# 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): January 9, 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.)** |

**99 Hayden Avenue, Suite 120, Building E**
**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 January 9, 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 9.01 Financial Statements and Exhibits.**
(d) Exhibits

| Exhibit No. | Description |
|---|---|
| 99.1 | Corporate Presentation dated January 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: January 9, 2023

KEROS THERAPEUTICS

# Corporate Presentation

January 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 and timing of its preclinical studies and clinical trials for KER-050, KER-047 and KER-012; the potential impact of COVID-19 on Keros’ ongoing and planned preclinical studies, clinical trials, business and operations; 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 lead product candidates, KER-050 and KER-047; 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; Keros’ dependence on third parties in connection with manufacturing, clinical trials and pre-clinical studies; and risks relating to the impact on our business of the COVID-19 pandemic or similar public health crises.

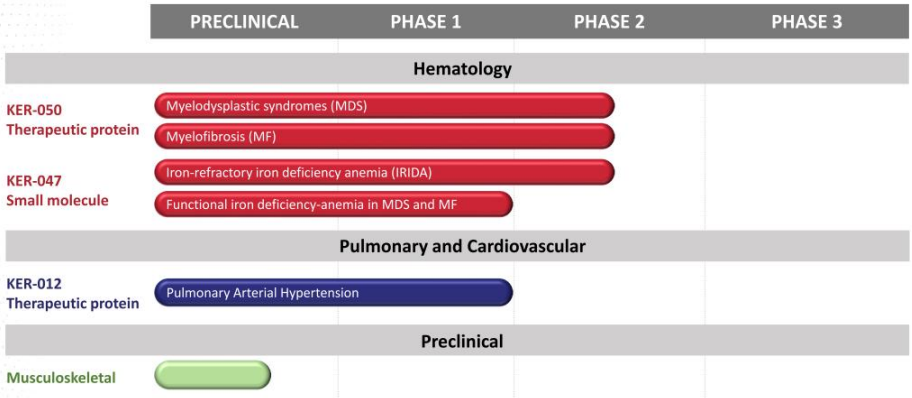
These and other risks are described more fully in Keros’ filings with the Securities and Exchange Commission (SEC), including the “Risk Factors” section of Keros' Annual Report on Form 10-K, filed with the SEC on March 9, 2022, and Keros’ Quarterly Reports on Form 10-Q, filed with the SEC on May 5, 2022, August 4, 2022 and November 3, 2022, 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.

# Keros is Focused on Transforming the Lives of Patients Suffering from Hematological, Pulmonary and Cardiovascular Disorders

- Keros is a clinical-stage biopharmaceutical company developing 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
  - Targeting such pathways has been clinically proven to elicit meaningful improvements in blood cells, blood vessels and heart tissue
- 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

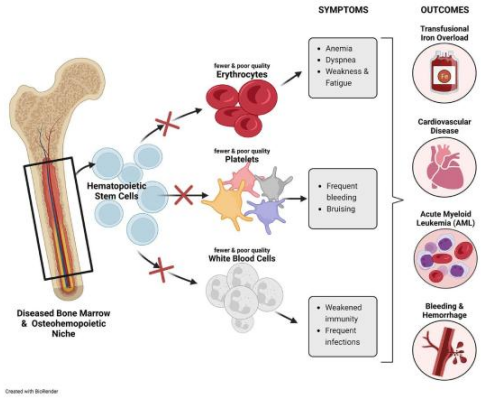
**Investigational Treatment for Anemia and Thrombocytopenia in Patients with Myelodysplastic Syndromes**

***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 is a collection of bone marrow disorders characterized by ineffective hematopoiesis and peripheral cytopenias
- The clinical consequences of MDS include anemia, bleeding, iron overload, cardiovascular disease and progression to acute myeloid leukemia (AML)
- Median survival ranges from approximately nine years for very low-risk patients to less than a year for high-risk patients
- 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

