HELP Study
Topline Results
June 2, 2020

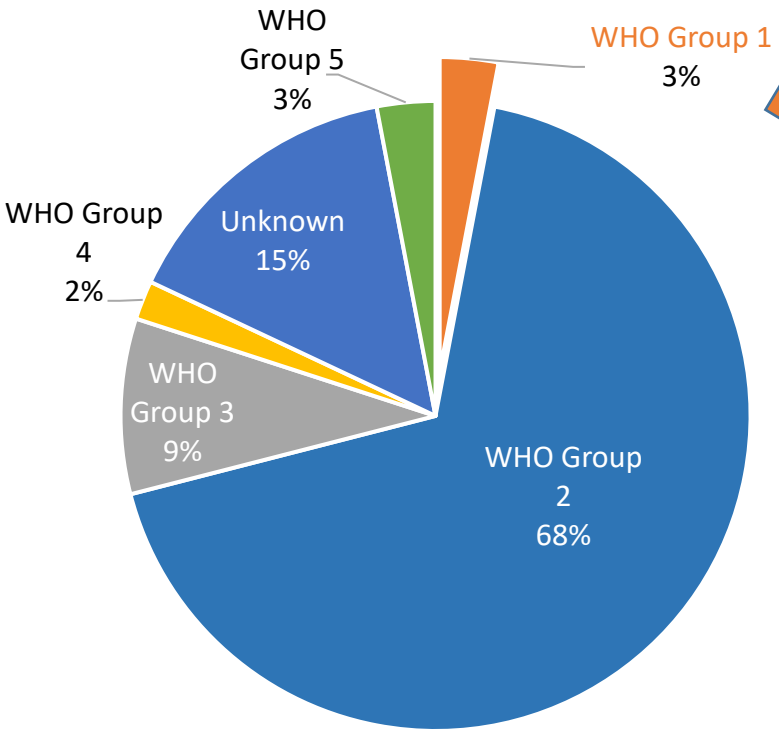
TENAX THERAPEUTICS

HELP Study Phase 2 Objectives

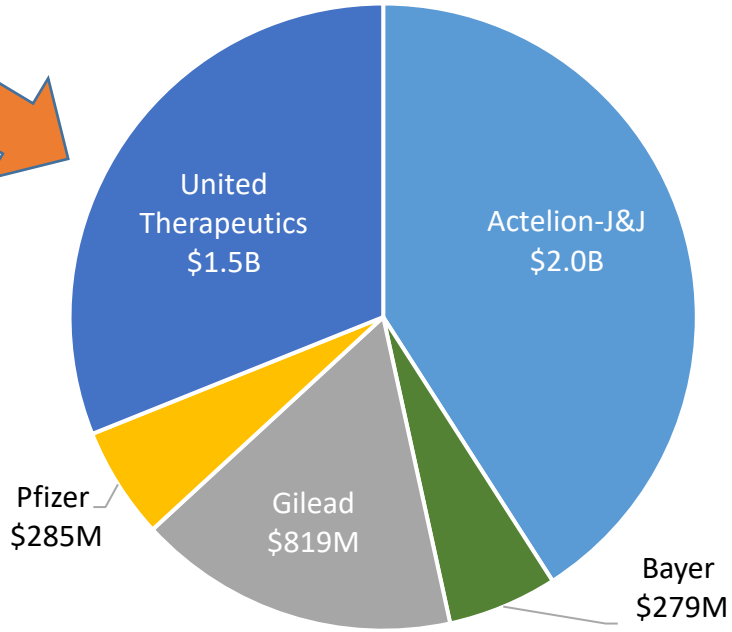
- HELP Study Objectives
  1. Explore hemodynamic markers of effectiveness in PH-HFpEF
  2. Explore safety of chronic Levosimendan dosing in PH-HFpEF
  3. Explore a potential signal of clinical effectiveness in PH-HFpEF
- We have achieved all these objectives in the HELP Study

