KEROS THERAPEUTICS

KER-012 Update

August 8, 2023

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Statements contained in this presentation regarding matters that are not historical facts are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, as amended. Words such as "anticipates," "believes," "expects," "intends," "plans," "potential," "projects," "would" and "future" or similar expressions are intended to identify forward-looking statements. Examples of these forward-looking statements include statements concerning: Keros' expectations regarding its growth, strategy, progress and the design, objectives, expected results and timing of its preclinical studies and clinical trials for KER-050, KER-047, KER-012 and KER-065; and the potential of KER-012 to treat diseases such as pulmonary arterial hypertension without a dose-limiting red blood cell effect (including with respect to the TROPOS trial). Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. These risks and uncertainties include, among others: Keros' limited operating history and historical losses; Keros' ability to raise additional funding to complete the development and any commercialization of its product candidates; Keros' dependence on the success of its product candidates, KER-050, KER-047, KER-012 and KER-065; that Keros may be delayed in initiating, enrolling or completing any clinical trials; competition from third parties that are developing products for similar uses; Keros' ability to obtain, maintain and protect its intellectual property; and Keros' dependence on third parties in connection with manufacturing, clinical trials and preclinical studies.

These and other risks are described more fully in Keros' filings with the Securities and Exchange Commission ("SEC"), including the "Risk Factors" section of the Company's Quarterly Report on Form 10-Q, filed with the SEC on August 7, 2023, and its other documents subsequently filed with or furnished to the SEC. All forward-looking statements contained in this presentation speak only as of the date on which they were made. Except to the extent required by law, Keros undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

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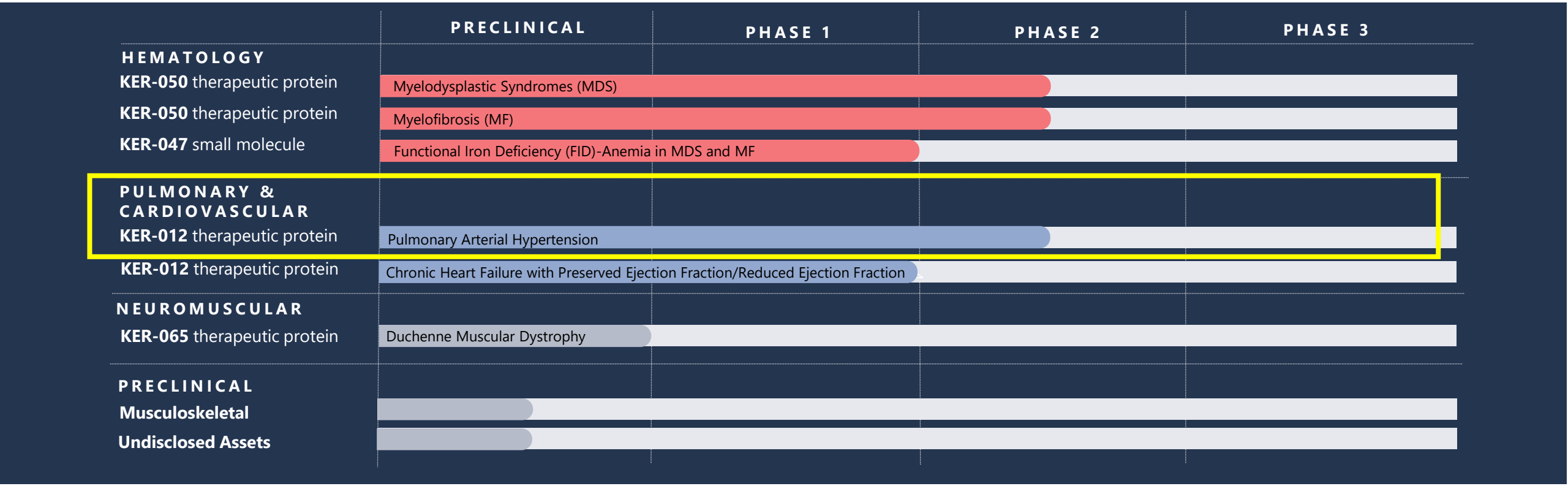
Agenda

Topic	Discussant(s)
Welcome and Introduction	Jasbir Seehra
PAH Overview and Unmet Medical Needs	Mardi Gomberg-Maitland
KER-012 Predicted MoA & Differentiation	Simon Cooper
KER012 Phase 2 PAH (TROPOS) Trial Rationale, Design	Mardi Gomberg-Maitland
Anticipated Key Milestone	Jasbir Seehra
Q&A	Open Panel
Closing Remarks & Adjourn	Jasbir Seehra

Focused on Transforming the Lives of Wide Range of Patients with Disorders Linked to Dysfunctional TGF-β superfamily signaling

Keros is a clinical-stage biopharmaceutical company
Developing potentially differentiated product candidates designed to alter transforming growth factor-beta (TGF-β) signaling and target pathways critical for the growth, repair and maintenance of a number of tissue and organ systems

We believe our product candidates have the potential to unlock the full therapeutic benefits of modulating the TGF-β superfamily and provide disease-modifying benefit to patients



Mardi Gomberg-Maitland, MD, MSC

TROPOS Steering Committee Chair

Director of the Pulmonary Hypertension Program at The George Washington University Heart and Vascular Institute.

Over 150 publications, including, *CHEST, Circulation, Circulation Heart Failure, European Respiratory Journal, Journal of American College of Cardiology (JACC), JACC Heart Failure, JAMA-Internal Medicine,* and the *New England Journal of Medicine*.

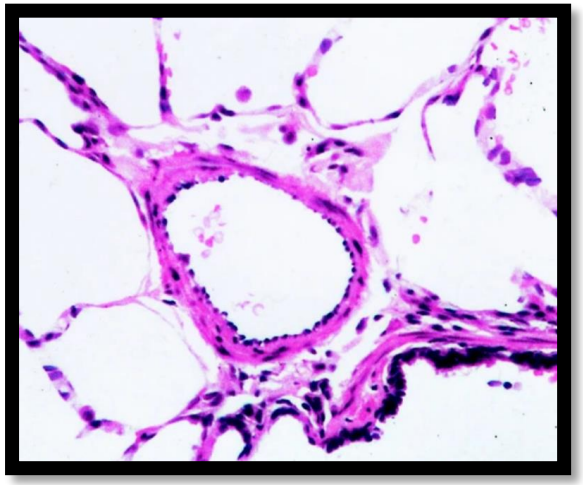
Past Chair of the Pulmonary Hypertension Council at the International Society of Heart and Lung Transplantation, Vice-Chair of the Education Committee at the International Society of Heart and Lung Transplantation, Section Editor at Journal of American College of Cardiology, and an Associate Editor at both CHEST and the European Respiratory Journal.

