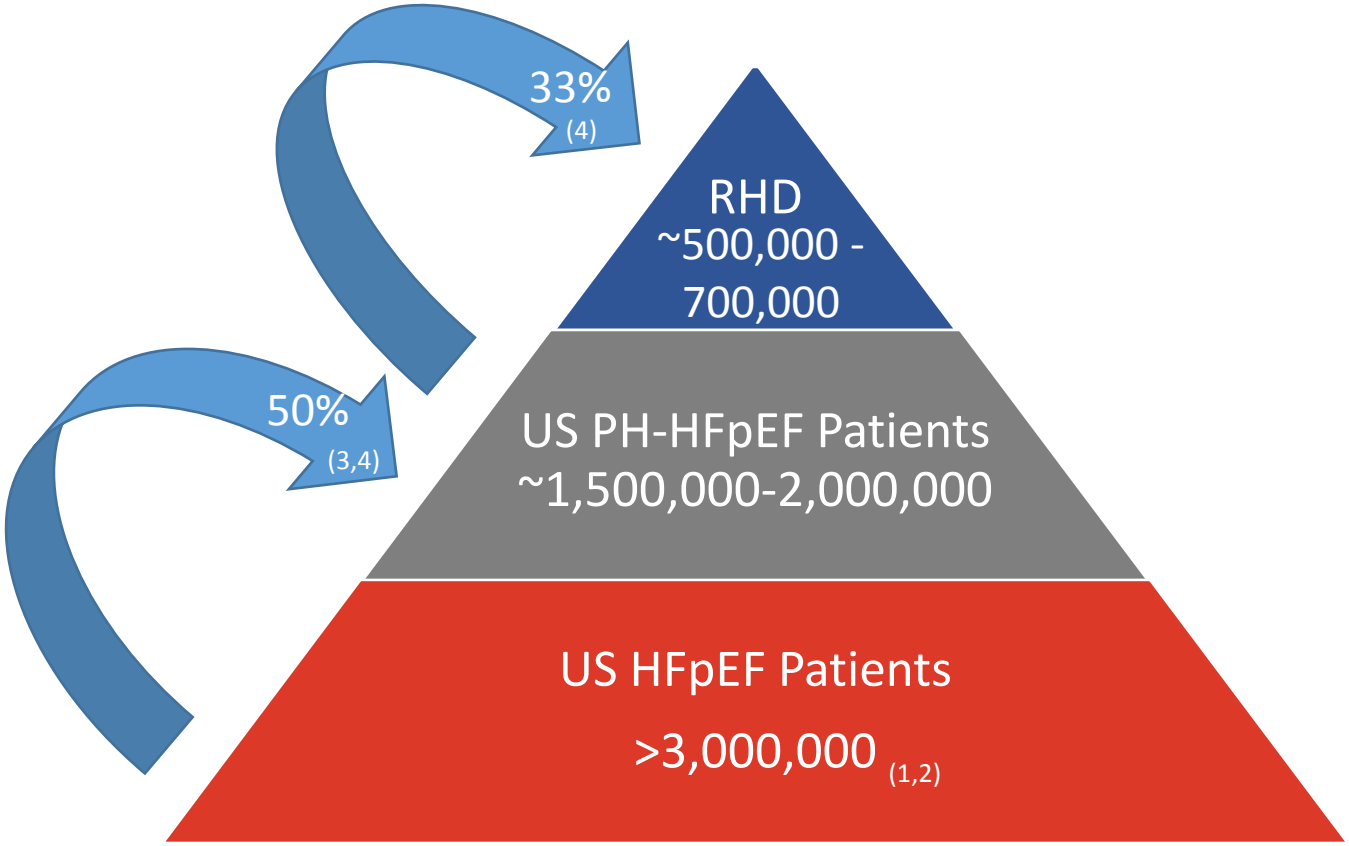
PH-HFpEF with Right Heart Dysfunction (RHD): Large Target Market with Very High Needs



Estimates based on

1) Benjamin, Emelia J., et al. "Heart disease and stroke statistics—2017 update: a report from the American Heart Association." *Circulation* 135.10 (2017): e146-e603.
2) Steinberg, Benjamin A., et al. "Trends in Patients Hospitalized with Heart Failure and Preserved Left Ventricular Ejection Fraction-Prevalence, Therapies, and Outcomes." *Circulation*(2012): CIRCULATIONAHA-111.
3) 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-HFpEFpatiients
4) Guazzi, Marco. "Pulmonary hypertension in heart failure preserved ejection fraction: prevalence, pathophysiology, and clinical perspectives." *Circulation: Heart Failure* 7.2 (2014): 367-377.