Pulmonary Hypertension Prevalence and Market Size

Estimated Prevalence by WHO Group



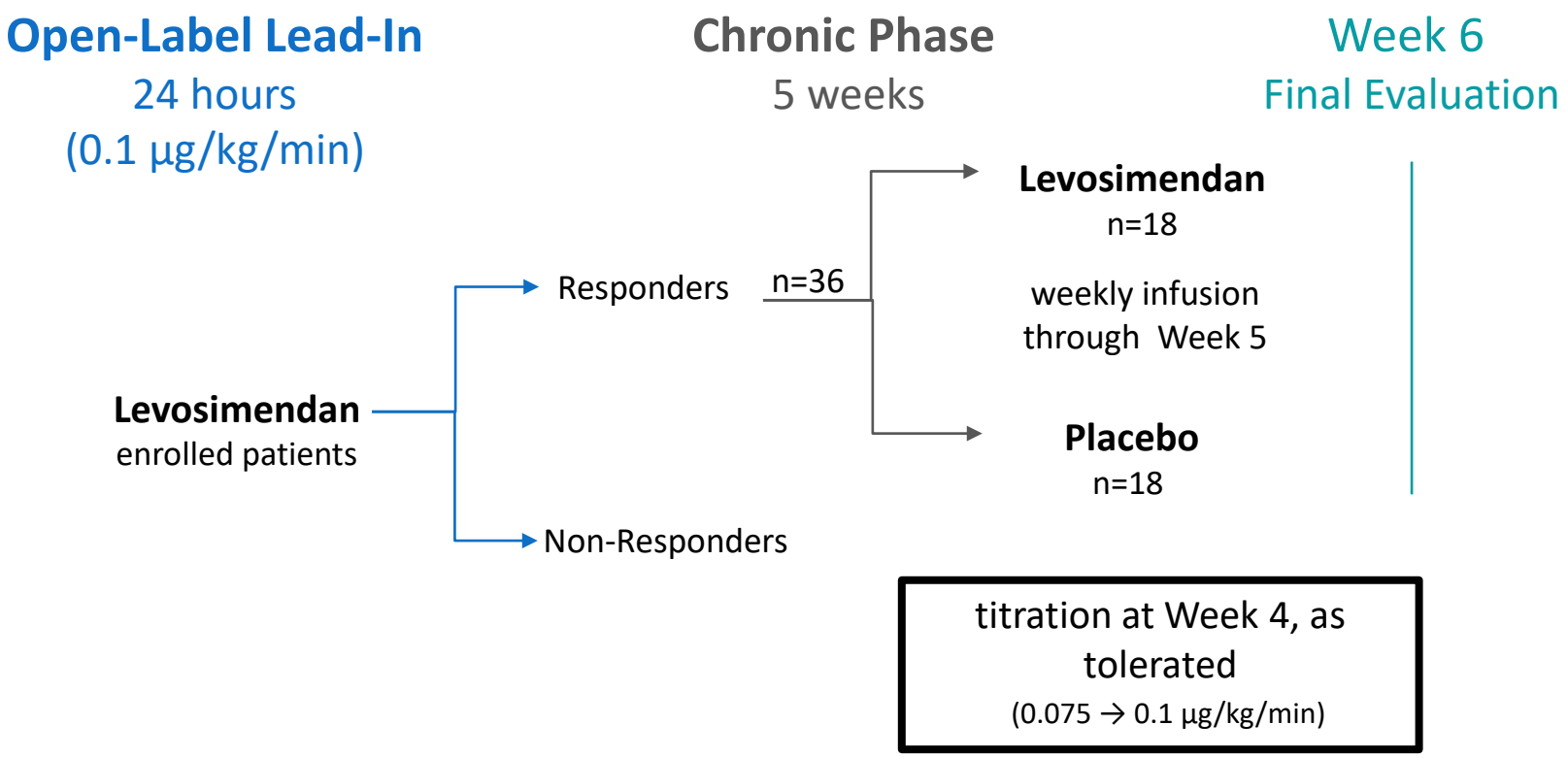
Pharmaceutical Sales >$5 billion in 2016 (primarily in Group 1)



