UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): August 7, 2023

Keros Therapeutics, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**001-39264**	**81-1173868**
(state or other jurisdiction of incorporation)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**

1050 Waltham Street, Suite 302
Lexington, Massachusetts **02421**
(Address of principal executive offices) **(Zip Code)**

Registrant's telephone number, including area code: (617) 314-6297

Not applicable

(Former name or former address, if changed since last report.)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol	Name of each exchange on which registered
Common Stock, $0.0001 par value per share	**KROS**	**The Nasdaq Stock Market LLC**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On August 7, 2023, Keros Therapeutics, Inc. (the "Company") updated its corporate presentation for use in meetings with investors, analysts and others. The presentation is available through the Company's website and a copy is attached as Exhibit 99.1 to this Current Report on Form 8-K.

The information under Item 7.01 in this Current Report on Form 8-K, including Exhibit 99.1 attached hereto, is being furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act") or otherwise subject to the liabilities of that section. Such information and the accompanying Exhibit 99.1 are not incorporated by reference in any filing of the Company under the Securities Act of 1933, as amended, or the Exchange Act, whether made before or after the date hereof, regardless of any general incorporation language in such filing, except as shall be expressly set forth by specific reference in such filing.

Item 8.01 Other Events.

During a conference call and webcast scheduled to be held at 8:00 a.m. Eastern time on August 8, 2023, the Company's management will provide an overview of TROPOS, its global Phase 2 clinical trial to evaluate KER-012 in combination with background therapy in patients with pulmonary arterial hypertension. A copy of the presentation for the conference call and webcast is attached as Exhibit 99.2 to this Current Report on Form 8-K and is incorporated by reference herein.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Corporate Presentation dated August 2023.
99.2	Investor Presentation dated August 2023.
104	Cover Page Interactive Data File (the cover page XBRL tags are embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

KEROS THERAPEUTICS, INC.

By: /s/ Jasbir Seehra
Jasbir Seehra, Ph.D.
Chief Executive Officer

Dated: August 7, 2023


KEROS
THERAPEUTICS
Corporate Presentation
August 2023

Disclaimer

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 Keros' proprietary discovery approach. 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.

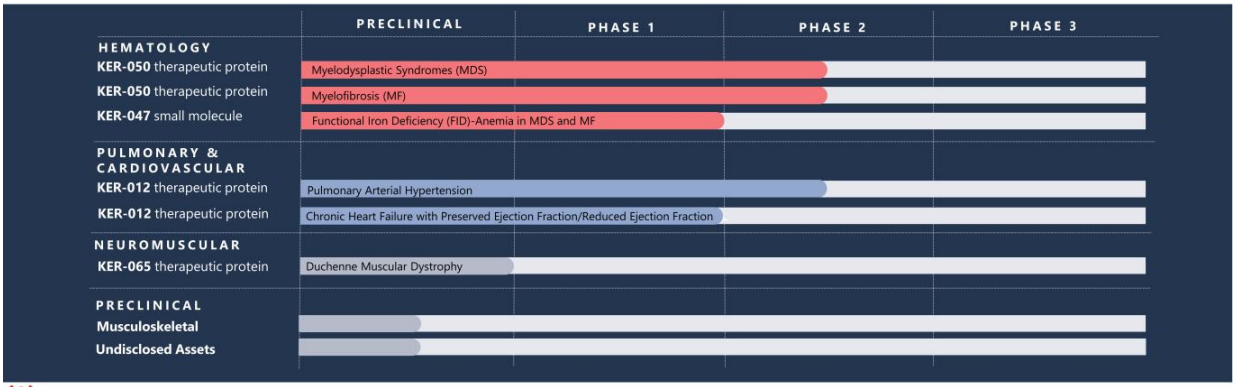
Certain information contained in this presentation relates to or is based on studies, publications, surveys and other data obtained from third-party sources and the Company's own internal estimates and research. While we believe these third-party sources to be reliable as of the date of this presentation, it has not independently verified, and makes no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third -party sources. Finally, while we believe our own internal research is reliable, such research has not been verified by any independent source.

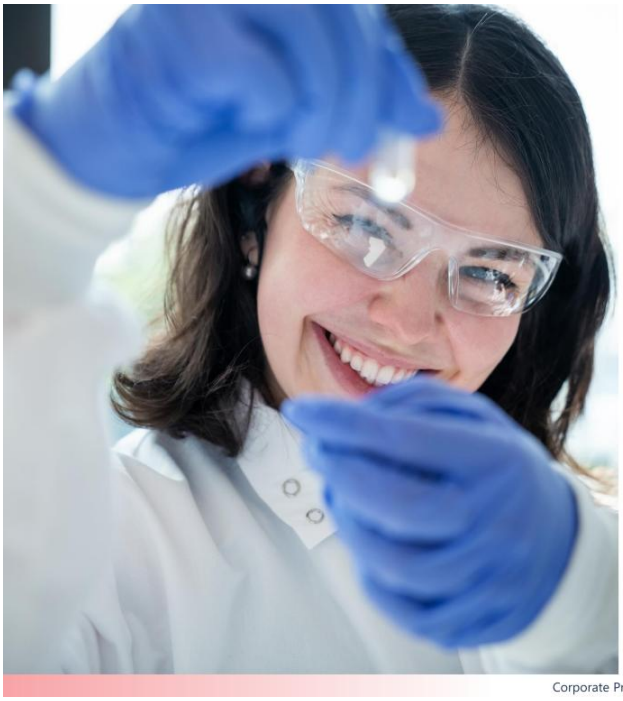
The trademarks included in this presentation are the property of the owners thereof and are used for reference purposes only.

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





Hematology Franchise

TGF-β Superfamily Plays a Critical Role in the Maintenance of the Bone Marrow Microenvironment

Hematopoiesis, the process by which blood cells are produced in the bone marrow, requires the coordinated control of cell division, differentiation and production of the specialized cellular machinery for each cell type

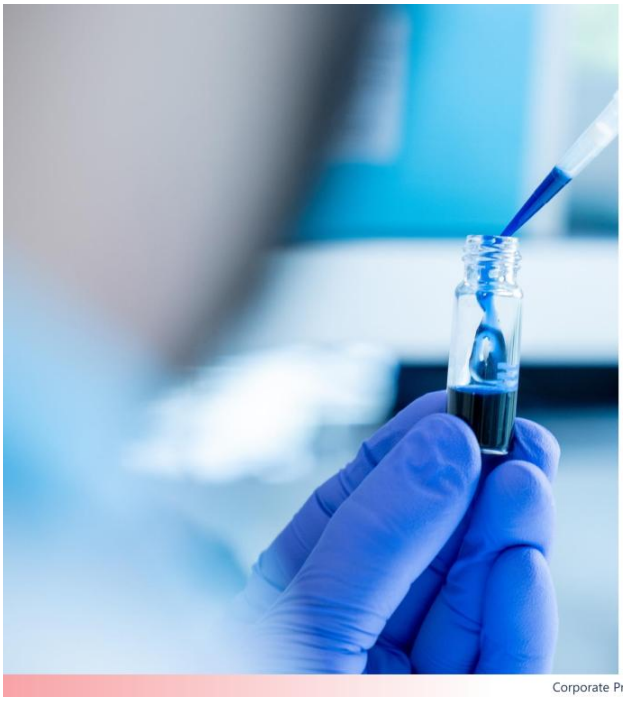
- Ineffective hematopoiesis is the failure of immature blood cells to properly develop into mature cells, and may lead to low levels of circulating red blood cells (anemia), white blood cells (neutropenia) or platelets (thrombocytopenia)