Pulmonary Arterial Hypertension Overview

PAH is Characterized by Vascular Remodeling and Dysfunction

Leads to Hemodynamic Abnormalities, Disease Progression, and Severe Morbidity

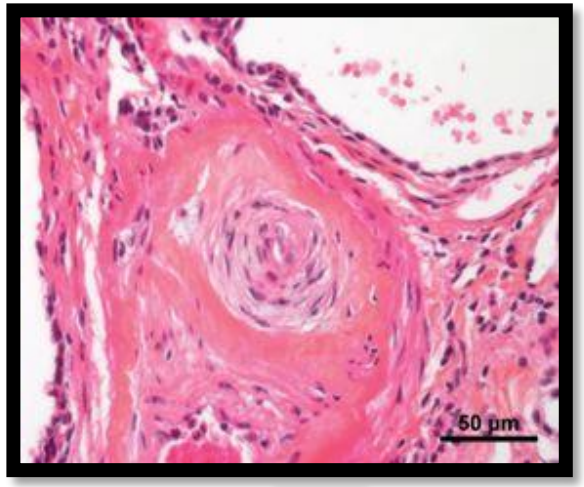
Normal/Healthy

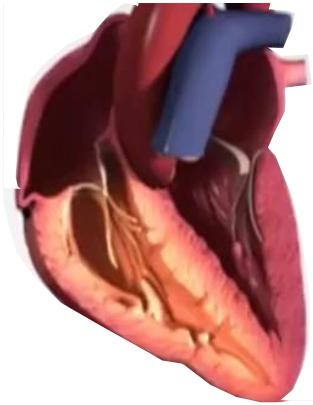


Vascular Smooth Muscle Pathology:

- Pulmonary Smooth Muscle & Endothelial Cell Proliferation
- Inflammation
- Vasoconstriction

PAH/Diseased





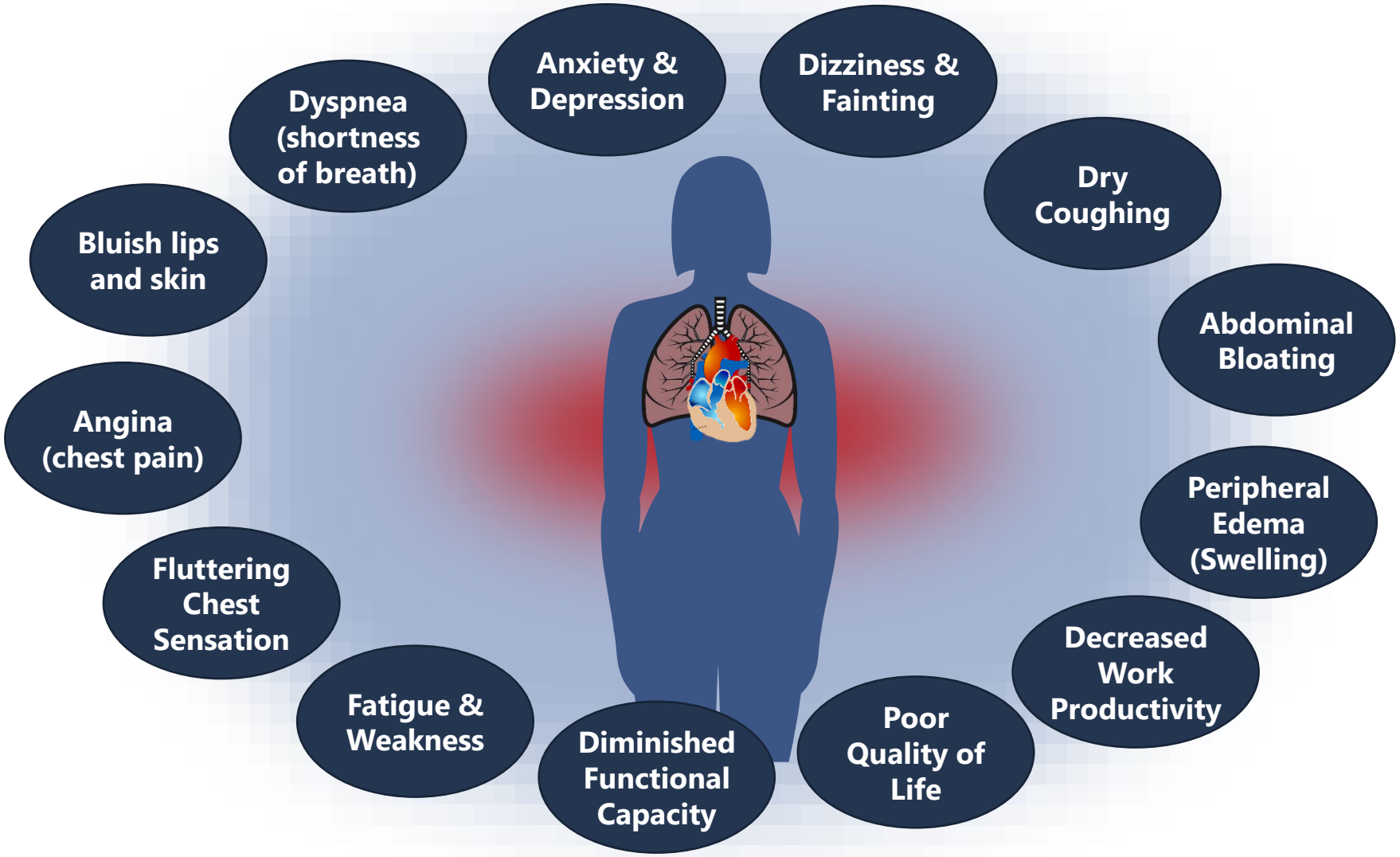
RV Remodeling & Failure

↑ mPAP ↑ PVR

Humbert M, et al. *Euro Resp J* 2019;53 (1801887) 1-14; mPAP=mean pulmonary arterial pressure; PVR=pulmonary vascular resistance ; RV=right ventricle