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

Source: Company Annual Reports

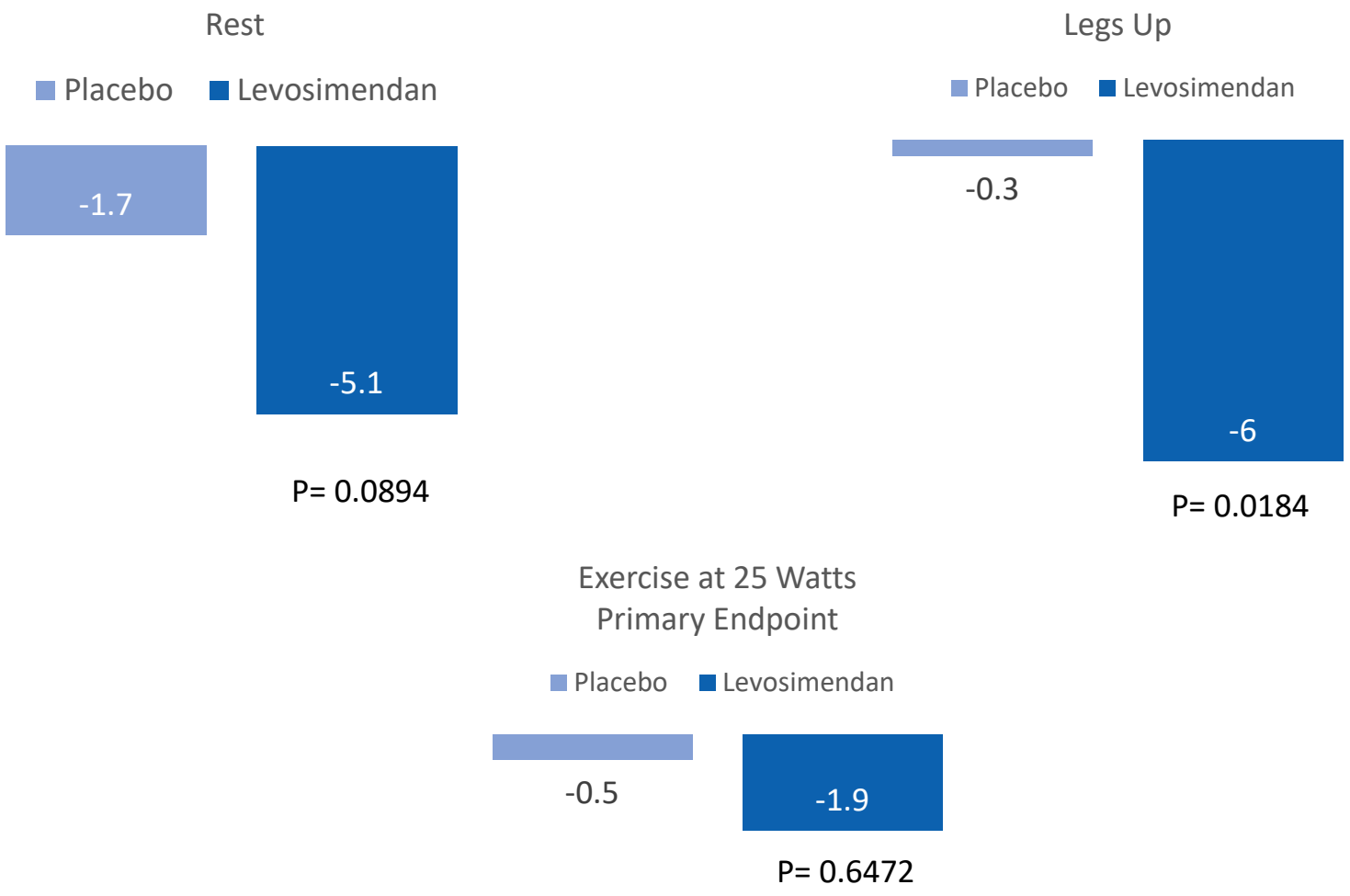
HELP Study Design



Baseline Characteristics

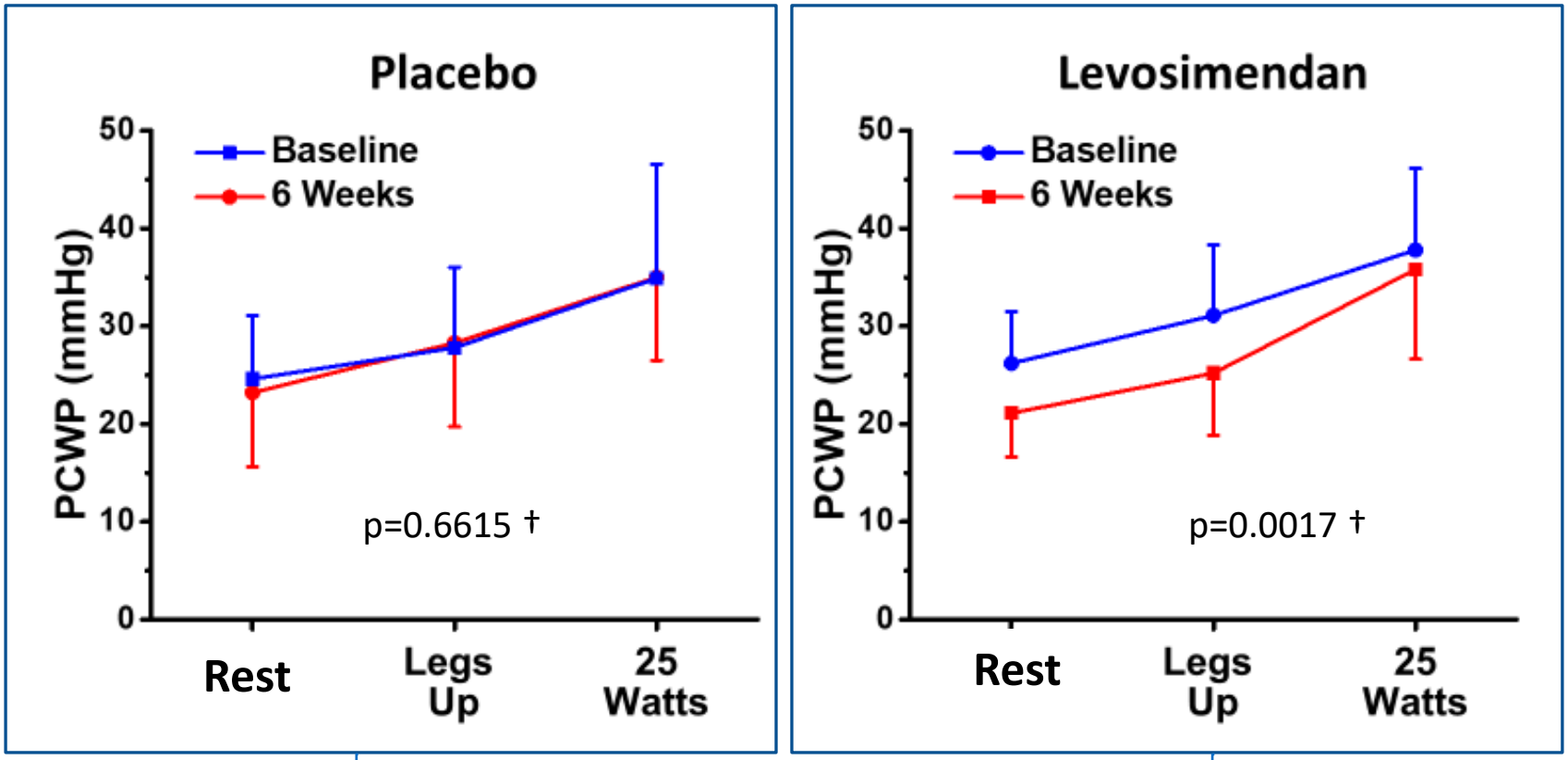
	Placebo n=18	Levosimendan n=18	p-value
Age, median (range), years	67.5 (43-81)	68.8 (54-80)	NS
< 65 % >=65 %	38.9 61.1	27.8 72.2	NS
Female sex, %	66.7	55.6	NS
White race, %	88.9	88.9	NS
Ethnicity (not hispanic or latino), %	100	94.4	NS
Body Mass Index, median (range), %	32.7 (22-52)	35.6 (23-57)	NS
Baseline Hemodynamics (exercise), median (range)			
Pulmonary Capillary Wedge Pressure (PCWP), mmHg	34.9 (14-55)	37.8 (23-53)	NS
Mean Pulmonary Arterial Pressure (mPAP), mmHg	55.1 (35-90)	57.4 (42-80)	NS
Pulmonary Vascular Resistance (PVR), dynes/sec/cm2	3.9 (-0.2-14.8)	3.1 (0.7-7.2)	NS
Right Atrial Pressure (RAP) , mmHg	27.4 (9-42)	27.7 (13-49)	NS
Cardiac Index (CO), L/min	3.0 (1.6-4.6)	3.5 (1.8-6.2)	NS
Right Ventricle Size (cm)	4.1 (2.9-5.6)	4.8 (3.5-6.2)	0.05
Baseline TAPSE (cm/s)	1.7 (1.0-2.4)	1.8 (1.35-2.5)	NS
6-min Walk Distance	282 (119-469)	290 (56-490)	NS