TGF-β superfamily signaling regulates many processes in the bone marrow microenvironment, including:

- Differentiation and maturation of hematopoietic cells
- Iron homeostasis
- Bone turnover
- Pro-inflammatory signaling
- Motility of malignant cells

Keros is developing product candidates with the potential to address ineffective hematopoiesis and functional iron deficiency:

- **KER-050:** Modified activin receptor IIA (ActRIIA) ligand trap designed to bind to and inhibit signaling of select TGF-β ligands, including activin A, activin B, GDF8 and GDF11, to promote growth and differentiation of erythroid cells and platelets
- **KER-047**: Small molecule product candidate designed to inhibit activin receptor-like kinase-2 (ALK2) to suppress hepcidin expression and mobilize iron for incorporation into hemoglobin



KER-050

Investigational Treatment for Anemia and Thrombocytopenia in Patients with Myelodysplastic Syndromes

Ongoing Phase 2 Clinical Trial of KER-050 for the Treatment of Anemia in Patients with Very Low-, Low- or Intermediate-Risk Myelodysplastic Syndromes

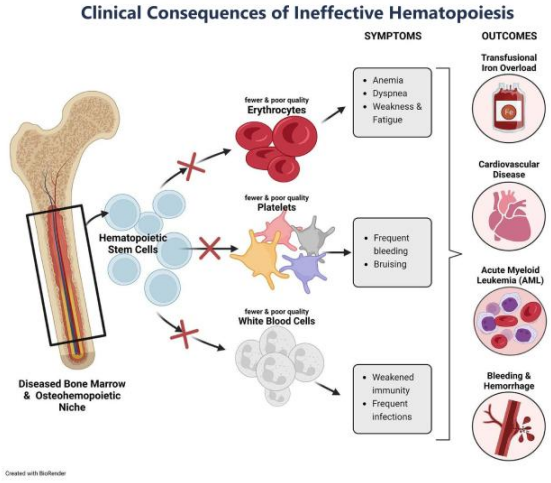
Myelodysplastic Syndromes (MDS)

MDS
MDS is a collection of bone marrow disorders characterized by ineffective hematopoiesis and peripheral cytopenias.

Clinical Consequences
The clinical consequences of MDS include anemia, bleeding, iron overload, cardiovascular disease and progression to acute myeloid leukemia (AML).

Survival Ranges
Median survival ranges from approximately nine years for very low-risk patients to less than a year for high-risk patients.

Scope
In the United States, there are 60,000 to 170,000 patients living with MDS and 15,000 to 20,000 new cases of MDS reported each year.



Novel Treatment Options are Needed to Address Unmet Need of Patients Living with MDS

Current treatment options for symptomatic anemia includes red blood cell (RBC) transfusions, erythropoiesis-stimulating agents (ESAs) and Reblozyl®

- RBC transfusions provide symptomatic relief of anemia, but are also associated with iron overload which can increase risk of AML and reduce overall survival
- ESAs' benefit is limited to patients with low transfusion burden and low endogenous erythropoietin levels
- Reblozyl® approved for treatment of anemia in RS+ patients requiring transfusions who have failed prior ESA treatment
  - Similar to ESAs, benefit primarily in low transfusion burden (LTB) patients. Only 20% of high transfusion burden (HTB) patients achieved 8-week transfusion independence with Reblozyl® versus 4% with placebo

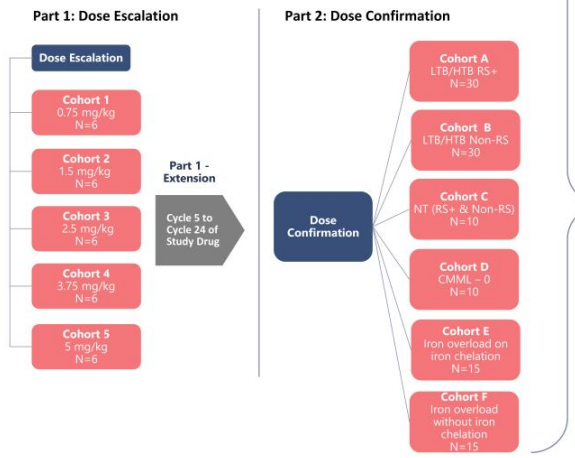
We believe KER-050 has the potential to improve the bone marrow and restore normal hematopoiesis by targeting multiple cell lineages in MDS

- Based on data from our completed Phase 1 clinical trial of KER-050 and multiple preclinical studies, we believe KER-050 has the potential to increase red blood cell and platelet production by acting across the spectrum of cellular differentiation and maturation in hematopoiesis while also improving bone health

RS+: patients that have ring sideroblasts.

Ongoing Phase 2 Clinical Trial of KER-050 for the Treatment of Anemia in Patients with Very Low-, Low- or Intermediate-Risk MDS

Amended Phase 2 Clinical Trial Design and Dose Levels



- KER-050 administered subcutaneously once every four weeks (Q4W)

Primary Objective:
- Assess safety and tolerability of KER-050

Select Efficacy Endpoints:
- IWG 2006 Hematological improvement-erythroid (HI-E):
  - Hemoglobin increase of ≥1.5 g/dL for 8 weeks (in NT and LTB patients)
  - Reduction of ≥4 RBC units transfused over 8 weeks compared to baseline (in HTB patients)
- Transfusion independence (TI) for at least 8 weeks in patients who require ≥ 2 RBC units transfused at baseline

Ongoing Trial – Status as of April 3, 2023:
- Part 1 Dose Escalation (N=31; completed)
- RP2D: 3.75 mg/kg with the ability to titrate to 5 mg/kg Q4W
- RP2D Experienced Patients: N=59
  - 25 patients from Part 1
  - 34 patients from Part 2

Data are presented as of a data cutoff date of April 3, 2023.
RP2D = Recommended Part 2 Dose; CMML: chronic myelomonocytic leukemia; high transfusion burden (HTB): ≥4 units of RBC/8 weeks for hemoglobin (Hgb) ≤9 g/dL; low transfusion burden (LTB): 1-3 units of RBC/8 weeks for Hgb ≤9 g/dL; non-transfused (NT): Hgb ≤10 g/dL; non-RS: patients that did not have ring sideroblasts.

