# 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): December 11, 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 8.01 Other Events.**

On December 11, 2023, Keros Therapeutics, Inc. (the "Company") issued a press release announcing additional data from its two ongoing Phase 2 clinical trials of KER-050, one in patients with very low-, low-, or intermediate-risk myelodysplastic syndromes ("MDS") and one in patients with myelofibrosis ("MF"), at the 65th American Society of Hematology Annual Meeting and Exposition, held in person and virtually from December 9 through 12, 2023. In addition, the Company presented preclinical data showing that a research form of KER-050 promoted erythropoiesis in an animal model of MF, as well as preclinical data evaluating the treatment effect of activin receptor-like kinase 2 inhibition in a mouse model of iron-refractory iron deficiency anemia. A copy of the press release is attached as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

During a conference call and webcast scheduled to be held at 8:00 a.m. Eastern time on December 11, 2023, the Company's management will discuss the additional data from its two ongoing Phase 2 clinical trials of KER-050, one in patients with MDS and one in patients with MF. 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 | Press release dated December 11, 2023. |
| 99.2 | Investor Presentation dated December 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: December 11, 2023

# Keros Therapeutics Presents Clinical Data from its KER-050 Program at the 65th American Society of Hematology Annual Meeting and Exposition

- *KER-050 (elritercept) achieved durable transfusion independence in lower-risk MDS, including in patients with high transfusion burden*
- *Durable clinical responses were associated with improvements in patient-reported measures of fatigue*
- *Biomarker data demonstrate that KER-050 treatment has potential to reduce NT-proBNP a measure of cardiac stress*
- *Preliminary findings from ongoing Phase 2 clinical trial in myelofibrosis demonstrate that KER-050 can not only ameliorate ineffective hematopoiesis and address cytopenias, but also provide broader clinical benefit seen through reduction of spleen size and improved symptoms*
- *Keros will be hosting a conference call and webcast today, December 11, 2023, at 8:00 a.m. ET*

LEXINGTON, Mass., Dec. 11, 2023 (GLOBE NEWSWIRE) -- Keros Therapeutics, Inc. (“Keros”) (Nasdaq: KROS), a clinical-stage biopharmaceutical company focused on developing and commercializing novel therapeutics to treat a wide range of patients with disorders that are linked to dysfunctional signaling of the transforming growth factor-beta (“TGF-ß”) family of proteins, today announced that it presented additional data from its two ongoing Phase 2 clinical trials of KER-050, one in patients with very low-, low-, or intermediate-risk myelodysplastic syndromes (“MDS”) and one in patients with myelofibrosis (“MF”), at the 65th American Society of Hematology (“ASH”) Annual Meeting and Exposition, held in person in San Diego and virtually from December 9 through 12, 2023. In addition, Keros presented preclinical data showing that a research form of KER-050 promoted erythropoiesis in an animal model of MF, as well as preclinical data evaluating the treatment effect of activin receptor-like kinase 2 inhibition in a mouse model of iron-refractory iron deficiency anemia.

“We believe the data presented at ASH from our ongoing KER-050 Phase 2 clinical trial in MDS supports the potential of KER-050 to ameliorate ineffective hematopoiesis and treat anemia and thrombocytopenia in difficult to treat patient populations, including those with greater transfusion burden and bone marrow dysfunction,” said Simon Cooper, MBBS, Chief Medical Officer of Keros. “Additionally, we are encouraged by the preliminary data from the lowest three dose cohorts from our ongoing Phase 2 clinical trial in MF. KER-050 treatment in combination with ruxolitinib and as KER-050 monotherapy led to improvements as assessed by changes in markers of hematopoiesis, reductions in spleen size and improvement in Total Symptom Score. We look forward to confirming this profile of benefit in the now enrolling dose confirmation part of our trial.”

“The encouraging broad profile of KER-050 that we have observed supports its potential to treat not just the disease-associated cytopenias, but also impact the pathogenesis of the respective diseases, as supported by the observed improvements in bone health and reduction of cardiac stress,” said Jasbir S. Seehra, Ph.D., President and Chief Executive Officer. “We are excited by the results we presented including the durability of transfusion independence observed with KER-050 and to engage with regulators in the first half of next year and look forward to sharing the design of a Phase 3 clinical trial evaluating KER-050 in lower-risk MDS following that feedback.”

Clinical Presentations

- *Durable Clinical Benefit with KER-050 treatment: Findings From an Ongoing Phase 2 Study in Participants with Lower-Risk MDS*

This ongoing, open-label, two-part, Phase 2 clinical trial is evaluating KER-050 in patients with very low-, low-, or intermediate-risk MDS. As of September 1, 2023 (the "data cut-off date"), 79 patients had received at least one dose of KER-050 at the recommended Part 2 dose ("RP2D") (collectively, the "safety population"). Of these patients, 60 had completed at least 24 weeks of treatment or discontinued as of the data cut-off date (collectively, the modified intent to treat 24-week population, or the "$mITT_{24}$ patients"). Data for hematological response and markers of hematopoiesis were presented from exploratory analyses of these $mITT_{24}$ patients. All data presented from this trial is as of the data cut-off date.