**Clinical Consequences of Ineffective Hematopoiesis in MDS**



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

**Current Treatment Options:**

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

- ESAs' benefit is limited to patients with low transfusion burden and low endogenous erythropoietin levels
- Reblozyl® approved for treatment of anemia in RS positive 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
- RBC transfusions provide symptomatic relief of anemia, but are also associated with iron overload which can increase risk of AML and reduce overall survival

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

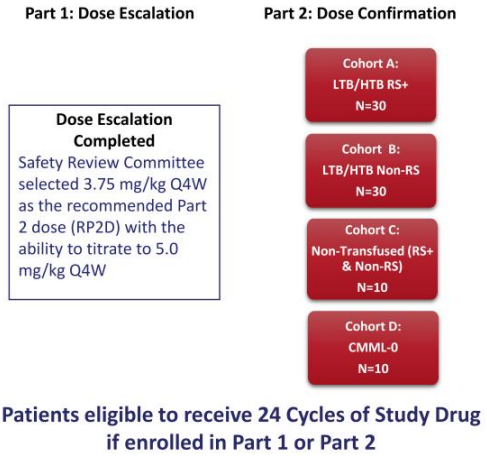
- Based on data from our completed Phase 1 clinical trial of KER-050 and multiple preclinical studies, we believe KER-050 has the potential to increase red blood cell and platelet production by acting across the spectrum of cellular differentiation and maturation in hematopoiesis while also improving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

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

- KER-050 administered subcutaneously once every four weeks (Q4W)
- **Trial objectives in Part 1 (Dose Escalation):**
  - *Evaluate safety, tolerability and pharmacokinetics*
  - *Evaluate pharmacodynamic effects and efficacy of KER-050*
- **Trial objectives in Part 2 (Dose Confirmation):**
  - *Confirm the safety, tolerability and efficacy of dose(s) selected from Part 1*

**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




**Patients eligible to receive 24 Cycles of Study Drug if enrolled in Part 1 or Part 2**



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; RS+: patients that have ring sideroblasts.

# KER-050 Safety and Efficacy Update in Patients Receiving the Recommended Part 2 Dose*

**In December 2022, we presented data from 36 patients receiving the RP2D as of the Oct 1-2022 data cut-off date**

- 36 patients were evaluable for safety
- 29 patients were evaluable for efficacy

**Demographics and Baseline Characteristics in RP2D Patients**

- Mean duration of treatment was 196 days as of the data cut-off date
- Majority of patients had multi-lineage dysplasia (MLD) and high transfusion burden at baseline

**KER-050 Generally Well-Tolerated at RP2D of 3.75 to 5.0 mg/kg***

- No dose-limiting toxicities and no progression to AML
- Most common treatment-emergent adverse events (TEAEs) that occurred in >5 patients were diarrhea (22.2%), fatigue (19.4%), dyspnea (16.7%), and nausea (16.7%)
- 3 TEAEs led to treatment discontinuation: injection-site reaction (related); dyspnea (unrelated); chronic obstructive pulmonary disease (unrelated)
- 1 TEAE unrelated to study treatment was fatality due to heart failure

| Parameter | RP2D Dataset (n=36) |
|---|---|
| Age, years, median (range) | 74.5 (61-88) |
| Male, n (%) | 20 (55.6) |
| RS status, n (%) | |
| RS+ | 23 (63.9) |
| Non-RS | 13 (36.1) |
| WHO MDS classification, n (%) | |
| MDS-MLD | 12 (33.3) |
| MDS-MLD-RS | 20 (55.6) |
| MDS-SLD | 0 |
| MDS-SLD-RS | 1 (2.8) |
| Unclassifiable/Unknown/Missing | 3 (8.4) |
| Prior ESA therapy, n (%) | 6 (16.7) |
| Iron chelator therapy, n (%) | 11 (30.6) |
| RBC transfusion status, units per 8 weeks | |
| NT | 10 (27.8) |
| LTB | 6 (16.7) |
| HTB | 20 (55.6) |
| 4 to <8 units | 11 (30.6) |
| ≥8 units | 9 (25.0) |