Enrolled Patient Population Included Difficult-to-Treat Patients With High Disease Burden

In June 2023, we presented data from 59 patients receiving the RP2D as of the April 3, 2023 data cut-off date

- 59 patients were evaluable for safety
- 37 patients were evaluable for efficacy

Most patients required transfusions at baseline

- Over half were high transfusion burden (HTB; ≥4 RBC units/8 wks)
  - Among HTB patients, 12/31 (38.7%) received ≥8 RBC units/8 wks
- Majority were ring sideroblast positive (RS+)
- Majority had multi-lineage dysplasia (MLD)

Exposure of overall MDS RP2D population

- Mean duration of treatment was 225 days as of the data cut-off date (≈32 weeks)
  - Range 6 to 649 days (≈1 to 93 weeks)
- Median doses received = 6
  - Range 1 to 22
    - 14 (23.7%) patients received ≥12 doses
    - 15 (25.4%) patients received <3 doses

Baseline Characteristics	RP2D dataset (n=59)
Age, years, median (range)	**74.0 (53-89)**
Male, n (%)	**34 (57.6)**
RBC transfusion status, units per 8 weeks, n (%)	
Non-transfused (NT), 0 units	12 (20.3)
Low Transfusion Burden (LTB), <4 units	16 (27.1)
High Transfusion Burden (HTB), ≥4 to <8 units	31 (52.5)
HTB, ≥8 units	12 (20.3)
Ring Sideroblast status, n (%)	
RS+	42 (71.2)
Non-RS	17 (28.8)
IPSS-R Risk Category, n (%)	
Very Low	8 (13.6)
Low	29 (66.1)
Intermediate	11 (18.6)
Missing	1 (1.7)
MDS WHO 2016 classification, n (%)	
MDS	2 (3.4)
MDS-MLD	12 (20.3)
MDS-RS-MLD	29 (49.2)
MDS-RS-SLD	5 (8.5)
Missing	11 (18.6)
Prior ESA therapy, n (%)	**13 (22.0)**
Iron chelator therapy, n (%)	**17 (28.8)**

Data are presented as of a data cutoff date of April 3, 2023.

KER-050 Was Generally Well-Tolerated

KER-050 generally well-tolerated at RP2D of 3.75 to 5.0 mg/kg

- Most frequent treatment-emergent adverse events (TEAEs) that occurred (in ≥15% patients) regardless of causality were:
  - Fatigue (22%), nausea (18.6%), diarrhea (18.6%), epistaxis (16.9%), COVID-19 (15.3%) and dyspnea (15.3%)
- 6 TEAEs led to treatment discontinuation:
  - Related TEAEs: Injection-site reaction (Grade 2)
  - Unrelated TEAEs: Nodular melanoma; dyspnea; chronic obstructive pulmonary disease and cardiac failure congestive (both in one patient), cardiac failure and myocardial infarction
- 2 fatal TEAEs (cardiac failure and myocardial infarction) determined to be unrelated to study treatment by the investigator

No patients progressed to AML

Category	RP2D dataset (n=59)
Any TEAE, n (%)	53 (89.8)
Any treatment related TEAE	19 (32.2)
Any TE serious AE (TESAE)	20 (33.9)
Any treatment-related TESAE	1 (1.7)
Any TEAE leading to death	2 (3.4)
Any TEAE leading to IMP Discontinuation[1]	6 (10.2)

[1] Related TEAEs leading to IMP discontinuation = injection site reaction; unrelated TEAEs = nodular melanoma, COPD and cardiac failure congestive (both in 1 patient), dyspnea, cardiac failure, and myocardial infarction

TEAE = Treatment Emergent Adverse Event
TESAE = Treatment Emergent Serious Adverse Event
IMP = Investigational Medicinal Product
AML = Acute Myeloid Leukemia

Data are presented as of a data cutoff date of April 3, 2023.

KER-050 Treatment Resulted in Hematological Response Across a Broad Population of Patients with Lower-Risk MDS

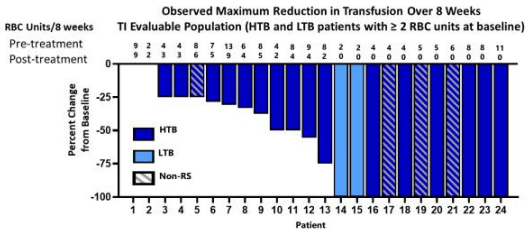
Response Summary	RP2D Patients[1]	
	All evaluable patients	HTB evaluable patients
Overall Erythroid Response (HI-E or TI), n (%)	19/37 (51.4)	11/22 (50)
IWG 2006 HI-E, n (%)	19/37 (51.4)	11/22 (50)
TI ≥8 weeks[2], n (%)	11/26 (42.3)	9/22 (40.9)
RS+, n (%)	8/19 (42.1)	6/17 (35.3)
Non-RS, n (%)	3/7 (42.9)	3/5 (60)

1 Includes data for weeks 0-24 in RP2D patients with ≥24 weeks of treatment or who discontinued
2 TI-evaluable patients received at least 2 RBC units in the 8 weeks prior to treatment initiation

- **Similar rates of HI-E and TI observed regardless of transfusion burden or RS status**
- **44.1%* of patients show a ≥30 x 10^9/L increase from baseline in platelet count sustained over at least 8 weeks**

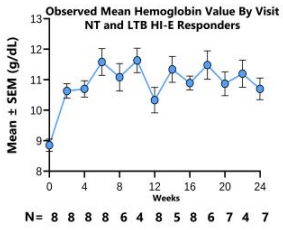
Data are presented as of a data cutoff date of April 3, 2023.
*Percentage based on 34 patients who had at least 24 weeks of treatment or discontinued AND had both baseline and 8weeks of post-baseline platelet data.

Reductions in Transfusion Burden and Sustained Increases in Hemoglobin Observed with KER-050 Treatment



KER-050 treatment led to reductions in transfusion burden[1]

- Reduced transfusion burden observed in majority of LTB and HTB patients
- TI observed in both RS+ and non-RS patients
- TI achieved in patients with baseline transfusion burden ranging from 2 to 11 units/8 weeks



KER-050 treatment demonstrated sustained increases in hemoglobin observed over 6 months[2]

- 8/15 (53.3%) NT and LTB patients with ≥6 months of treatment (or discontinued) achieved HI-E response in first 24 weeks of treatment
- Observed sustained increases in hemoglobin support durable response with KER-050

Data are presented as of a data cutoff date of April 3, 2023.

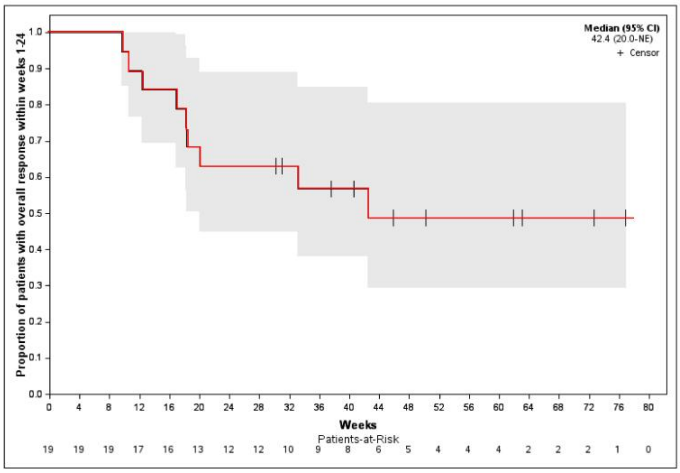
1. 2 patients discontinued with insufficient data to determine 8-week transfusion reduction, and are not included in this plot; 2. Baseline hemoglobin calculated as average over 8-week pre-treatment period. Hemoglobin values within 14 days following a transfusion censored except for pre-transfusion values. Per protocol, KER-050 dose must be held at hemoglobin levels ≥12 g/dL.