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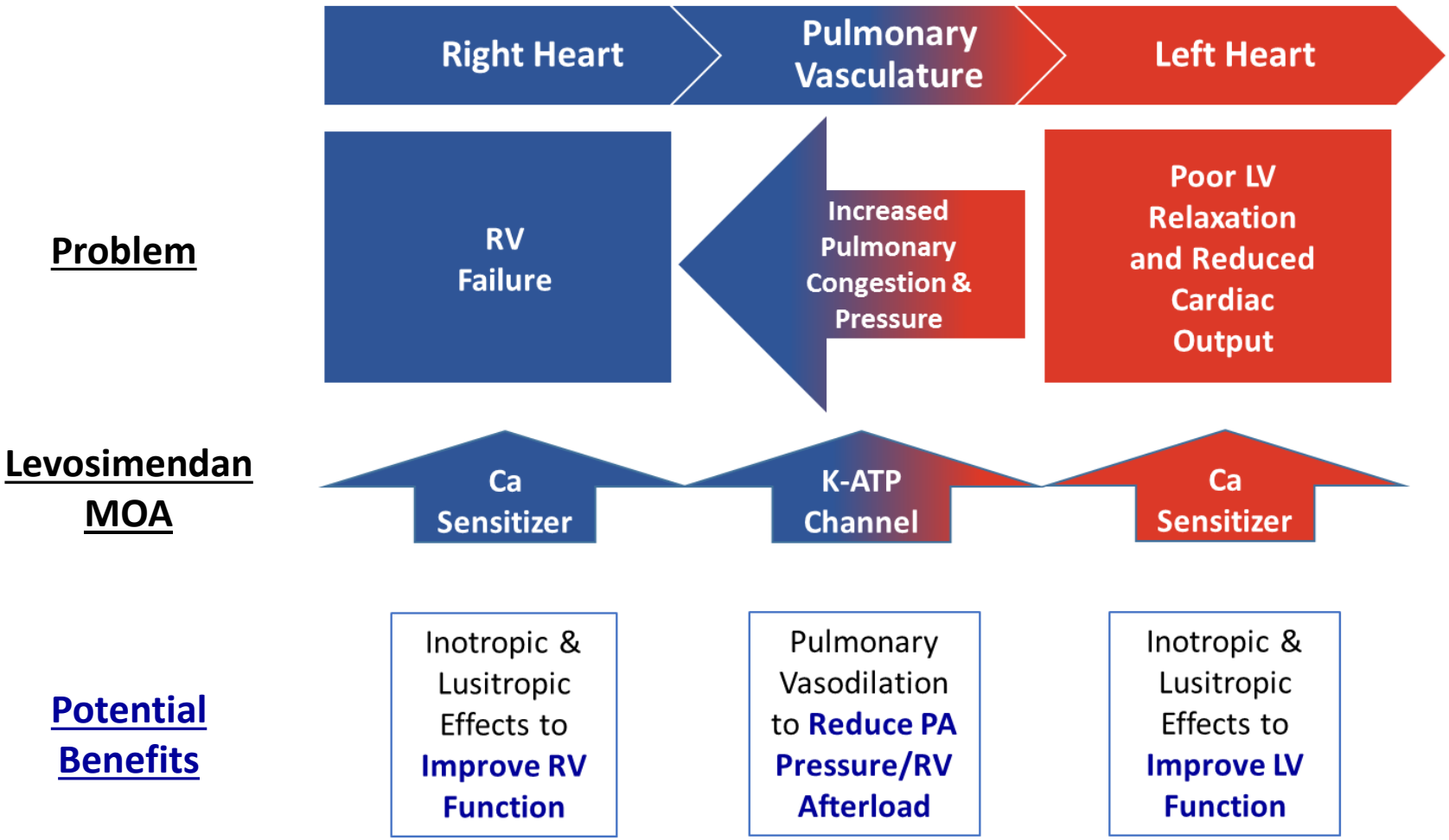
Mechanistic Rationale for Levosimendan in PH-HFpEF – More than just a Vasodilator