SLD: Single lineage dysplasia
WHO: World Health Organization

*Data cutoff date: 1-Oct-2022

# Observed a Sustained Transfusion Independence Response with Longer-Term Treatment with KER-050 at the RP2D*

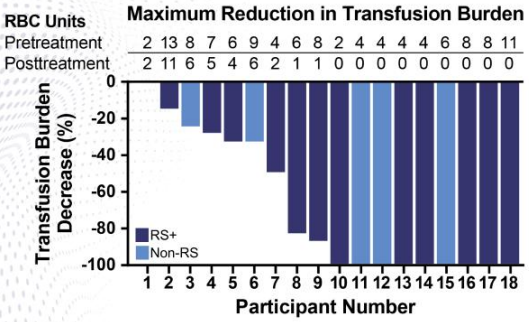
- Transfusion independence at ≥12 weeks was achieved in 53% of evaluable patients treated at RP2D and eligible for long-term treatment
  - Mean duration of treatment was 196 days as of the data cut-off date
- Transfusion independence was observed in both RS+ and non-RS patients regardless of transfusion burden

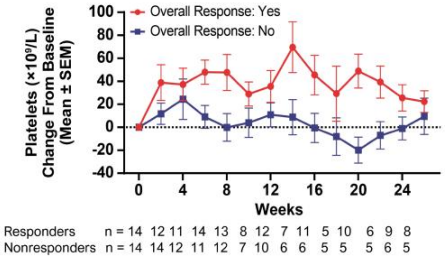
| Response Summary | Response Rate, n/m (%) | |
|---|---|---|
| | All evaluable patients | HTB evaluable patients |
| Overall Erythroid Response (HI-E or TI) | 15/29 (51.7%) | 10/16 (62.5%) |
| IWG 2006 HI-E | 15/29 (51.7%) | 10/16 (62.5%) |
| **TI ≥8 weeks** | **9/18 (50%)** | **8/16 (50%)** |
| RS+ | 6/12 (50%) | 5/11 (45.5%) |
| Non-RS | 3/6 (50%) | 3/5 (60%) |
| **TI ≥12 weeks** | **8/15 (53.3%)** | **7/14 (50%)** |

- *HI-E evaluable: ≥8 weeks postbaseline hemoglobin assessments (NT and LTB) or transfusion assessments (HTB)*
- *TI evaluable: ≥8 (or ≥12) weeks postbaseline transfusion assessments with ≥2 units RBC transfusion at baseline*

*Data cutoff date: 1-Oct-2022

# KER-050 Treatment Resulted in HI-E and TI in Transfusion-Dependent Non-RS and RS+ Patients with Sustained Increase in Platelets*



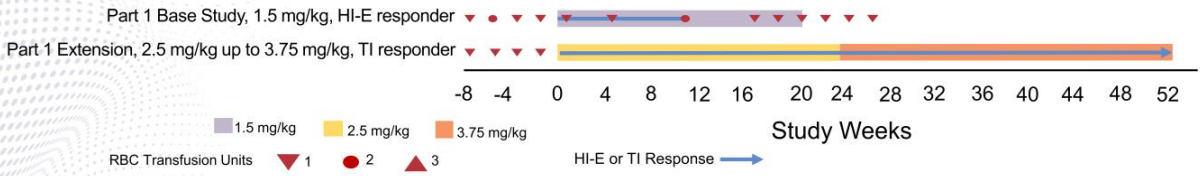

Altered visit schedules for patients re-baselined in Part 1 Extension following treatment gap contribute to fluctuating numbers across visits.

- KER-050 treatment led to improved transfusion burden in both LTB and HTB patients
- 8 out of 16 HTB patients achieved transfusion independence

- The observed increases in platelets for HI-E and TI responders suggest that KER-050 has a differentiated mechanism of action in that it potentially promotes hematopoiesis across multiple cell lineages