Data Suggest KER-050 Elicited a Durable Response

19 patients achieved HI-E or TI
- During weeks 0-24 in RP2D patients with ≥24wk of treatment or who discontinued

Median duration of response was 42.4 weeks

10/19 patients (52.6%) had ongoing response at time of data cutoff
- Patients with ongoing response censored at time of data cutoff, denoted by vertical



Data are presented as of a data cutoff date of April 3, 2023.

KER-050

Investigational Treatment for Anemia and Thrombocytopenia in Patients with Myelofibrosis

Ongoing Phase 2 Open-Label Clinical Trial to Evaluate the Safety and Efficacy of KER-050 as Monotherapy or in Combination with Ruxolitinib in Participants with Myelofibrosis

Myelofibrosis (MF)

MF

MF is a rare cancer of the bone marrow in which the marrow is replaced by scar tissue and is not able to produce healthy blood cells

Clinical Consequences

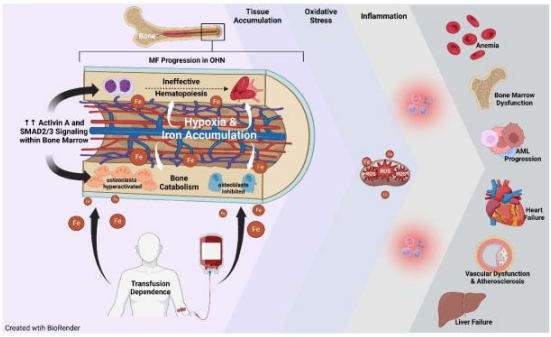
MF is characterized by ineffective hematopoiesis, an enlarged spleen, bone marrow fibrosis and shortened survival. Patients often experience multiple disease-associated and treatment-emergent cytopenias, including anemia and thrombocytopenia

Current Treatments

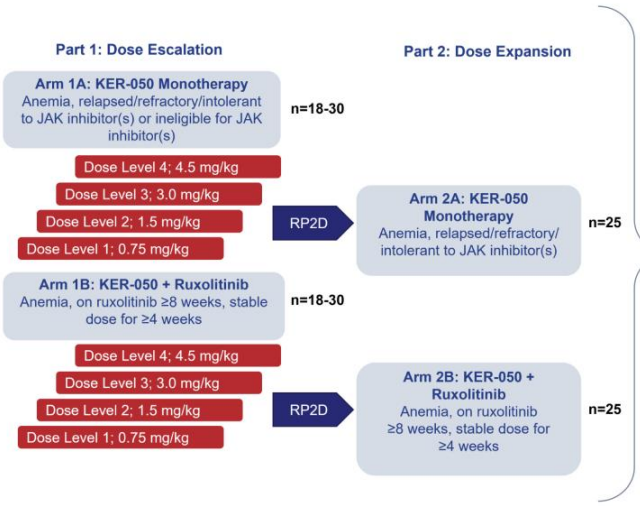
Currently, there are limited therapeutic options to address the MF-associated cytopenias. Within a year of diagnosis, 26% of patients with MF will develop thrombocytopenia and 51% will develop anemia. Additionally, within a year of diagnosis, 38% of patients with MF are RBC transfusion dependent

Scope

In the United States, there are 16,000 to 18,500 patients living with MF and approximately 3,000 newly diagnosed each year



Ongoing Phase 2 Clinical Trial to Evaluate KER-050 as Monotherapy or in Combination with Ruxolitinib in Patients with MF



Primary Objective:

- Part 1: Assess safety and tolerability of KER-050
- Part 2: Confirm safety and tolerability of the dose(s) selected from Part 1

Secondary Endpoints include:

- Evaluate the pharmacokinetics, pharmacodynamics and efficacy of KER-050 administered with or without ruxolitinib

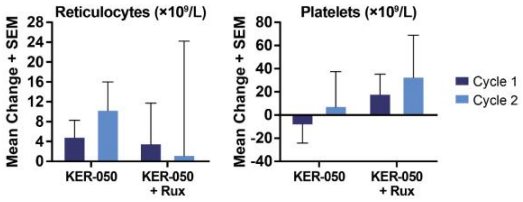
KER-050 was generally well tolerated at 0.75mg/kg:

- No dose-limiting toxicities
- Most frequent TEAEs reported by ≥ 2 patients were diarrhea (25.0%) and fatigue, dyspnea and COVID-19 (16.7% each)
- 1 TEAE led to KER-050 dose modification: amyloidosis (unrelated)
- No TEAEs led to either study treatment or study discontinuation

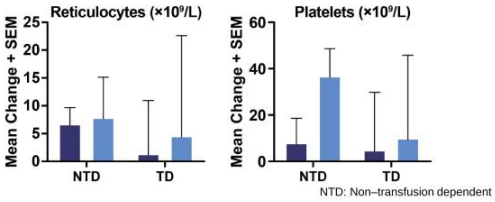
Data are presented as of a data cutoff date of October 1, 2022.

KER-050 Treatment Increased Reticulocytes and Platelets in Patients with MF

Change by Study Arm



Change by Transfusion Status



NTD: Non–transfusion dependent

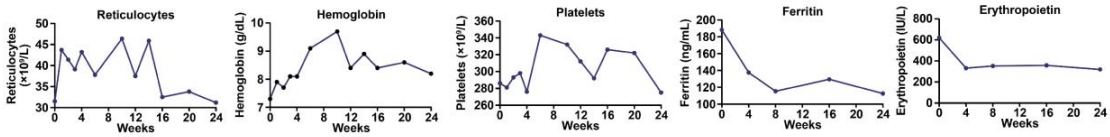
Although variability was observed amongst the patients, treatment with KER-050 at the lowest dose in this trial (0.75 mg/kg) resulted in increased reticulocytes and platelets on aggregate, both as monotherapy and in combination with ruxolitinib, and regardless of transfusion status

- This is consistent with prior preclinical and clinical findings on the pharmacodynamic effects of KER-050

These data support the potential of KER-050 to promote differentiation of erythroid and megakaryocytic precursors and ameliorate anemia and thrombocytopenia in patients with MF

Data are presented as of a data cutoff date of October 1, 2022.

Observed Increases in RBC Parameters and Platelets in a Patient with KER-050 Treatment (Monotherapy)



Case Study of Patient on KER-050 Monotherapy Treatment at 0.75mg/kg Q4W

- 60-year-old non-transfusion dependent female with primary MF
- Treatment with KER-050 increased hematopoiesis
  - A robust increase in reticulocytes observed after a single dose of KER-050 was followed by a sustained increase in hemoglobin (≥1.5 g/dL over baseline) and corresponding decrease in ferritin and erythropoietin with continued dosing
  - An increase in platelets was also observed

Data are presented as of a data cutoff date of October 1, 2022.