Pulmonary Arterial Hypertension is All Encompassing

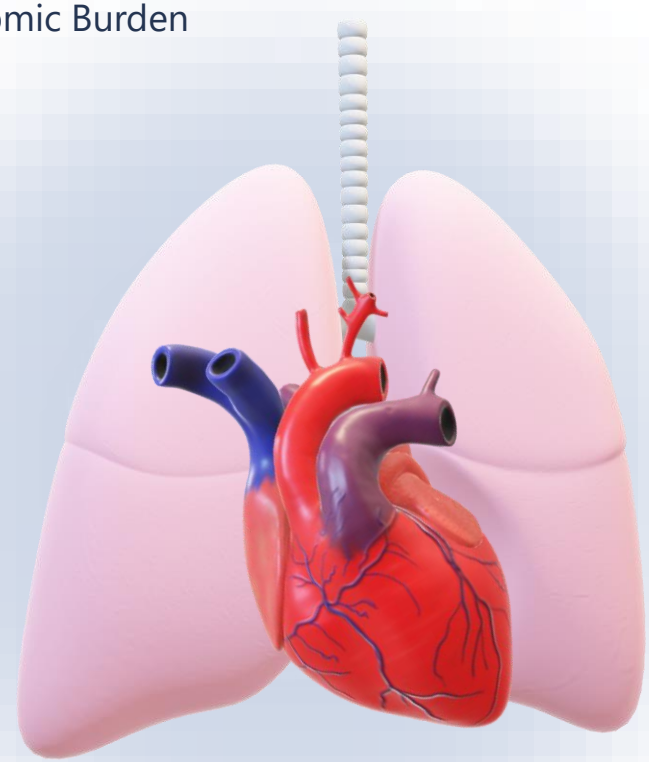
Symptoms and Complications Negatively Impact Most Aspects of Patients' Lives



Pulmonary Arterial Hypertension at a Glance

A Rare, Progressive and Debilitating Disease Resulting in Significant Health and Economic Burden

Epidemiology:	**~40,000 addressable PAH patients in U.S. (~59-81% Female[1])**	**Reported average age at diagnosis: 36-71 years[2]**
Cause & Prognosis:	**~50-60% idiopathic origin (U.S./Europe)[1]**	**Slightly above 50% survival at 5 years**



- **Current standard of care (SOC) for PAH is the use of drugs that promote vasodilation**
- **Currently available treatments do not correct the underlying biology**

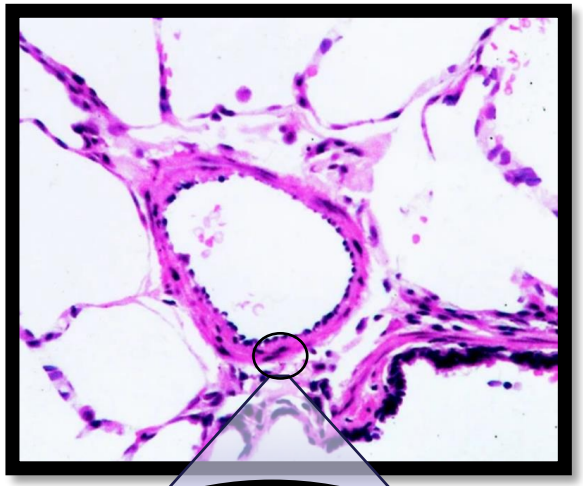
1. Hoeper MM, et al. *Lancet Resp Med* DOI:https://doi.org/10.1016/S2213-2600(15)00543-3; 2. Rothbard N, et al. *Cardiol J.* 2020; 27(2):184-193.

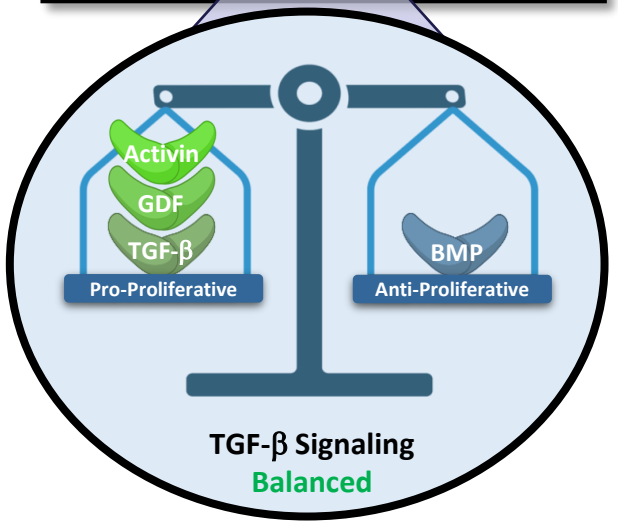
KER-012 MOA and Differentiation in PAH

PAH Pathophysiology and Disease Progression

Characterized by TGF-β Signaling Imbalance in Pulmonary Artery Vascular Wall (and Endothelial Cells)

Normal/Healthy

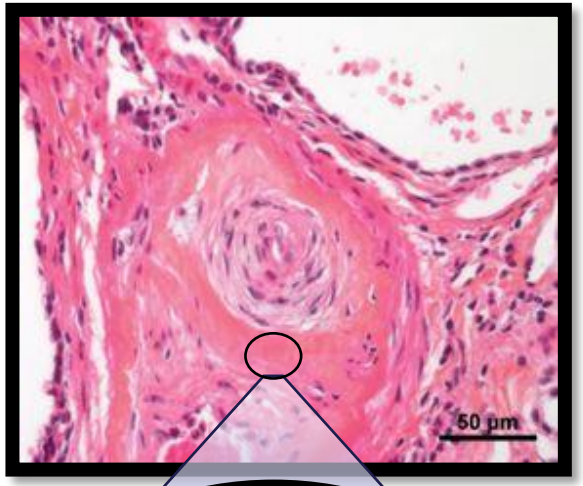


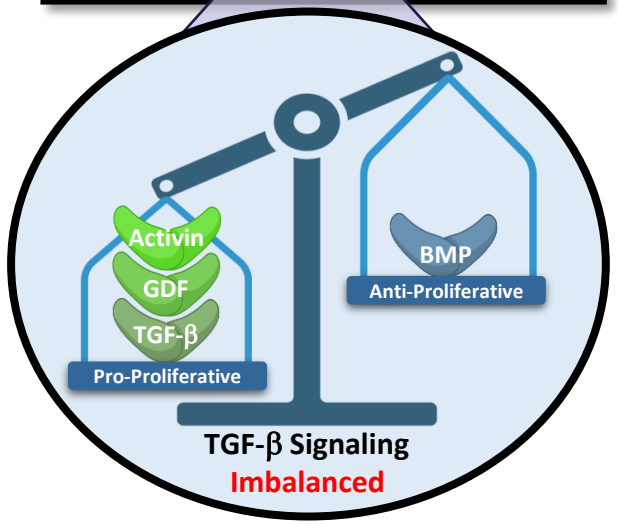


Vascular Smooth Muscle Pathology:
- Pulmonary Smooth Muscle & Endothelial Cell Proliferation
- Inflammation
- Vasoconstriction