*Data cutoff date: 1-Oct-2022

# Long-term Transfusion Independence Achieved in a Patient Dosed at RP2D




**Case Study: 72-year-old male, Non-RS, MDS-MLD, HTB, Concomitant Iron Chelation Therapy**

- This patient achieved an initial HI-E response (but not TI) when treated with four doses of KER-050 1.5 mg/kg in Part 1 Dose Escalation (top bar)
- The patient was rescreened and initiated Part 1 Extension (bottom bar) following a 112-day gap between the last dose in Dose Escalation and first dose in the Extension
- The patient then achieved TI upon recommencement of treatment at 2.5 mg/kg every 4 weeks
- The patient dose escalated to 3.75 mg/kg every 4 weeks per the clinical trial protocol (after 24 weeks) and has remained TI for more than one year as of November 30, 2022

# 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)

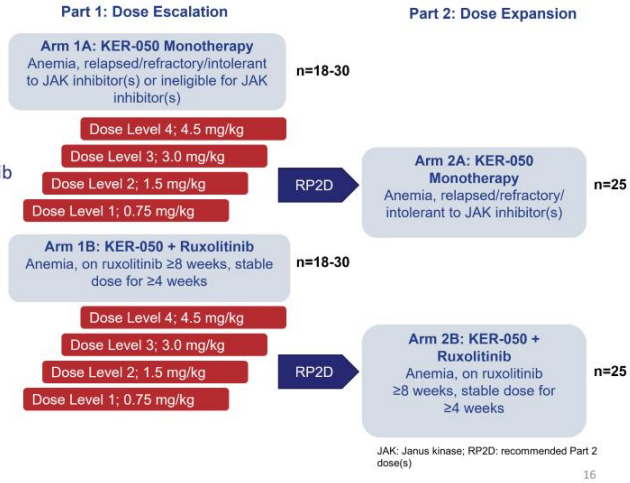
- MF is a group of rare cancers of the bone marrow in which the marrow is replaced by scar tissue and is not able to produce healthy blood cells
- MF is characterized by ineffective hematopoiesis, an enlarged spleen, bone marrow fibrosis and shortened survival. Patients often experience multiple disease-associated and treatment-emergent cytopenias, including anemia and thrombocytopenia
- The ineffective hematopoiesis in MF is driven by molecular abnormalities in the JAK-STAT signaling pathway, which leads to proliferation of red blood cell progenitors and platelet progenitors, or megakaryocytes
- The inability of megakaryocytes to fully differentiate leads to the release of pro-inflammatory and pro-fibrotic factors that results in scarring of the bone marrow, which further exacerbates the MF-associated cytopenias
- 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

**Ongoing, two-part, open-label Phase 2 clinical trial evaluating KER-050 administered with or without ruxolitinib in patients with MF who have anemia**

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

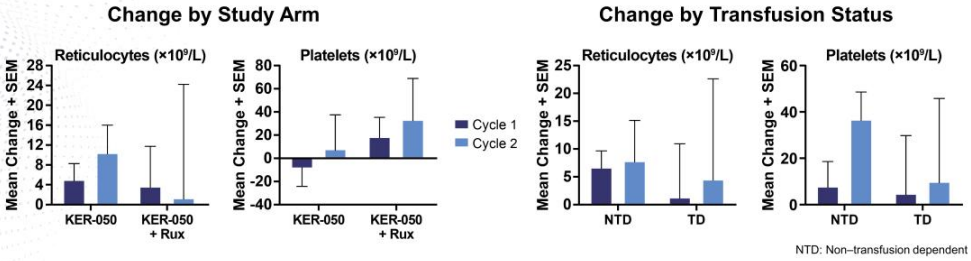
- **KER-050 was generally well tolerated at 0.75mg/kg***
  - No dose-limiting toxicities
  - Most frequent TEAEs reported by ≥ 2 patients were diarrhea (25.0%) and fatigue, dyspnea and COVID-19 (16.7% each)
  - 1 TEAE led to KER-050 dose modification: amyloidosis (unrelated)
  - No TEAEs led to either study treatment or study discontinuation




JAK: Janus kinase; RP2D: recommended Part 2 dose(s)