KER-047

A Novel Product Candidate Designed to Treat Functional Iron Deficiency That is a Consequence of Elevated ALK2 Signaling

Increased Hepcidin Expression Leads to Functional Iron Deficiency

ALK2 signaling controls hepcidin expression, a hormone that controls iron homeostasis

Hepcidin is the master regulator of iron flux into and out of storage tissues

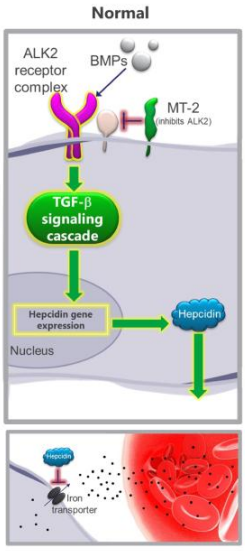
- The body responds to demands for iron by increasing or reducing the production of hepcidin, which leads to a reduction or increase in iron availability, respectively.

Elevated hepcidin is observed in chronic inflammation, iron overload or results from mutations in the regulatory proteins that control hepcidin expression

Functional iron deficiency is a condition when the body has adequate iron in the body, but the iron cannot be mobilized out of storage tissues and incorporated into RBCs, resulting in anemia

- RBC transfusions, which are used to treat anemia, can lead to iron overload and toxicity in cardiovascular and other tissues

Modulating ALK2 signaling will normalize high hepcidin levels, restore serum iron and ameliorate anemia in functional iron deficiency

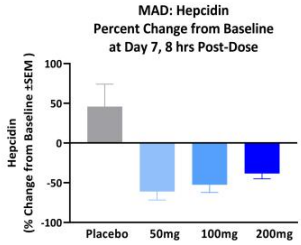


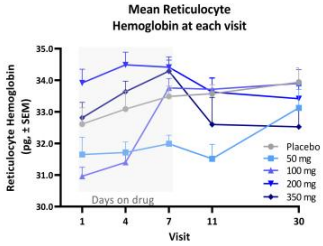
KER-047 Treatment Reduced Hepcidin Levels and Increased Hemoglobin Content in Reticulocytes in a Phase 1 Clinical Trial

KER-047 is a novel, oral, investigational small molecule inhibitor of ALK2 with low nanomolar IC_{50}

PK/ADME: Suitable for 1x daily oral dosing

There were no serious adverse events reported in the randomized, double-blind, placebo-controlled two-part Phase 1 clinical trial of KER-047 in healthy volunteers





- Consistent with ALK2 inhibition, decreases in serum hepcidin were observed in Cohorts 1 through 3 of Part 2 of the trial
- Treatment related decreases in hepcidin were associated with increased serum iron

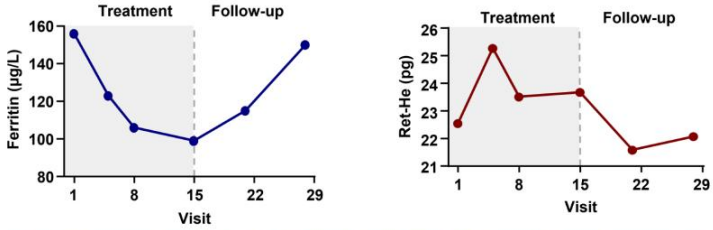
- An increase in reticulocyte hemoglobin was observed in Cohorts 1 through 4 of Part 2 of the trial, starting on Day 4 of treatment
- Pronounced increase in reticulocyte hemoglobin observed in cohorts with lower baseline reticulocyte hemoglobin

KER-047 Treatment of One IRIDA Patient Resulted in a Decrease in Hepcidin and an Increase in Reticulocyte Hemoglobin

In December 2022, we presented data from one patient enrolled in our open label, two-part, dose-escalation and dose-expansion Phase 2 clinical trial to evaluate KER-047 in patients with iron-refractory iron deficiency anemia (IRIDA). The patient completed 14 days of treatment with KER-047 (25mg once daily) and a 14 day-follow up

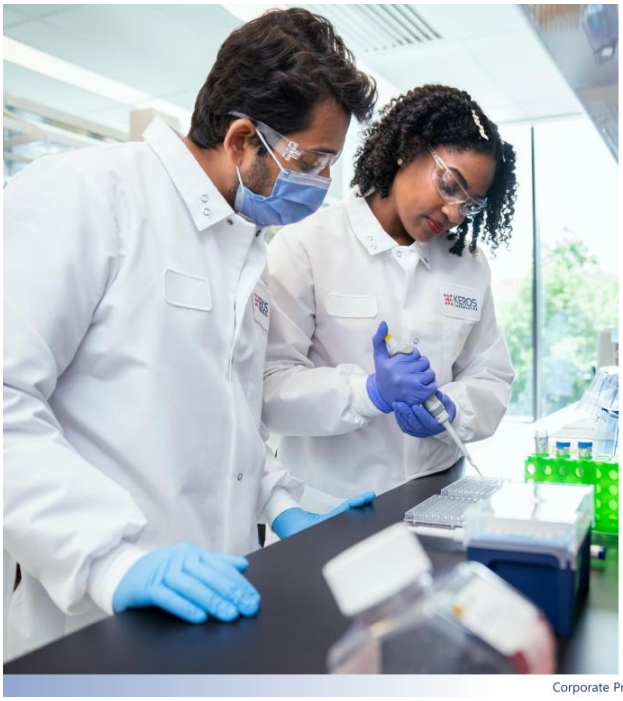
- A dose of 25mg once daily was generally well tolerated; no serious adverse events or dose limiting toxicities were observed during treatment
- Consistent with results from our Phase 1 clinical trial of KER047 in healthy volunteers, we observed decreases in hepcidin and serum ferritin as well as increases in reticulocyte hemoglobin

Laboratory Results Before, During, and After Administration of KER-047 for the First Low-Dose Cohort (n=1)



We terminated this trial early, having observed data in the one patient enrolled that we believe is suggestive of proof of mechanism. The early termination was not on the basis of any safety concerns

We are conducting an open label, two-part Phase 2 clinical trial to evaluate response-guided dose titration of KER-047 in MDS and MF patients with functional iron deficiency. The primary objectives of this trial are to assess the safety and tolerability of KER-047. The secondary objectives of this trial are to evaluate the pharmacokinetics, pharmacodynamics and preliminary efficacy of KER-047.