Cellular Signaling Defects:
- Increased Activin Signaling
- Reduced BMP Signaling

PAH/Diseased

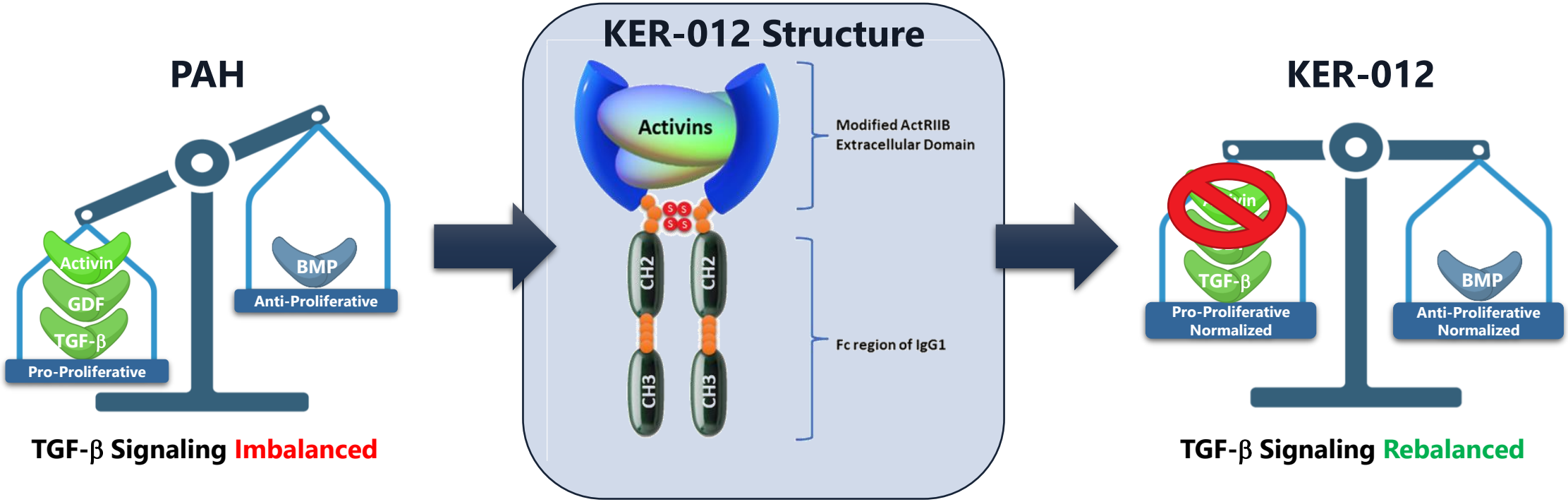




Humbert M, et al. *Euro Resp J* 2019;53 (1801887) 1-14; GDF=growth differentiation factors; BMP=bone morphogenic proteins

KER-012

A Novel, Investigational Activin Receptor Type IIB Ligand Trap



KER-012 is designed to inhibit select TGF-β superfamily ligands to:

- **Inhibit pro-proliferative activins and GDFs without increasing RBCs**
- **Spare BMP binding to permit anti-proliferative BMP signaling**

KER-012 vs. Native ActRIIA

In Vitro Binding Studies Support Comparable Activin/GDF Specificity and Greater BMP-Sparing of KER-012

***In Vitro* Ligand Binding Affinity**

Strong	Semi-Strong	Semi-Weak	Weak

	Activin/GDF Ligand Binding	
	ActRIIA-Fc	KER-012 (Modified ActRIIB-Fc)
Activin A	Strong	Strong
Activin B	Strong	Strong
Activin C	Weak	Weak
GDF-8	Strong	Strong
GDF-11	Strong	Strong

	BMP Ligand Binding	
	ActRIIA-Fc	KER-012 (Modified ActRIIB-Fc)
BMP-2	Semi-Weak	Weak
BMP-3	Weak	Weak
BMP-4	Semi-Weak	Weak
BMP-5	Strong	Semi-Strong
BMP-6	Strong	Weak
BMP-7	Strong	Semi-Strong
BMP-9	Semi-Weak	Weak
BMP-10	Strong	Strong

- **KER-012 affinity for SMAD2/3 ligands is comparable to ActRIIA**
- **KER-012 had lower affinity for multiple BMPs compared to ActRIIA**

Gudelsky A et al American Thoracic Society 2023 Annual Meeting. Am J Respir Crit Care Med 2023;207:A378

KER-012 vs. Native ActRIIA

In Vitro Binding Studies Support Comparable Activin/GDF Specificity and Greater BMP-Sparing of KER-012

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Strong	Semi-Strong	Semi-Weak	Weak

	Activin/GDF Ligand Binding	
	ActRIIA-Fc	KER-012 (Modified ActRIIB-Fc)
Activin A	Strong	Strong
Activin B	Strong	Strong
Activin C	Weak	Weak
GDF-8	Strong	Strong
GDF-11	Strong	Strong

	BMP Ligand Binding	
	ActRIIA-Fc	KER-012 (Modified ActRIIB-Fc)
BMP-2	Semi-Weak	Weak
BMP-3	Weak	Weak
BMP-4	Semi-Weak	Weak
BMP-5	Strong	Semi-Strong
BMP-6	Strong	Weak
BMP-7	Strong	Semi-Strong
BMP-9	Semi-Weak	Weak
BMP-10	Strong	Strong