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Increasing Number of Scientific Publications on Levosimendan in Pulmonary Hypertension

- **Clinical Studies**
  - **2017**- Jiang, Rong, et al. "Efficacy and Safety of a Calcium Sensitizer, Levosimendan, in Patients with Right Heart Failure due to Pulmonary Hypertension." *The Clinical Respiratory Journal* (2017).
  - **2016** -Guerrero-Orriach, José Luis, et al. "Cardiac, renal, and neurological benefits of preoperative levosimendan administration in patients with right ventricular dysfunction and pulmonary hypertension undergoing cardiac surgery: evaluation with two biomarkers neutrophil gelatinase-associated lipocalin and neuronal enolase." *Therapeutics and clinical risk management* 12 (2016): 623
  - **2012**- Martyniuk TV, Arkhipova OA, Kobal' EA, Danilov NM, Chazova IE. Possibilities of using levosimendan in patients with idiopathic pulmonary hypertension. Ter Arkh. 2012;84(9):83-8.
  - **2009** -Kleber, Franz X., et al. "Repetitive dosing of intravenous levosimendan improves pulmonary hemodynamics in patients with pulmonary hypertension: results of a pilot study." *The Journal of Clinical Pharmacology* 49.1 (2009): 109-115.
- **Preclinical Studies**
  - **2018-** Hansen, M. S., et al. "Levosimendan improves cardiac function and myocardial efficiency in rats with right ventricular failure." *Pulmonary circulation* 8.1 (2018): 2045893217743122-2045893217743122
  - **2017**- Hansen, Mona Sahlholdt, et al. "Levosimendan prevents and reverts right ventricular failure in experimental pulmonary arterial hypertension." *Journal of Cardiovascular Pharmacology* (2017).
  - **2017-** Tavares-Silva, Marta, et al. "Dose–Response Head-to-Head Comparison of Inodilators Dobutamine, Milrinone, and Levosimendan in Chronic Experimental Pulmonary Hypertension." *Journal of Cardiovascular Pharmacology and Therapeutics* (2017): 1074248417696818.
  - **2012**- Wiklund, Annaeva, David Kylhammar, and Göran Rådegran. "Levosimendan attenuates hypoxia-induced pulmonary hypertension in a porcine model." *Journal of cardiovascular pharmacology* 59.5 (2012): 441-449.
  - **2011**- Revermann, M., et al. "Levosimendan attenuates pulmonary vascular remodeling." *Intensive care medicine* 37.8 (2011): 1368-1377.

Results from a Multicenter, Randomized, Placebo Controlled, Pilot Study of Levosimendan in Pulmonary Hypertension Patients

Kleber, Franz X., et al. "Repetitive dosing of intravenous levosimendan improves pulmonary hemodynamics in patients with pulmonary hypertension: results of a pilot study." *The Journal of Clinical Pharmacology* 49.1 (2009): 109-115.