Pulmonary and Cardiovascular Franchise

KER-012

Investigational Treatment for Pulmonary Arterial Hypertension (PAH) and for Cardiovascular Disorders

Ongoing Randomized, Phase 2, Double-blind, Placebo-Controlled Clinical Trial to Evaluate the Safety and Efficacy of KER-012 in Combination with Background Therapy in Adult Participants with Pulmonary Hypertension

Imbalances in TGF-β Superfamily Signaling Underlies Vascular Remodeling in PAH

PAH is a debilitating disorder characterized by elevated pulmonary vascular resistance due to increased vascular smooth muscle cell proliferation and inflammation

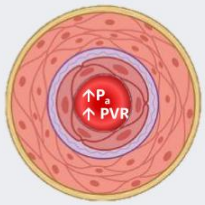
- This results in diminished oxygenation, impaired cardiac output, and right ventricle (RV) overload
- Patients experience shortness of breath, fatigue, fainting, chest pain, palpitations and swelling of extremities and abdomen. Despite current treatment options, the 5-year survival remains only slightly above 50%
- PAH is associated with imbalanced TGF-β superfamily signaling, including insufficient bone morphogenic protein (BMP) signaling and increased signaling by activins and GDFs

KER-012 is a modified activin receptor IIB ligand trap

- Designed to rebalance TGF-β superfamily signaling
- Being developed for the treatment of pulmonary and cardiovascular disorders, including PAH
- KER-012 is designed to preferentially inhibit select ligands (activin A, activin B, GDF 8 and GDF 11) to potentially rebalance TGF-β superfamily signaling without a dose-limiting increase in RBCs

Pulmonary Arterial Hypertension

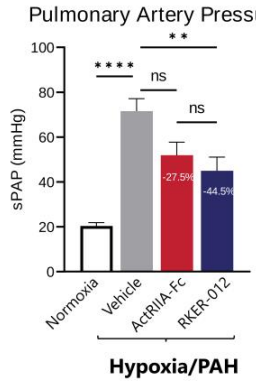
Thickened Vasculature

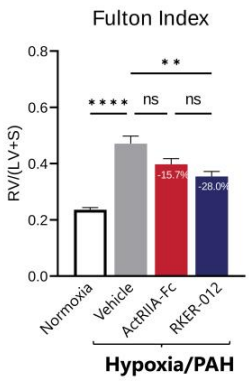


↑ Myogenic & Fibrogenic Differentiation

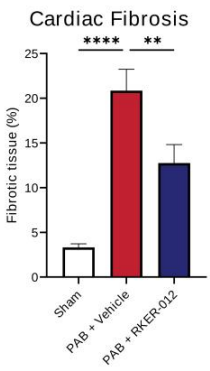
RKER-012 Reduced Pulmonary Arterial Pressure, Right Ventricle Hypertrophy and Cardiac Fibrosis Observed in Rodent PAH Models

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, * $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$. 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

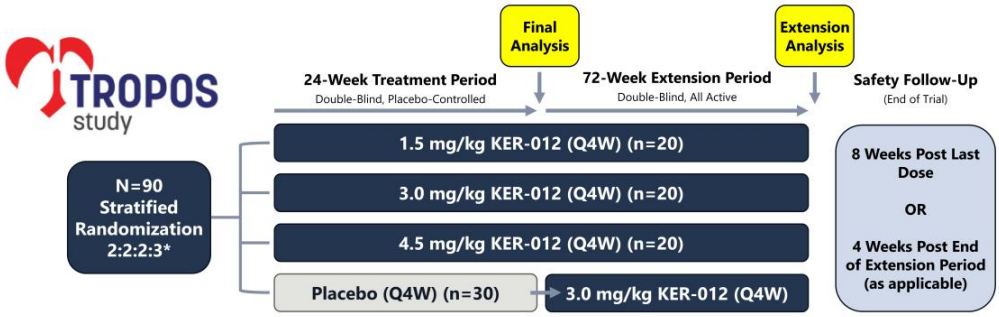
Keros completed a randomized, double-blind, placebo-controlled, two-part Phase 1 clinical trial to evaluate single and multiple ascending doses of KER-012 in healthy volunteers.

- 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 ↓ Pulmonary arterial pressure ↓ Right ventricular hypertrophy ↓ 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

TROPOS Trial: Global Phase 2 Clinical Trial of KER-012 in Patients with PAH



Primary Objective:

- To evaluate the effect of KER-012 on hemodynamics compared to placebo in participants on background PAH therapy

Primary Endpoint:

- Change from baseline in pulmonary vascular resistance (PVR) at Week 24

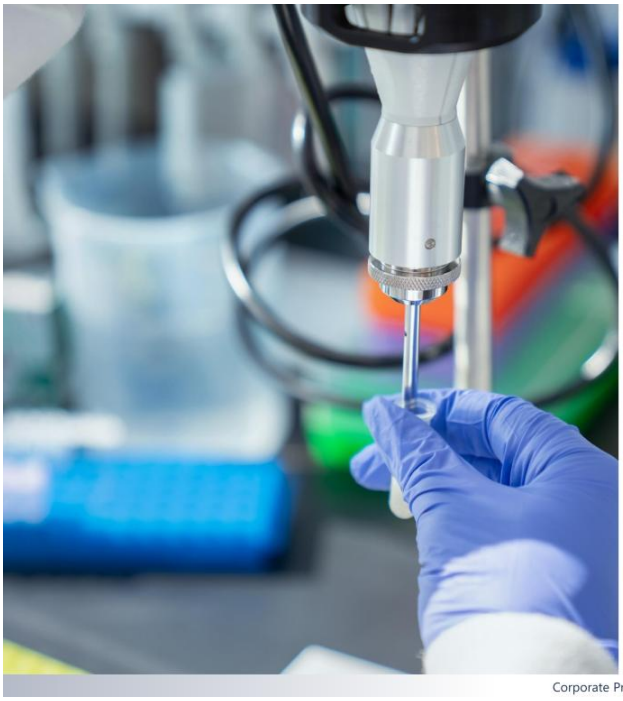
Key Secondary Objective:

- To evaluate the effect of KER-012 on exercise capacity compared to placebo in participants on background PAH therapy

Key Secondary Endpoint:

- Change from baseline in 6-minute walk distance at Week 24

*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.



Neuromuscular Franchise

KER-065

Designed to Address Neuromuscular Diseases, with an initial focus on Duchenne Muscular Dystrophy (DMD)

KER-065 Overview

KER-065 is a selective activin receptor ligand trap

- Designed to inhibit the biological effects of myostatin and activin to increase skeletal muscle and bone mass, increase fat metabolism and reduce fibrosis
- Being developed for the treatment of neuromuscular diseases, with an initial focus on DMD

In preclinical studies, KER-065 showed high affinity for and potent inhibition of ligands involved in the regulation of muscle and bone homeostasis. Additionally, in preclinical studies, the research form of KER-065 (RKER-065):

- Increased muscle mass, muscle function and bone mass in wild-type mice
- Increased muscle mass, grip strength and trabecular bone in a mouse model of DMD

We expect to initiate a randomized, double-blind, placebo-controlled, two-part Phase 1 clinical trial to evaluate the safety and tolerability of single and multiple ascending doses of KER-065 in healthy volunteers in Q1 2024

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


KEROS
THERAPEUTICS
KER-012 Update
August 8, 2023

Disclaimer

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.