PCWP Change from Baseline at Week 6 Levosimendan vs Placebo



PCWP Endpoint

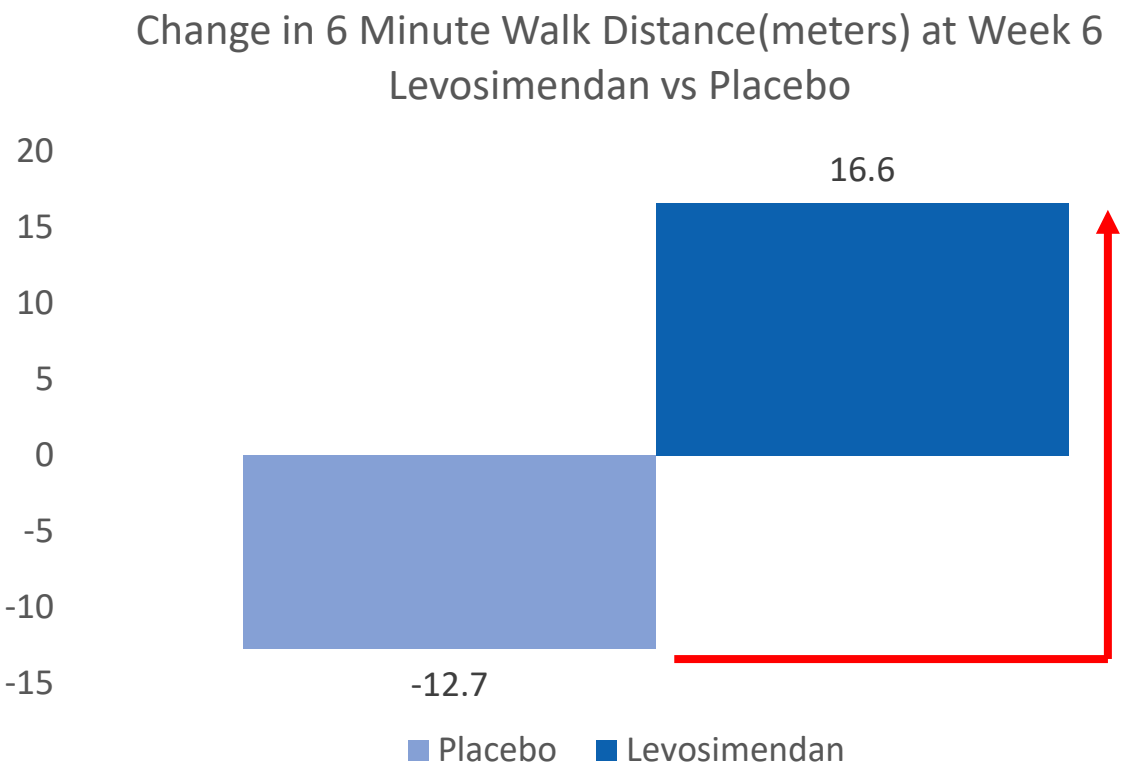
Baseline versus 6 Weeks



Levosimendan effect on PCWP across positions significant vs placebo

† Tested in a mixed effect model using treatments as factors and position as a random effect