*Data cutoff date: 1-Oct-2022

# KER-050 Treatment Increased Reticulocytes and Platelets in MF Patients*



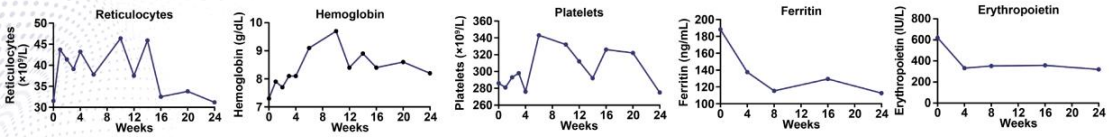

NTD: Non–transfusion dependent

- 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 effect of KER-050

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

*Data cutoff date: 1-Oct-2022

# Observed Increases in Red Blood Cells 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 was observed after a single dose of KER-050, and 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 cutoff date: 1-Oct-2022

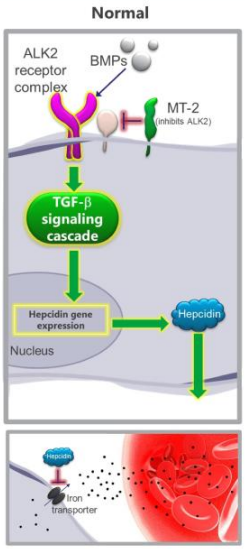
# KER-047

**A Novel Product Candidate Designed to Address Anemia in Patients with:**

- *Iron-Refractory Iron Deficiency Anemia (IRIDA)*
- *Functional Iron Deficiency (FID) in MDS and MF*

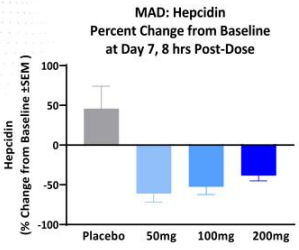
# Increased Hepcidin Expression Leads to Functional Iron Deficiency

- 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 exerts control and 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 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

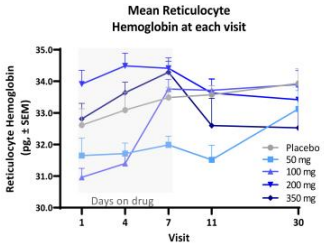


# KER-047 Treatment Reduced Hepcidin Levels and Increased Hemoglobin Content in Reticulocytes in a Phase 1 Clinical Trial

- 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

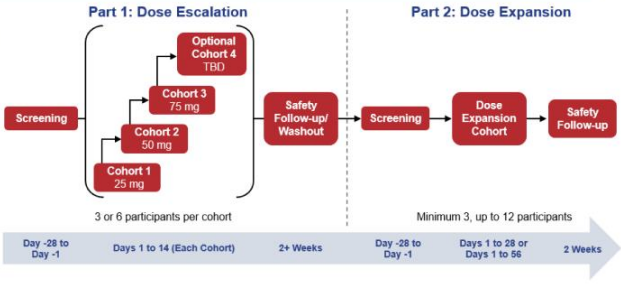



- An increase in reticulocyte hemoglobin was observed in Cohorts 1 through 4 of Part 2 of the trial, starting on Day 4 of treatment
- Pronounced increase in reticulocyte hemoglobin observed in cohorts with lower baseline reticulocyte hemoglobin

# KER-047 Treatment of One IRIDA Patient in a Phase 2 Clinical Trial Resulted in a Decrease in Hepcidin and an Increase in Reticulocyte Hemoglobin

**Ongoing, two-part, open-label dose-escalation and dose-expansion Phase 2 clinical trial in patients with IRIDA (an inherited form of iron deficiency anemia)**

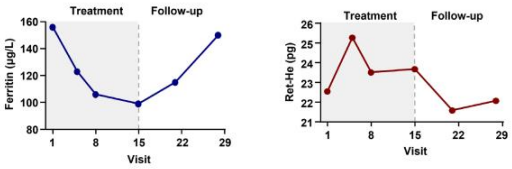
- Patients treated once daily with KER-047 for a 2-week period followed by a 2-week washout period
- **Primary objective:** Safety
- **Secondary objectives:** Pharmacokinetic and pharmacodynamic analyses




**In December 2022, we presented data from one patient that enrolled in Cohort 1 of this trial and completed 14 days treatment (KER-047 25 mg once daily) and 14-day follow-up:**