Certain information contained in this presentation relates to or is based on studies, publications, surveys and other data obtained from third-party sources and the Company's own internal estimates and research. While we believe these third-party sources to be reliable as of the date of this presentation, it has not independently verified, and makes no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third -party sources. Finally, while we believe our own internal research is reliable, such research has not been verified by any independent source.

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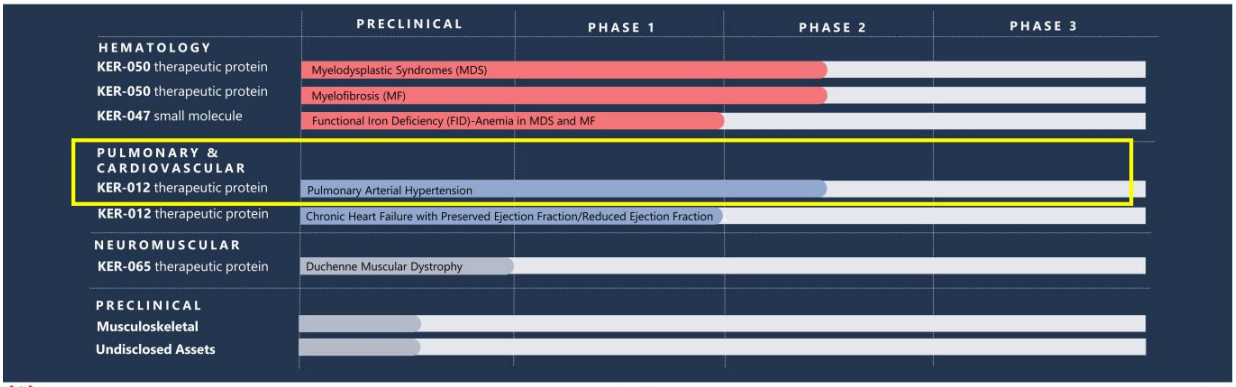
Agenda

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

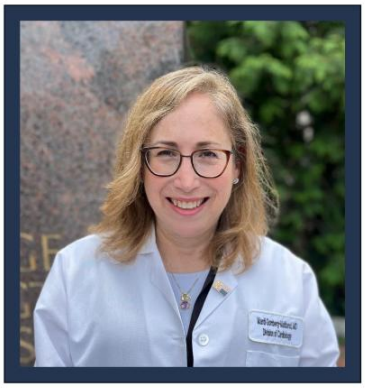
Keros is a clinical-stage biopharmaceutical company
Developing potentially differentiated product candidates designed to alter transforming growth factor-beta (TGF-β) signaling and target pathways critical for the growth, repair and maintenance of a number of tissue and organ systems

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.

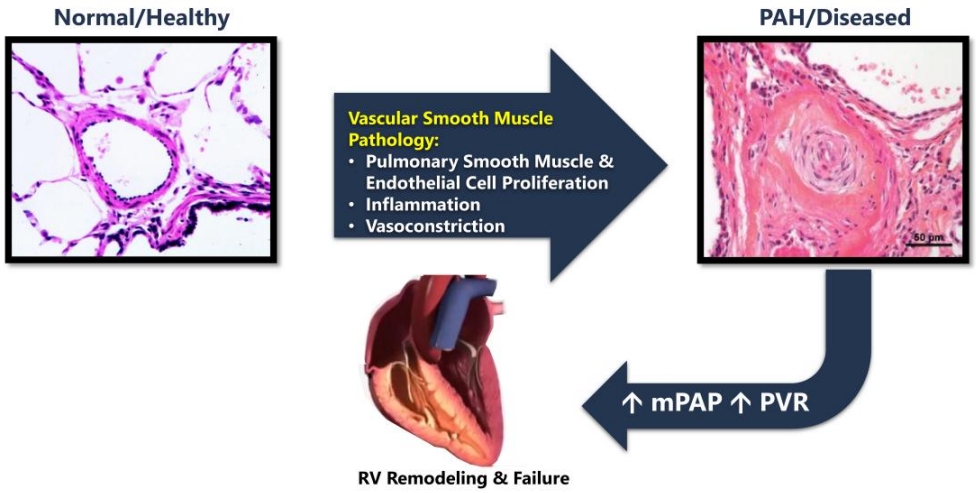
Over 150 publications, including, *CHEST, Circulation, Circulation Heart Failure, European Respiratory Journal, Journal of American College of Cardiology (JACC), JACC Heart Failure, JAMA-Internal Medicine,* and the *New England Journal of Medicine*.

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

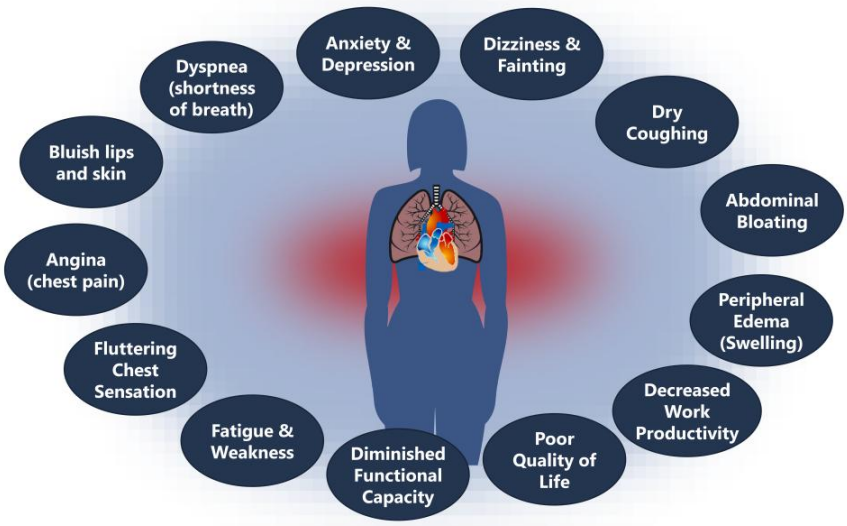
Leads to Hemodynamic Abnormalities, Disease Progression, and Severe Morbidity



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

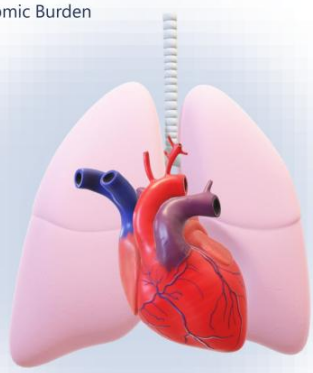
Symptoms and Complications Negatively Impact Most Aspects of Patients' Lives