- **KER-012 affinity for SMAD2/3 ligands is comparable to ActRIIA**
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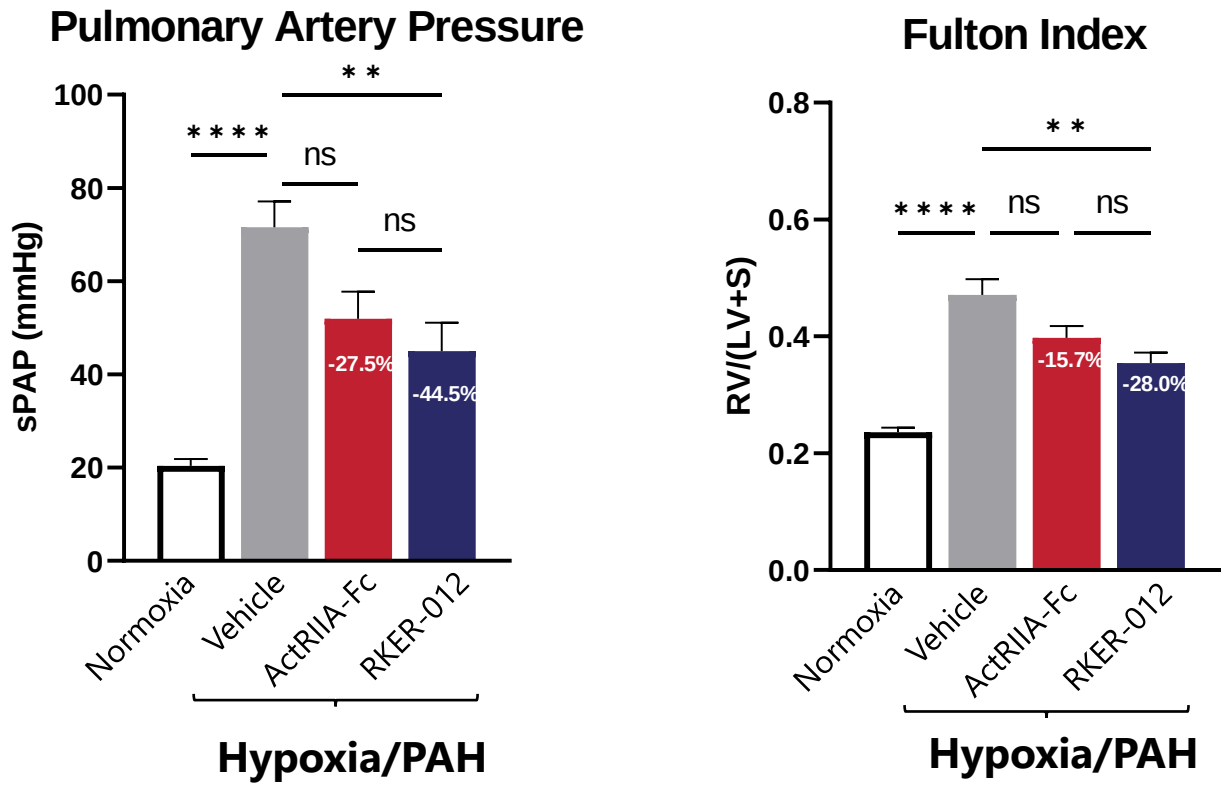
Gudelsky A et al American Thoracic Society 2023 Annual Meeting. Am J Respir Crit Care Med 2023;207:A378

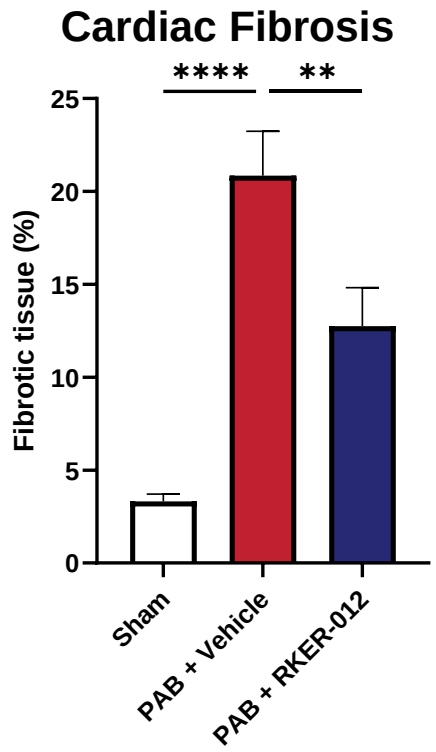
RKER-012 Preclinical Data

Reduced Pulmonary Arterial Pressure, Right Ventricle Hypertrophy, and Cardiac Fibrosis Observed in Rodent PAH Models

Sugen-Hypoxia Model of PAH[1]



Pulmonary Artery Banding[2] (Direct Cardiac Effects)



One way ANOVA followed by Sidak post-hoc test. Ns – not significant, * p ≤ 0.05, ** p ≤ 0.01, *** p ≤ 0.001, **** p ≤ 0.0001. Percent change compared to hypoxia + vehicle rats.

1. K. Babbs, et al. Am J Respir Crit Care Med 2022;205:A5776; 2. Babbs K, et al. Am Heart Association Scientific Sessions 2021; RKER-012 = Research KER-012 fused with Fc region of murine IgG1

Observed KER-012 Profile Supports Therapeutic Rationale in PAH

- Keros completed a randomized, double-blind, placebo-controlled, two-part Phase 1 clinical trial to evaluate single and multiple ascending doses of KER-012 in healthy volunteers.
  - The primary objectives of this trial were safety, tolerability and pharmacokinetics.