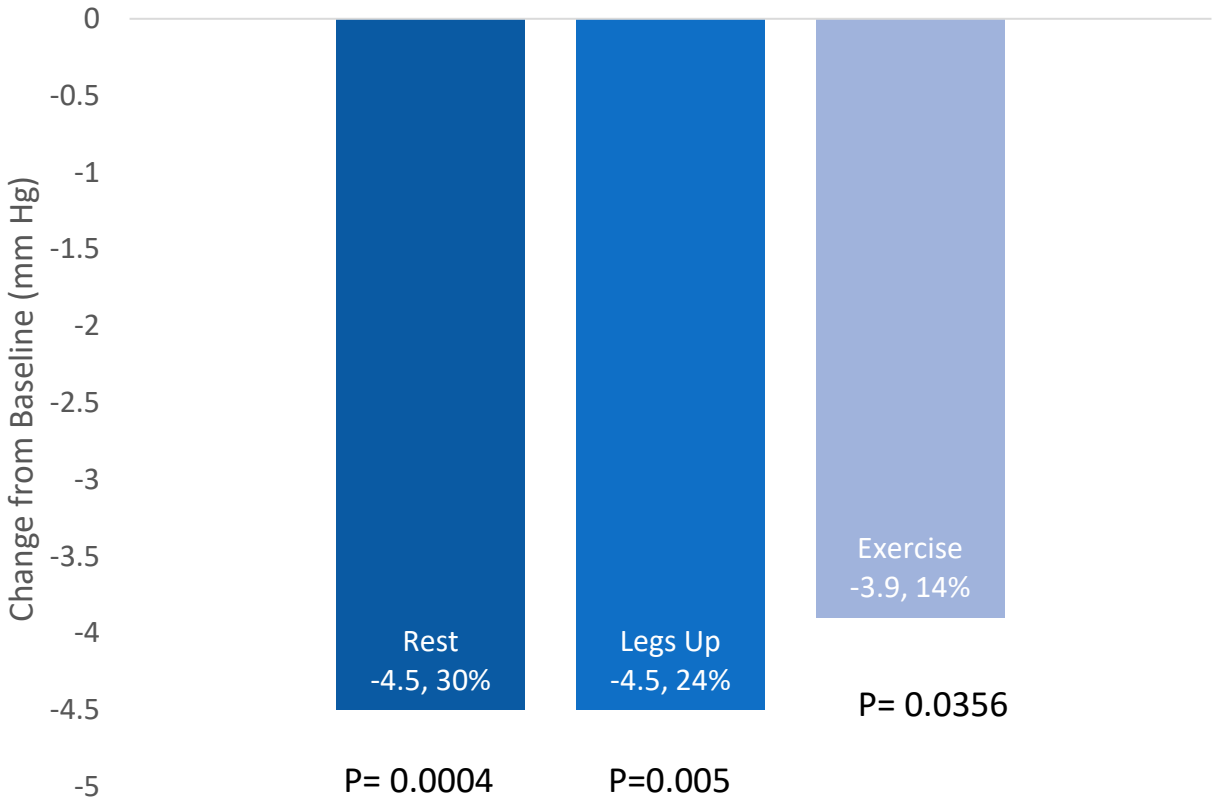
6 Minute Walk Change from Baseline Levosimendan vs Placebo