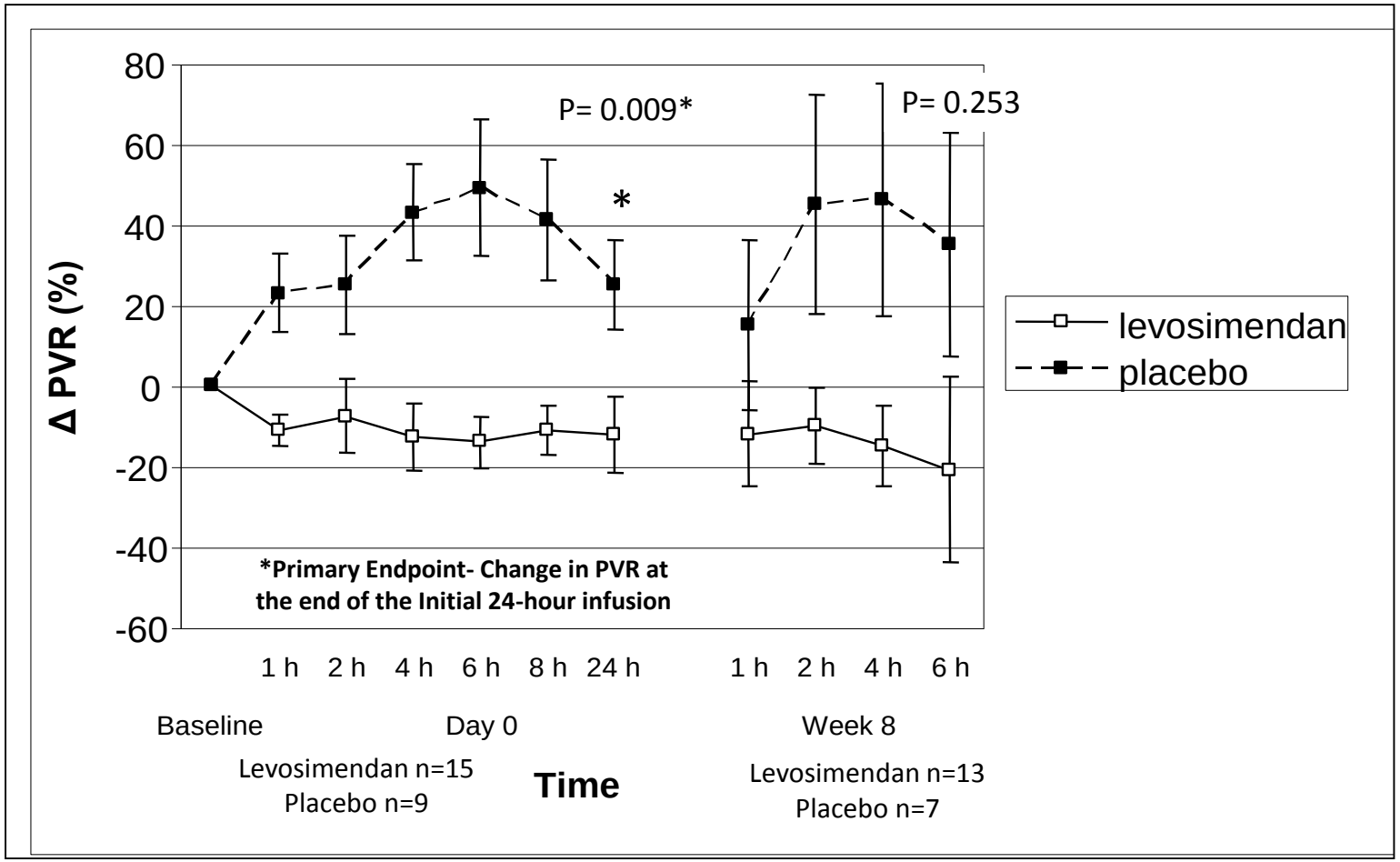
Kleber et al Patient Demographics

	Levosimendan (n = 18)	Placebo (n = 10)
Age, y	62 ± 11	58 ± 12
Sex, M/F	9/9	8/2
Etiology of pulmonary hypertension[a]		
Pulmonary arterial hypertension	7 (39)	4 (40)
Idiopathic	6	2
Portal hypertension	1	1
Congenital systemic to pulmonary shunts		1
Pulmonary venous hypertension due to left-sided heart disease	10 (56)	4 (40)
Pulmonary hypertension due to chronic thrombotic and/or embolic disease	1 (5)	2 (20)
Signs of right heart failure		
Jugular venous distension	12 (67)	7 (70)
Peripheral edema	14 (78)	8 (80)
Known response to vasodilator testing	18 (100)	10 (100)
Systemic hemodynamics		
Systolic blood pressure	121 ± 23	116 ± 15
Diastolic blood pressure	72 ± 10	75 ± 12
Heart rate	75 ± 18	70 ± 13
New York Heart Association class		
III	15 (83)	9 (90)
IV	3 (17)	1 (10)
mRAP		
Mean ± SD	12 ± 5.9 (n = 15)	14 ± 4.9 (n = 9)
Range	5-29	7-24
Use of vasoactive medication		
Diuretics	15 (83)	8 (80)
Angiotensin-converting enzyme inhibitor/ AT2-blocker	14 (78)	6 (60)
β-Blocker	10 (56)	7 (70)
Calcium channel blocker	6 (33)	4 (40)
Bosentan	3 (17)	2 (20)