PAH Domain	Preclinical Data	Phase 1 Clinical Trial[1,2]
 **MOA & Ligand Specificity:**	• Strong activin/GDF binding observed • Observed to be BMP-sparing vs. ActRIIA-Fc	• We believe PD data support potential for maximal target engagement with doses in Phase 2
 **Fibrosis & Inflammation:**	↓ Inflammation ↓ Fibrosis	↓ Pro-inflammatory biomarkers ↑ Anti-inflammatory biomarkers ↓ Pro-fibrotic biomarkers ↑ Anti-fibrotic biomarkers
 **CV & Hemodynamics:**	↓ Smooth muscle hypertrophy ↓ PAP ↓ RVH ↓ Cardiac fibrosis (direct) ↓ Ventricular dysfunction biomarkers	↓ Ventricular dysfunction biomarkers ↓ Remodeling biomarkers
 **Erythropoiesis (Hb/RBCs):**	No increase observed	No clinically meaningful changes observed
 **Safety & Tolerability:**	N/A	• Generally well tolerated up to 4.5 mg/kg (multiple doses) in Part 2 of the trial • AEs generally mild

1. Natarajan H., et al. American Society for Bone and Mineral Research 2022 Annual Meeting; 2. Natarajan H., et al. 2023 American Thoracic Society International Conference; PAP=pulmonary arterial pressure; RVH=right ventricular hypertrophy

Rationale of TROPOS Trial in PAH

Mardi Gomberg-Maitland, MD, MSc

George Washington University School of Medicine and Health Sciences

Targeting the TGF-β Superfamily in PAH

Phase 3 STELLAR Trial Presented at American College of Cardiology 2023 Scientific Sessions

- Sotatercept is an investigational activin receptor IIA-Fc (native ActRIIa fused to Fc region of IgG1) ligand trap
- A third-party Phase 3 clinical trial of sotatercept[1] demonstrated the importance of the TGF-β superfamily in patients with PAH
  - Improved 6-minute walking distance (6MWD) along with hemodynamics, biomarkers, World Health Organization Functional Class, Risk Scores, delayed time to clinical worsening, and improved 2 of 3 quality of life domains was reported in this trial[1]
  - Adverse events that occurred more frequently with sotatercept than with placebo in that Phase 3 trial included increased hemoglobin levels, epistaxis and telangiectasia[1]

1. Hoeper M, et al. *New Eng J Med* 2023; 388 (16):1478-90

Sotatercept Dosing in PAH Limited Due to On-Target AEs

Doses between 0.3 mg/kg and 0.7 mg/kg administered every 21 days

- **Maximum dose in PAH limited to 0.7 mg/kg in the clinical trial due to increased hemoglobin observed in earlier-phase clinical trials[1,2]**

Sherman et al 2013 (Phase 1)

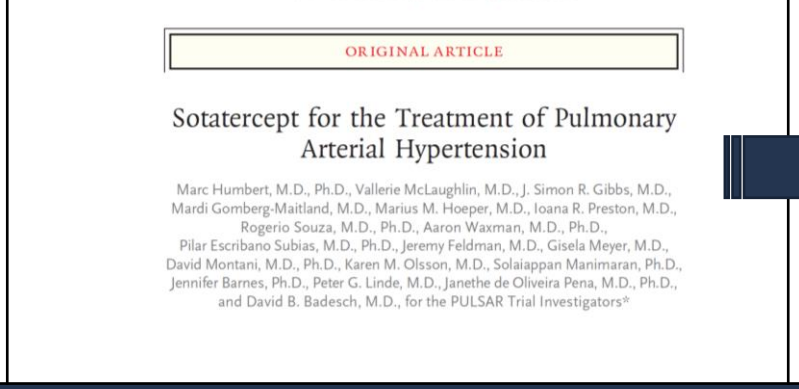
Pharmacokinetics and Pharmacodynamic

Multiple-Dose, Safety, Pharmacokinetic, and Pharmacodynamic Study of Sotatercept (ActRIIA-IgG1), a Novel Erythropoietic Agent, in Healthy Postmenopausal Women

The Journal of Clinical Pharmacology 53(11) 1121–1130 © 2013, The American College of Clinical Pharmacology DOI: 10.1002/jcph.160

Matthew L. Sherman, MD[1], Niels G. Borgstein, MD[1], Louisa Mook, MD[1], Dawn Wilson, BS[1], Yijun Yang, ScD[1], Nianhang Chen, PhD[2], Ravindra Kumar, PhD[1], Kenneth Kim, MD[3], and Abderrahmane Laadem, MD[2]

Humbert et al 2021 (Phase 2 PAH)



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Sotatercept for the Treatment of Pulmonary Arterial Hypertension

Marc Humbert, M.D., Ph.D., Vallerie McLaughlin, M.D., J. Simon R. Gibbs, M.D., Mardi Gomberg-Maitland, M.D., Marius M. Hoeper, M.D., Ioana R. Preston, M.D., Rogerio Souza, M.D., Ph.D., Aaron Waxman, M.D., Ph.D., Pilar Escribano Subias, M.D., Ph.D., Jeremy Feldman, M.D., Gisela Meyer, M.D., David Montani, M.D., Ph.D., Karen M. Olsson, M.D., Solaiappan Manimaran, Ph.D., Jennifer Barnes, Ph.D., Peter G. Linde, M.D., Janethe de Oliveira Pena, M.D., Ph.D., and David B. Badesch, M.D., for the PULSAR Trial Investigators*

Cappellini et al 2019 (Phase 2 β-thalassemia)

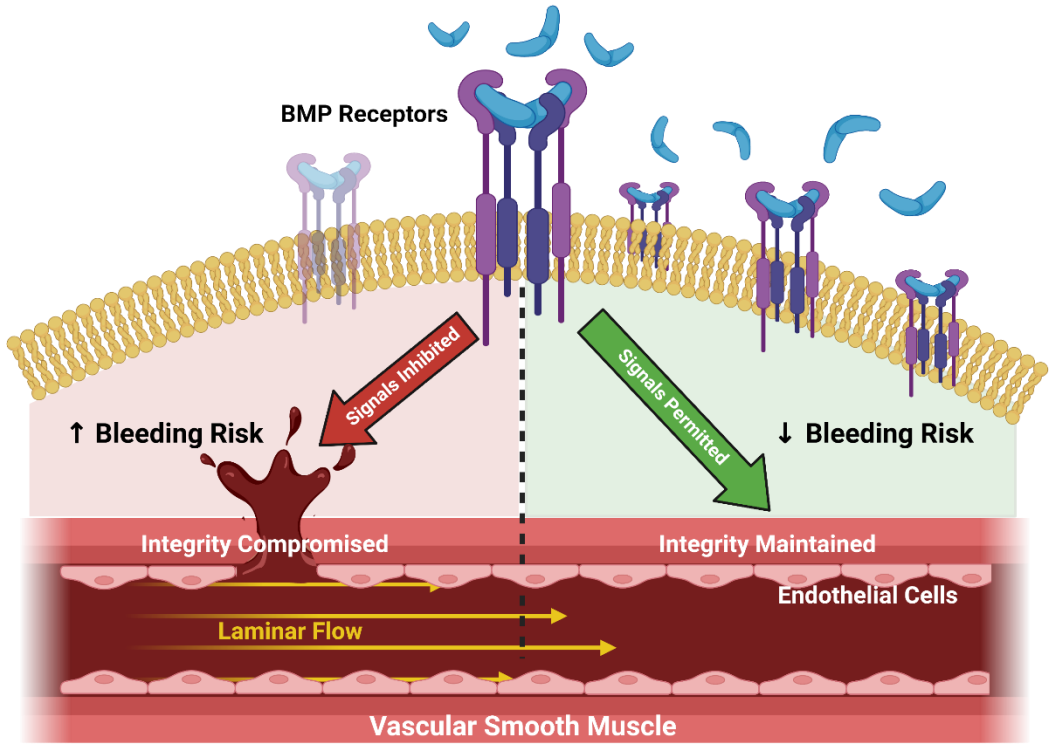
Sotatercept, a novel transforming growth factor β ligand trap, improves anemia in β-thalassemia: a phase II, open-label, dose-finding study