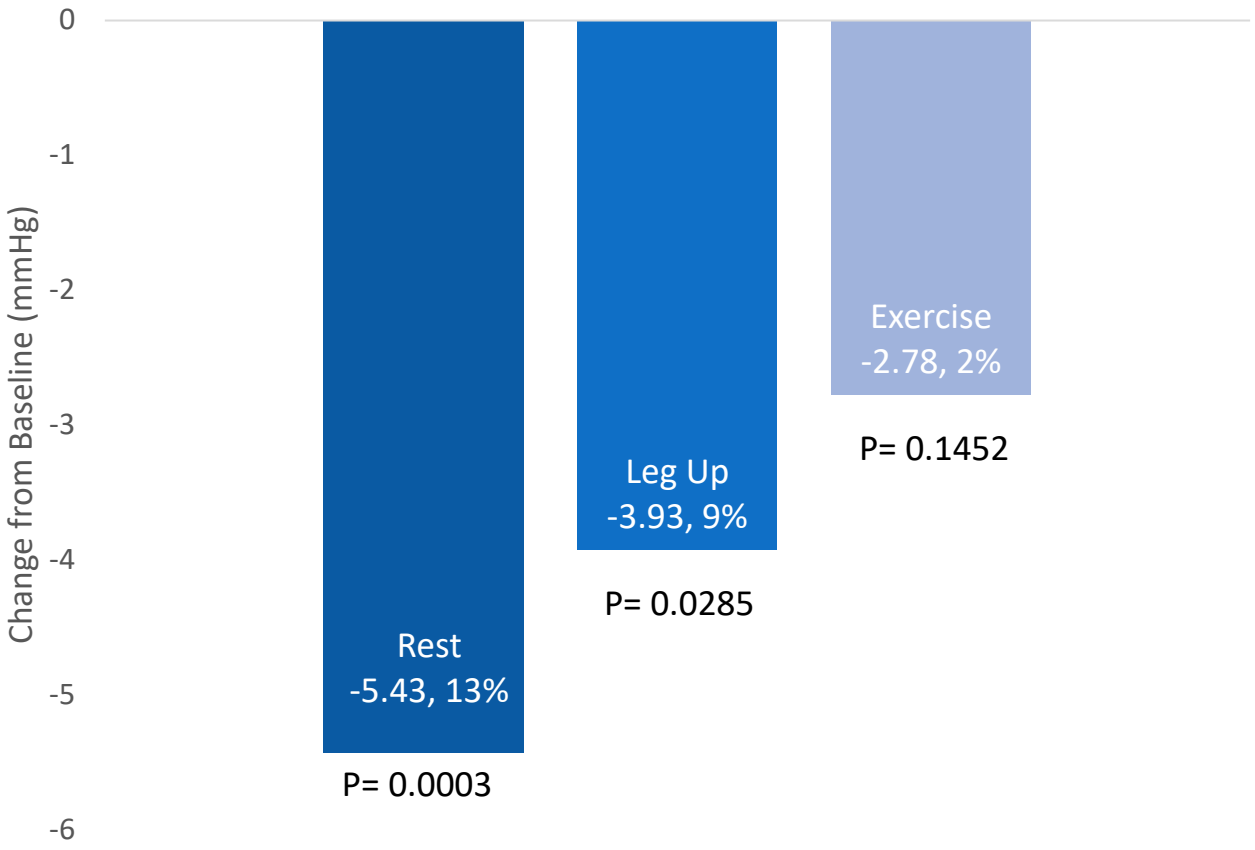
+29 Meters

Mean Diff	29.3
SE	13.14
95% CI	(2.5, 56.1)
p-value	**0.0329**

RAP Change from Baseline at Week 6 Levosimendan Treated Patients



mPAP Week 6
Levosimendan Change from Baseline



Treatment Emergent Adverse Events

	Placebo n=18	Levosimendan n=18
Any Treatment Emergent AEs (TEAEs)	8 (44%)	13 (72%)
TEAEs by Severity Mild Moderate Severe	 5 (28%) 2 (11%) 1 (6%)	 9 (50%) 2 (11%) 2 (11%)
Any Drug-Related TEAEs	5 (28%)	9 (50%)
TEAEs of Special Interest †	0	0
Serious TEAEs	1 (6%)	3 (17%)

† hypotension, atrial fibrillation, other significant arrhythmia, resuscitated death stroke

Treatment Emergent Adverse Events
(Incidence of 2 or more)

	Placebo n=18	Levosimendan n=18
Headache	1 (6%)	3 (17%)
Heart Rate Increased	0 (0%)	2 (11%)
Fatigue	2 (11%)	1 (6%)
Cardiac Failure Acute	1 (6%)	2 (11%)
Dyspnea	1 (6%)	2 (11%)
Vascular Access Site Pain	2 (11%)	0 (0%)
Muscle Spasms	0 (0 %)	2 (11%)
Hypokalaemia	1 (6%)	2 (11%)

Serious Adverse Events

Event on Levosimendan	Severity	Relatedness/ Change in Dose
Infections and Infestations, Device related infection	severe	not related, dose interrupted
Infections and Infestations, Bacteremia	moderate	not related, dose not changed
Cardiac disorders, Cardiac failure acute	mild	not related, dose not changed
Cardiac disorders, Cardiac failure acute	moderate	not related, dose not changed

HELP Study Topline Results Support Phase 3 Development in PH-HFpEF

1. **Evidence of levosimendan efficacy in PH-HFpEF**
   - Evidence of hemodynamic improvements with biventricular effects(PCWP,RAP,PAP)
   - Evidence of significant improvement in exercise performance, 6-Minute Walk
     - Statistically significant increase in 6-Minute Walk distance compared to placebo (29 meters, p=0.03)
2. **Evidence of Levosimendan safety and tolerability in PH-HFpEF**
   - AEs were few and limited to known events associated with the drug and disease
   - No adverse events of special clinical interest were identified
   - Serious adverse events were few, including infusion-related infection and events expected in the population (cardiac failure)
   - No arrhythmia concerns identified from cardiac monitoring
3. **Results provide strong rationale for Phase 3 PH-HFpEF Development**
   - Plan to publish/present data ASAP
   - Plan to schedule FDA End of Phase 2 Meeting
   - 6-Minute Walk response provides important reference for Phase 3 design/scope