- A dose of 25 mg once daily was generally well tolerated; no serious adverse events or dose-limiting toxicities were observed during treatment
- **Changes in markers of iron metabolism:**
  - Consistent with results from our Phase 1 clinical trial of KER-047 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)**



# KER-012

A Clinical Program Designed to Address:

- *Pulmonary Arterial Hypertension (PAH)*
- *Cardiovascular Disorders*

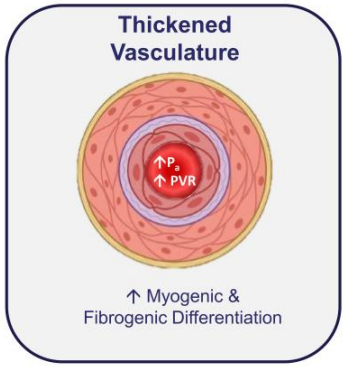
# Imbalances in TGF-β Superfamily Signaling Underlies Vascular Remodeling in PAH

- 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**

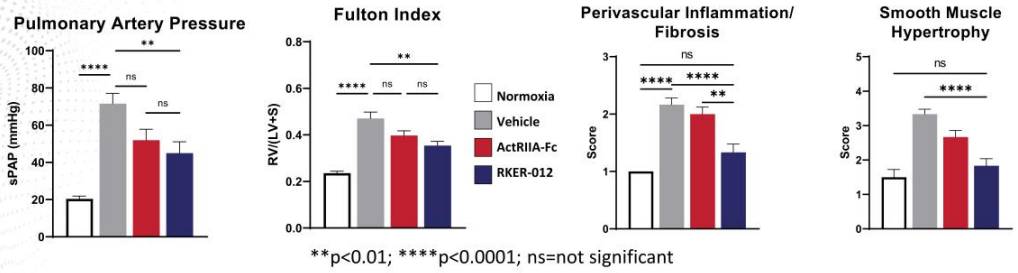
- Designed to rebalance TGF-β superfamily signaling
- Being developed for the treatment of pulmonary and cardiovascular disorders, including PAH
- KER-012 is designed to preferentially inhibit select ligands (activin A, activin B, GDF 8 and GDF 11) to potentially rebalance TGF-β superfamily signaling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

**Pulmonary Arterial Hypertension**



# RKER-012 Reduced Pulmonary Arterial Pressure and Right Ventricle (RV) Hypertrophy in a Rat PAH Model

In a head-to-head preclinical study, ActRIIA-Fc and RKER-012 demonstrated activity in the Sugen/hypoxia rat model of PAH:




**p<0.01; ****p<0.0001; ns=not significant

- Hypoxic rats were dosed with vehicle, ActRIIA-Fc (10 mg/kg) or RKER-012 (10 mg/kg), twice weekly for three weeks
  - Normoxic rats were dosed with vehicle
- Relative to vehicle-treated hypoxic rats, RKER-012:
  - Statistically significantly reduced RV hypertrophy and pulmonary arterial pressure
  - Statistically significantly reduced lung inflammation, fibrosis and smooth muscle hypertrophy

***RKER-012 consistently showed a trend towards improved activity relative to ActRIIA-Fc in this preclinical study***

# KER-012 was Well Tolerated in a Phase 1 Clinical Trial in Healthy Volunteers

**Key Inclusion Criteria:**

- Postmenopausal females aged 45 to 70 years
- Serum follicle stimulating hormone (FSH) levels > 40 IU/L
- BMI >18.5 kg/m$^2$ to <32.0 kg/m$^2$

**Part 1 and Part 2 Endpoints:**

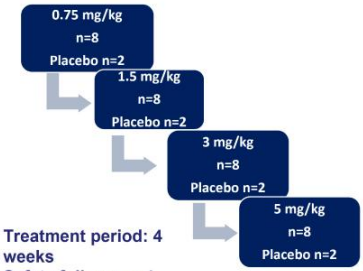
- Safety and pharmacokinetics
- Pharmacodynamic markers
  - FSH and serum biomarkers of bone formation and resorption