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**



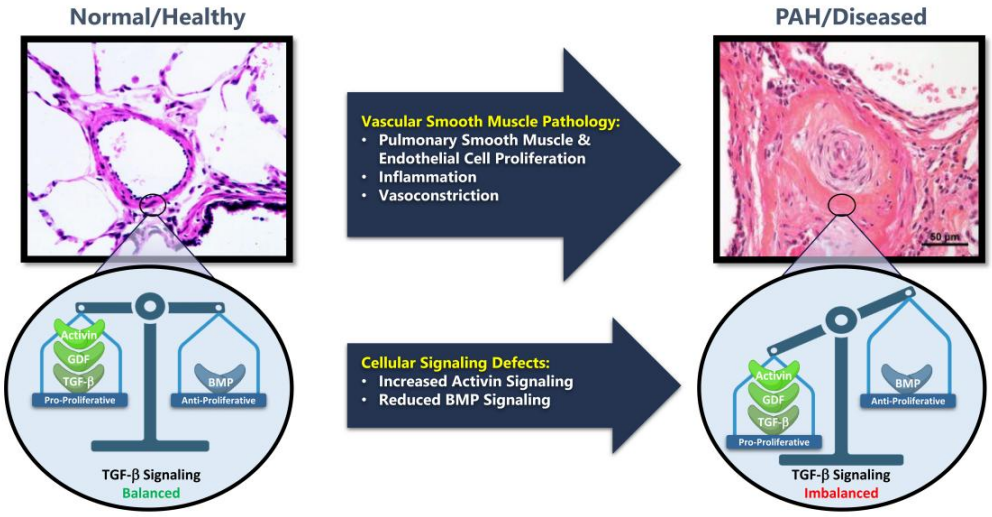
- **Current standard of care (SOC) for PAH is the use of drugs that promote vasodilation**
  - **Currently available treatments do not correct the underlying biology**

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

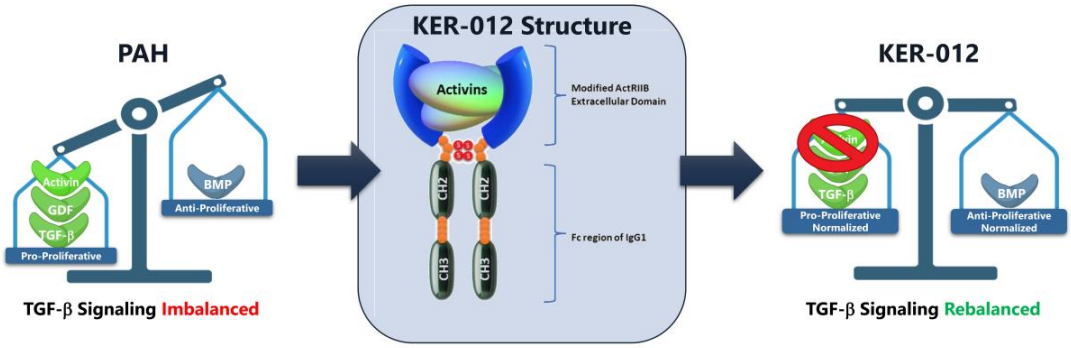
Characterized by TGF-β Signaling Imbalance in Pulmonary Artery Vascular Wall (and Endothelial Cells)



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

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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

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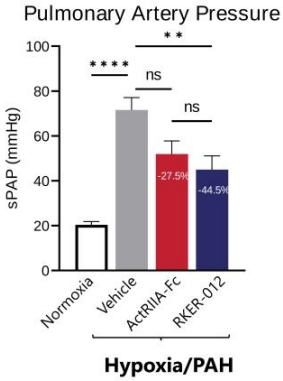
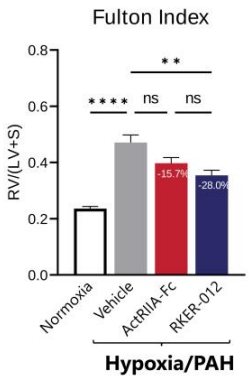
Gudelsky A et al American Thoracic Society 2023 Annual Meeting. Am J Respir Crit Care Med 2023;207:A378

RKER-012 Preclinical Data

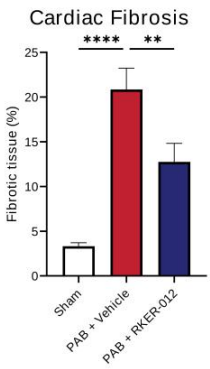
Reduced Pulmonary Arterial Pressure, Right Ventricle Hypertrophy, and Cardiac Fibrosis Observed in Rodent PAH Models

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, * $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$. Percent change compared to hypoxia + vehicle rats.

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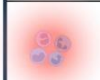
Observed KER-012 Profile Supports Therapeutic Rationale in PAH

- 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

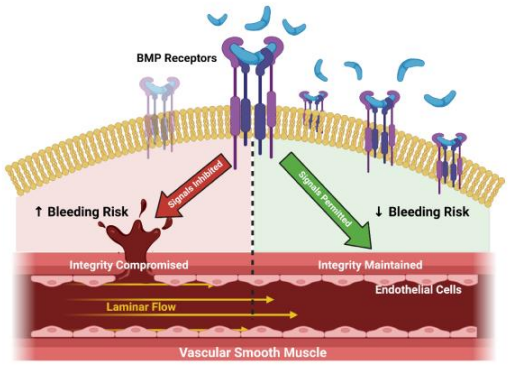
Sotatercept Dosing in PAH Limited Due to On-Target AEs

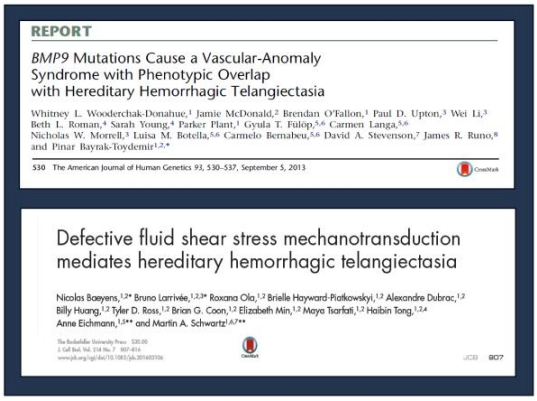
Doses between 0.3 mg/kg and 0.7 mg/kg administered every 21 days

- **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]**

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

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

Defective fluid shear stress mechanotransduction mediates hereditary hemorrhagic telangiectasia

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JCB 807

- **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).

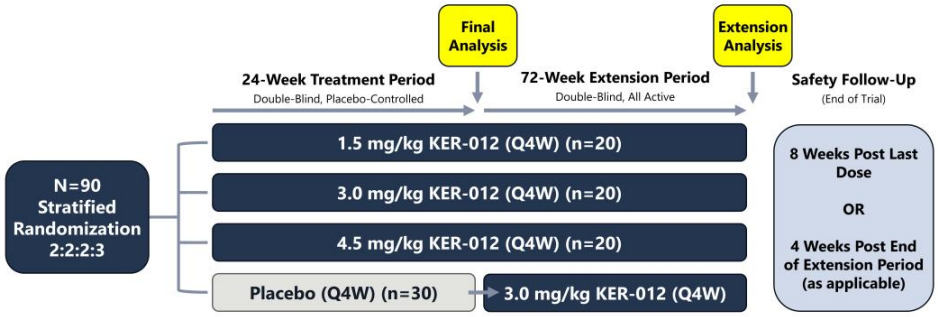
Six-minute walk distance (6MWD) ≥ 150 and ≤ 500 meters

- 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