Maria Domenica Cappellini,[1] John Porter,[2] Raffaella Origa,[3] Gian Luca Forni,[4] Ersi Voskaridou,[5] Frédéric Galactéros,[6] Ali T. Taher,[7] Jean-Benoît Arlet,[8,9,10] Jean-Antoine Ribeil,[11] Maciej Garbowski,[2] Giovanna Graziadei,[1] Chantal Brouzes,[11] Michaela Semeraro,[11] Abderrahmane Laadem,[12] Dimana Miteva,[13] Jun Zou,[12] Victoria Sung,[14] Tatiana Zinger,[13] Kenneth M. Attie[15] and Olivier Hermine[9,10,16]

[1]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Department of Clinical

1. Sherman et al 2013 *J. Clin Pharmacol* 53(11) 1121–1130; 2. Humbert M et al, *New Engl J Med* 2023; 384:1204-15; 3. Cappellini MD et al. *Haematologica* 2019; 104(3) 477-484

Loss of BMP Signaling Impairs Endothelial Function and Vascular Integrity



REPORT

BMP9 Mutations Cause a Vascular-Anomaly Syndrome with Phenotypic Overlap with Hereditary Hemorrhagic Telangiectasia

Whitney L. Wooderchak-Donahue,[1] Jamie McDonald,[2] Brendan O'Fallon,[1] Paul D. Upton,[3] Wei Li,[3] Beth L. Roman,[4] Sarah Young,[4] Parker Plant,[1] Gyula T. Fülöp,[5,6] Carmen Langa,[5,6] Nicholas W. Morrell,[3] Luisa M. Botella,[5,6] Carmelo Bernabeu,[5,6] David A. Stevenson,[7] James R. Runo,[8] and Pinar Bayrak-Toydemir[1,2,*]

530 The American Journal of Human Genetics *93*, 530–537, September 5, 2013

Defective fluid shear stress mechanotransduction mediates hereditary hemorrhagic telangiectasia

Nicolas Baeyens,[1,2*] Bruno Larrivée,[1,2,3*] Roxana Ola,[1,2] Brielle Hayward-Piatkowskyi,[1,2] Alexandre Dubrac,[1,2] Billy Huang,[1,2] Tyler D. Ross,[1,2] Brian G. Coon,[1,2] Elizabeth Min,[1,2] Maya Tsarfati,[1,2] Haibin Tong,[1,2,4] Anne Eichmann,[1,5**] and Martin A. Schwartz[1,6,7**]

The Rockefeller University Press $30.00
J. Cell Biol. Vol. 214 No. 7 807–816
www.jcb.org/cgi/doi/10.1083/jcb.201603106

- **BMP-sparing ligand trap has the potential to reduce bleeding risk**

TROPOS is a Global Phase 2 Clinical Trial in PAH

A Randomized, Phase 2, Double-blind, Placebo-controlled Trial to Investigate the Safety and Efficacy of KER-012 in Combination with Background Therapy in Adult Participants with Pulmonary Arterial Hypertension

TROPOS study

Planning for ~60 sites

Key Eligibility Criteria for Participation

Adult patients ≥ 18 years of age.

Primary diagnosis of symptomatic PAH (WHO Group 1) in subgroups:

- Idiopathic
- Heritable
- Drug or toxin-induced
- PAH associated with:
  - Connective tissue disease,
  - Congenital systemic-pulmonary intracardiac shunt
- Hemodynamic parameters consistent with PAH diagnosis:
  - Mean pulmonary arterial pressure (mPAP) > 20 mmHg at rest, AND
  - Pulmonary artery wedge pressure (PAWP) ≤ 15 mmHg, AND
  - Pulmonary vascular resistance (PVR) ≥ 5 Wood Units (400 dyn·sec·cm−5).

WHO/NYHA FC II or III symptoms

Stable PAH-specific background therapy (ERA/PDE5-I/sGC stimulator/prostacyclin analogue or receptor agonist).