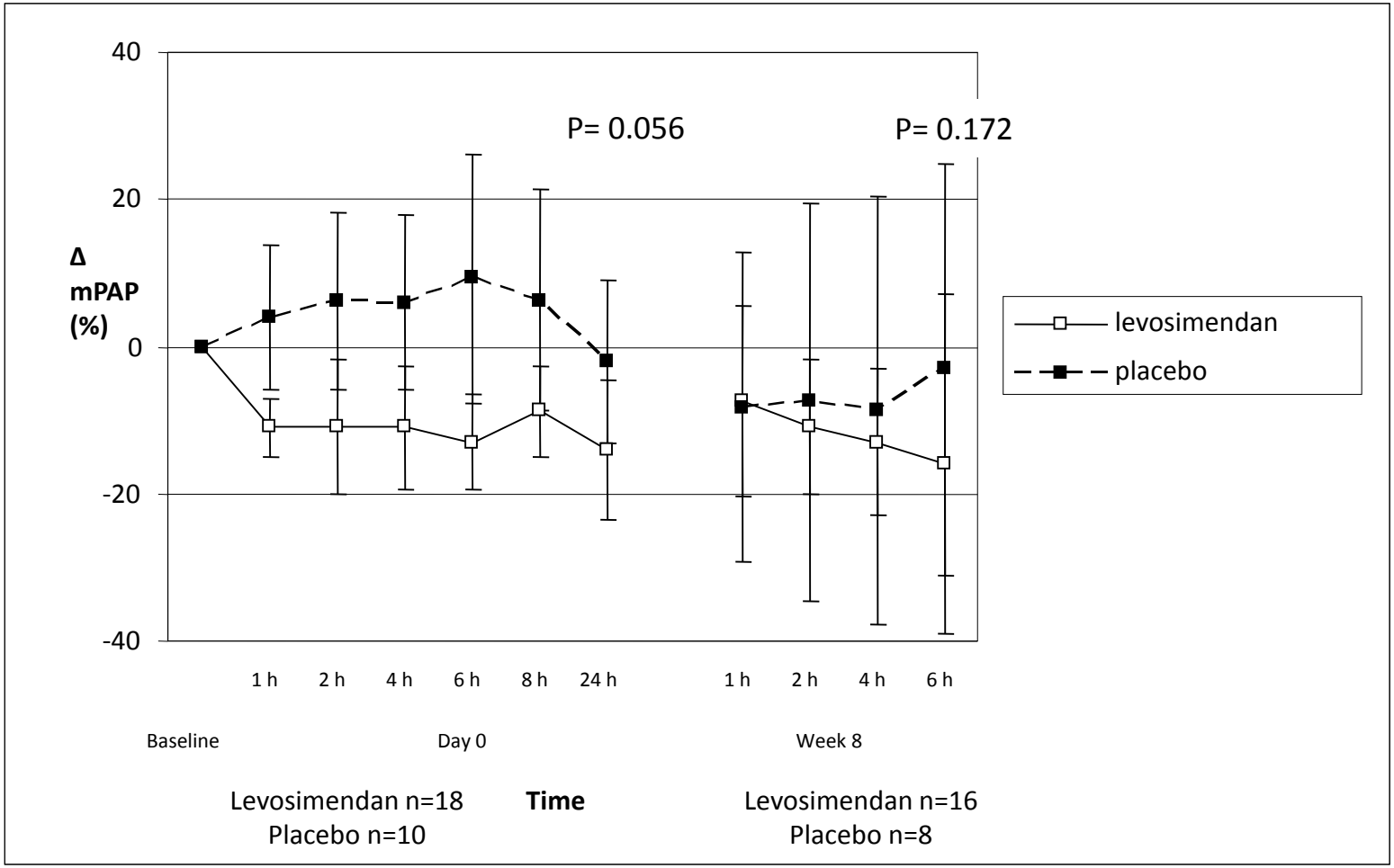
Values are mean ± SD or n (%). Medication is expressed as the number of patients taking the drug (%).
a. According to the Venice classification.[24]

Kleber, Franz X., et al. "Repetitive dosing of intravenous levosimendan improves pulmonary hemodynamics in patients with pulmonary hypertension: results of a pilot study." *The Journal of Clinical Pharmacology* 49.1 (2009): 109-115.