**Safety:**

KER-012 was generally well tolerated

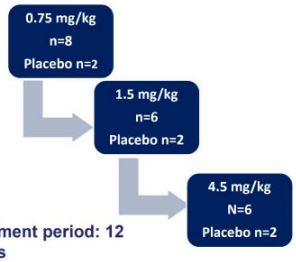
- No dose-limiting toxicities
- Most common adverse events were headache, backpain, diarrhea, COVID-19, pain in extremity and injection site erythema (increased incidence with increasing dose in Part 2 of the trial)
- No TEAEs led to either study treatment or study discontinuation

**Part 1: Single Ascending Dose (Double-blinded)**



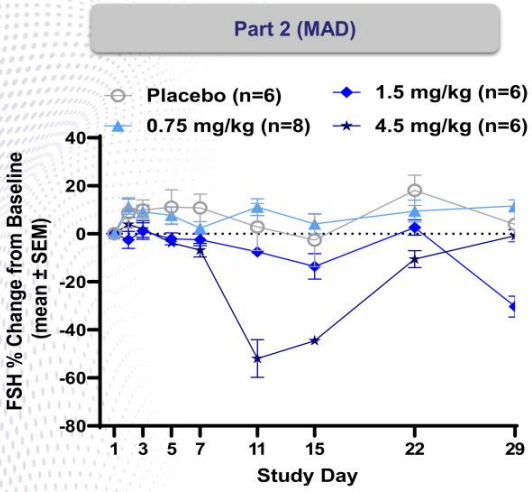

**Treatment period: 4 weeks**
**Safety follow up: 4 weeks**
**Single subcutaneous dose**

**Part 2: Multiple Ascending Dose (Double-blinded)**




**Treatment period: 12 weeks**
**Safety follow up: 4 weeks**
**Three subcutaneous doses (28 days apart)**

# KER-012 Treatment Indicate Maximal Target Engagement at the Highest Doses Tested in Phase 1 Clinical Trial




**Follicle stimulating hormone (FSH) secretion by the pituitary is controlled through signaling by the activin receptor and Gonadotropin Releasing Hormone (GnRH)**

- Approximately 50% of the FSH secretion is regulated via activin signaling and the other 50% by GnRH[1]
- Complete inhibition of activin signaling therefore would be expected to reduce FSH by ~50% in postmenopausal women, who have elevated FSH levels

**KER-012 treatment resulted in suppression of FSH**

- FSH suppression was observed in Part 1 (SAD) and Part 2 (MAD) of the trial
- In Part 2, maximal suppression was observed at the 4.5 mg/kg dose level with 5 of 6 subjects achieving ≥ 40% reduction in FSH

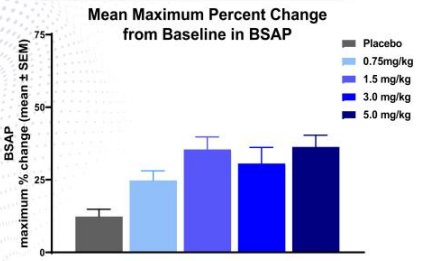
**The magnitude of FSH reduction in the highest doses tested suggest that KER-012 treatment maximally inhibited activin signaling**



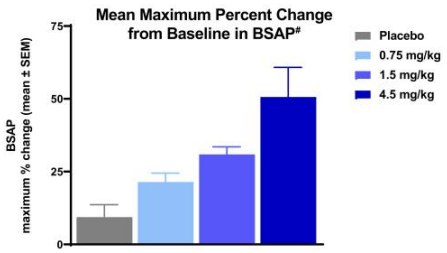
1. Rivier and Vale, Endocrinology 1991;129: 2160-2165

# KER-012 Treatment Changed Pharmacodynamic Markers Consistent with Increased BMP Signaling in the Bone in Phase 1 Clinical Trial