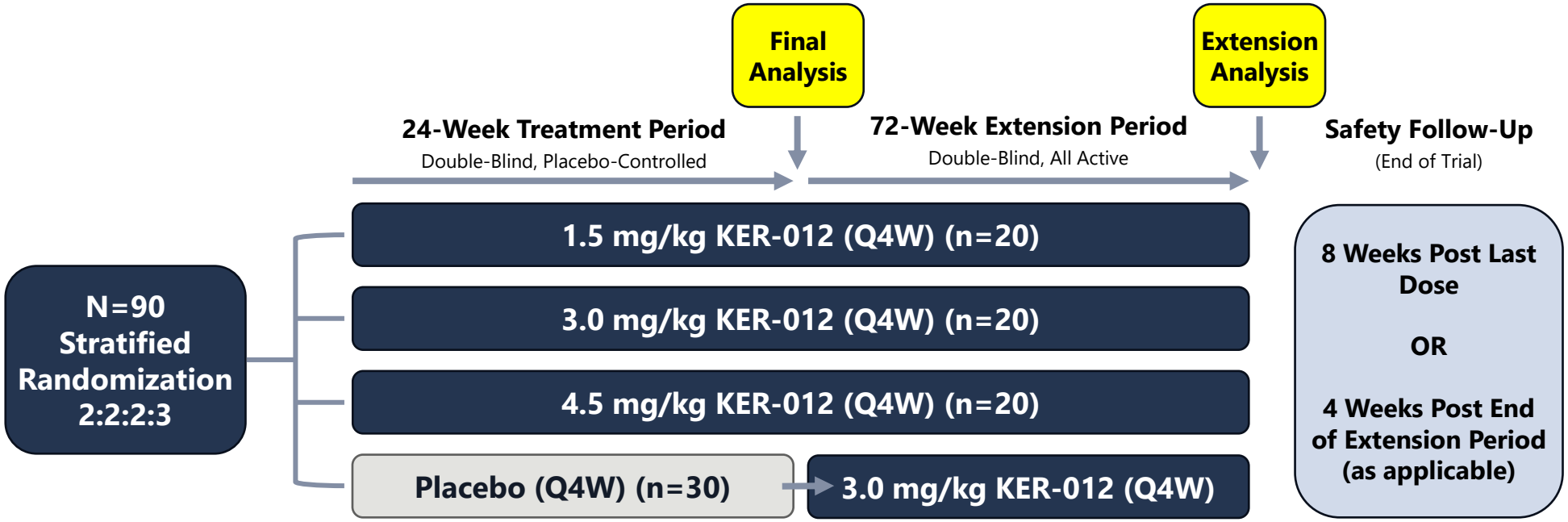
Six-minute walk distance (6MWD) ≥ 150 and ≤ 500 meters

- Note: Right-heart catheterization will be performed during Screening

Key Exclusion Criteria

- Evidence or history of left ventricular dysfunction and/or clinically significant cardiac disease
- Has pulmonary function tests (PFTs) with evidence of significant obstructive or parenchymal lung disease
- Evidence of thromboembolic disease assessed by ventilation perfusion (V/Q) lung scan or other local standard of care diagnostic evaluation at the time of PAH diagnosis or after
- Has uncontrolled systemic hypertension
- Hemoglobin < 9 g/dL at screening
- Prior heart or heart-lung transplants, active on the lung transplant list, or life expectancy of < 12 months per Investigator assessment
- Diagnosis of pulmonary veno-occlusive disease or pulmonary capillary hemangiomatosis
- Initiation or discontinuation of an exercise program for cardiopulmonary rehabilitation within 90 days prior to baseline or planned initiation during the study
- Prior participation in a KER-012 study or prior treatment with a therapy targeting TGF-β superfamily (e.g. sotatercept)
- Prior participation in another interventional clinical study with medicinal products within 30 days or 5 half-lives prior to screening, whichever is longer.

TROPOS Trial Design



Approximately 90 patients diagnosed with PAH and on stable PAH background therapy will be randomized and assigned in a 2:2:2:3 ratio to the 1.5 mg/kg, 3.0 mg/kg, and 4.5 mg/kg KER-012 doses and placebo treatment arms.

TROPOS Primary & Key Secondary Objective & Endpoint

Pooled-Arm KER-012 Hemodynamics and Exercise Capacity Evaluated vs. Placebo over a 24-week Treatment Period

Primary Objective	Primary Endpoint
To evaluate the **effect** of KER-012 **on hemodynamics** compared to placebo in participants on background PAH therapy	Change from baseline in pulmonary vascular resistance (PVR) at Week 24
Key Secondary Objective	**Key Secondary Endpoint**
To evaluate the **effect** of KER-012 **on exercise capacity** compared to placebo in participants on background PAH therapy	Change from baseline in 6MWD at Week 24

TROPOS Secondary Objectives and Endpoints

Evaluated vs. Placebo over a 24-week Treatment and 72-week Extension Period

Secondary Objective	Secondary Endpoint
To evaluate the **safety and tolerability** of KER-012	Incidence of treatment-emergent AEs, treatment related AEs and discontinuation due to AEs; change from baseline in clinical lab values, vital signs and ECG; Incidence of ADA
To evaluate the effects of KER-012 on **hemodynamics**	Change from baseline in mPAP, CO, CI, PAWP, mRAP, SvO2, SV, SVI and PAC at Week 24 and Week 96
To evaluate the **effects** of KER-012 on **NT-proBNP**	Change from baseline in NT-proBNP by visit
To evaluate improvement **in functional class** of KER-012 compared to placebo	Proportion of participants who achieved improvement from baseline in NYHA FC/WHO by visit

ECG=electrocardiogram; CO=carbon monoxide; CI=cardiac index; mRAP=; Sv02=venous oxygen saturation;SV=stroke volume; SVI=stroke volume index; PAC=premature atrial contractions; NT-proBNP=n-terminal pro-b-type natriuretic peptide

TROPOS Exploratory Objectives and Endpoints

Evaluated vs. Placebo over a 24-week Treatment and 72-week Extension Period

Exploratory Objectives	Exploratory Endpoints
To evaluate **physical activity**	Change from baseline in overall activity as measured by actigraphy
To evaluate **improvement in additional risk stratification measures**	Proportion of patients who achieve improvement in REVEAL Lite 2 and COMPERA 2.0 by visit
To evaluate the effect of KER-012 **on clinical worsening**	Incidence of and time to first clinical worsening
To evaluate the **PD effect** of KER-012 **on biomarkers**	Change from baseline in PAH-related biomarkers and other biomarkers by visit
To evaluate the **HRQoL**	Change from baseline in HRQoL measures by visit (PAH-SYMPACT and emPHasis-10)

HRQoL=health-related quality of life

Anticipated Key Milestones

- **KER-050**
  - Complete enrollment in transfusion-dependent cohorts in Phase 2 MDS trial — H2 2023
  - Announce additional data from Part 2 of Phase 2 MDS trial — H2 2023
  - Announce dose escalation data from Phase 2 MF trial — H2 2023
  - Initiate Part 2 of Phase 2 MF trial — H2 2023
- **KER-047**
  - Announce initial data from Phase 2 FID (MDS and MF) trial — H1 2024
- **KER-012**
  - Initiate Phase 2 open-label biomarker trial in patients with chronic heart failure with preserved ejection fraction and in such patients with reduced ejection fraction — H2 2023
- **KER-065**
  - Commence Phase 1 healthy volunteer trial — Q1 2024

Questions & Answers