Change in PVR (mean ± SEM) during 24-hour infusion and 6-hour infusion at week 8



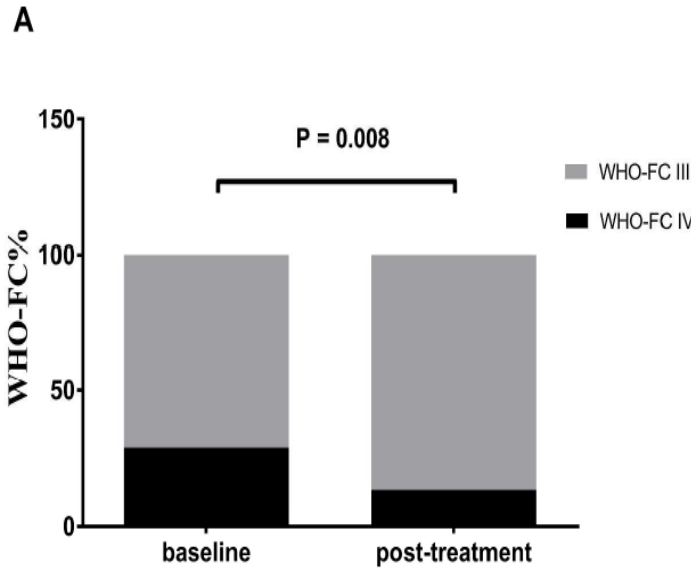
Change in mPAP (mean ± SEM) during 24-hour infusion and 6-hour infusion at week 8



Levosimendan in Pulmonary Hypertension

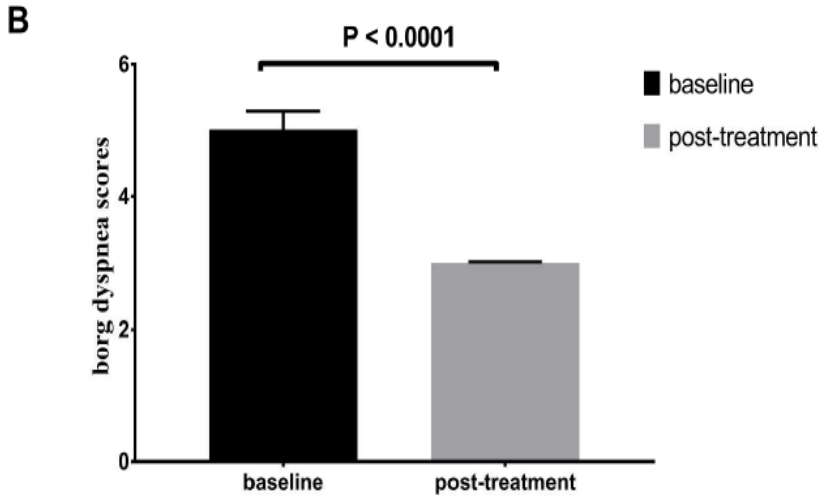
The Clinical Respiratory Journal (September 2017)

Primary endpoint-Change in WHO Functional Class



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

Primary Endpoint- Change in Dyspnea Scores



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

Jiang, Rong, et al. "Efficacy and Safety of a Calcium Sensitizer, Levosimendan, in Patients with Right Heart Failure due to Pulmonary Hypertension." *The Clinical Respiratory Journal* (2017).

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Phase 2 Study Design

- Double-blind study of PH-HFpEF Patients
  - PAP ≥35, PCWP ≥20, CI ≤2.2, NYHA Class III/IV, LVEF ≥40%
- Targets: 50 patients; 20 sites; 14-18 months
- Primary Endpoint:
  - hemodynamic effect (with exercise) at 6 weeks compared to the baseline measurements manifested by:
    - ↓5mmHg in pulmonary capillary wedge pressure (PCWP), and/or
    - ↑10% in cardiac index (CI)
- 90% power; assuming responses of 67% (levosimendan) and 13% (placebo)
- Secondary Endpoints:
  - Change in resting PCWP and CI
  - Change in PVR effect at rest and with exercise
  - Change in PCWP when supine, legs elevated, and at max exercise
  - Patient global assessment (based on a 7-point Likert scale) at Wk 6
  - Exercise duration at Wk 6

Summary
The Opportunity for Levosimendan in PH-HFpEF

- PH-HFpEF is an area of high unmet medical need
  - High mortality (up to 50% at 5 years)
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  - No approved therapies in PH-HFpEF
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