**Part 1 (SAD)**




**Part 2 (MAD)**

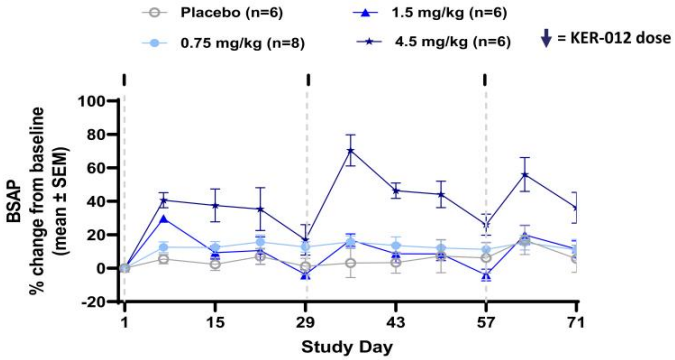



- Dose-dependent increases in serum bone specific alkaline phosphatase (BSAP) with maximal increase observed at the highest doses evaluated in this trial
- KER-012 is designed to inhibit activins and growth differentiation factor ligands (GDFs) in bone, which potentially results in reduced SMAD 2/3 signaling and increased signaling of the bone morphogenetic protein (BMP) pathway (SMAD 1/5/9)
  - The increased BMP signaling potentially promotes bone formation through a dual mechanism of activation/recruitment of bone forming osteoblasts and repression of osteoclasts, as demonstrated in preclinical studies[1]
- Increases in BSAP, a marker of osteoblast activity, were observed starting at the lowest dose tested in this trial

1. Materna C et al., Am Society Bone Mineral Res 2021 Annual Meeting. Sept 9-12, 2021, # Data shown post first dose only

# In Part 2 of the Phase 1 Clinical Trial, Treatment with KER-012 Resulted in an Increase in Serum BSAP After Each Administration

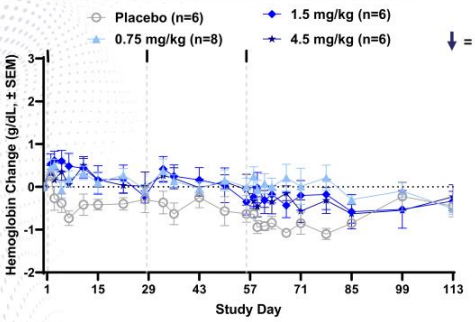
**Part 2: Multiple Ascending Doses**



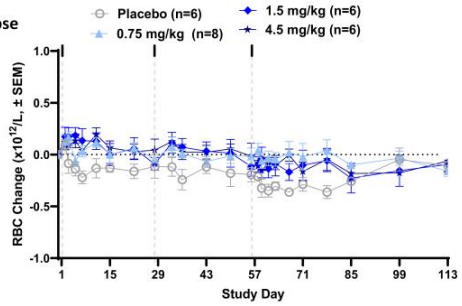

- KER-012 was administered at a 28-day interval in Part 2 (MAD) of the Phase 1 clinical trial in healthy volunteers
- **Observed increases in BSAP after each dose in Part 2 are supportive of activation of osteoblasts after each dose**

# KER-012 Did Not Elicit Dose-Limiting Increases in Red Blood Cells in Phase 1 Clinical Trial

**Mean Hemoglobin Change**




**Mean RBC Change**




- **KER-012 treatment did not elicit changes in hemoglobin or red blood cells**
  - No changes in RBCs observed after second or third dose
- The lack of effect on erythropoiesis in humans was consistent with lack of effect in multiple preclinical models[1,2]

1. Babbs K, et al. American Thoracic Society 2021 Annual Meeting; 2. Babbs K, et al. American Thoracic Society 2022 Annual Meeting

# Keros Summary

# 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 | H1 and H2 2023 |
| • Expand Phase 2 MDS trial to MDS patients with iron overload | 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 dose escalation data from Phase 2 IRIDA trial | H2 2023 |
| • Announce initial data from Phase 2 FID (MDS and MF) trial | H2 2023 |
| **KER-012** | |
| • Initiate Phase 2 PAH trial | H1 2023 |
| • Initiate Phase 2 open-label biomarker trial | H2 2023 |

*Anticipated clinical milestones are subject to the impact of COVID-19 on our business.