Of the 79 patients in the safety population, 55.7% (n=44) were high transfusion burden ("HTB") while 25.3% (n=20) were low transfusion burden and 19.0% (n=15) were non-transfused ("NT"). KER-050 was generally well tolerated by the 79 patients in the safety population. The most commonly reported treatment-emergent adverse events ("TEAEs") (in ≥15% of patients) were diarrhea, dyspnea, fatigue, nausea and headache. No patients had progressed to acute myeloid leukemia.

50% (n=30/60) of the $mITT_{24}$ patients achieved an overall erythroid response over the first 24 weeks of treatment, which is defined as meeting either modified IWG 2006 Hematological improvement-erythroid ("HI-E") or transfusion independence ("TI") for at least eight weeks in transfusion-dependent patients who required ≥ 2 red blood cell ("RBC") units transfused at baseline.

Additional data from the $mITT_{24}$ patients include:

- 39.1% (n=18/46) of the TI-evaluable patients achieved TI for at least eight weeks over the first 24 weeks of treatment. 13 of those 18 patients (72.2%) achieved TI for at least 24 weeks over the first 48 weeks of treatment.
- Of the patients with HTB, 33.3% (n=11/33) achieved TI for at least eight weeks during the first 24 weeks of treatment. 7 of those 11 patients (63.6%) achieved TI for at least 24 weeks over the first 48 weeks of treatment.
- Of the patients with baseline erythropoietin level less than 500 U/L, 44.7% (n=17/38) achieved TI for at least eight weeks over the first 24 weeks of treatment. Of the patients with baseline erythropoietin level less than 500 U/L and HTB, 38.5% (n=10/26) achieved TI for at least eight weeks over the first 24 weeks of treatment.

The FACIT-Fatigue scale, a measure of self-reported fatigue and its impact upon daily activities and function, was utilized to assess health-related quality of life in 45 of the $mITT_{24}$ patients who were TI-evaluable and with baseline FACIT-F assessment. A difference of three in the FACIT-Fatigue scale is considered a minimally clinically important difference. In this group, patients who achieved TI had durable and clinically meaningful improvements in self-reported fatigue. At Week 24, patients achieving TI of eight weeks or longer within first 24 weeks had a mean score of 5.8 (n=10) versus patients who did not achieve TI who reported a mean score of -3.2 (n=11), for a mean difference of 9.0. At Week 24, patients achieving TI of 24 weeks or longer with first 48 weeks had a mean score of 7.8 (n=9) versus patients who did not achieve TI who reported a mean score of -3.9 (n=12), for a mean difference of 11.7.

The majority of patients enrolled in this ongoing trial had HTB or multi-lineage dysplasia, indicating a difficult-to-treat trial population. Durable TI responses were observed in a broad range of patients with lower-risk MDS, including in those with HTB, which support the potential for KER-050 to ameliorate ineffective hematopoiesis across multiple lineages in patients with MDS. Patients who achieved TI showed clinically meaningful improvements in FACIT-Fatigue scores, indicating that KER-050 may improve quality of life in patients with lower-risk MDS.

- *KER-050 Treatment Reduced Iron Overload and Increased Bone Specific Alkaline Phosphatase in Participants with Lower-risk MDS Supporting Potential to Restore Balance to the Osteohematopoietic Niche*

Exploratory analysis of biomarkers that may indicate MDS disease modification were evaluated as of the data cut-off date in the ongoing Phase 2 clinical trial of KER-050 in patients with MDS. Observations from these biomarkers included improvements in:

- Iron metabolism: 48.3% (n=14/29) of patients with baseline ferritin ≥ 1,000 ng/ml had a decreased ferritin to < 1000 ng/ml and 69.0% (n=20/29) of patients decreased ferritin by ≥20%. Two patients, including one who was NT, discontinued iron chelator therapy due to observed decreases in ferritin. These data support potential of KER-050 to ameliorate iron overload.
- Hematopoiesis: Sustained increases in hemoglobin for 24 weeks coincided with observed increases in soluble transferrin receptor and concomitant decreases in serum ferritin, suggesting KER-050 resulted in durable restoration of erythropoiesis and improved iron metabolism.
- Bone turnover: Increases in bone-specific alkaline phosphatase, a marker of osteoblast activity, were observed with KER-050 treatment regardless of hematological response, baseline transfusion burden or RS status, suggesting KER-050 can potentially restore a bone marrow microenvironment conducive to functional hematopoiesis.
- Cardiac stress: Levels of N-terminal prohormone of brain natriuretic protein, a biomarker of myocardial stress, decreased in both HI-E and/or TI responders and non-responders, suggesting that KER-050 may ameliorate cardiac strain directly via inhibition of activin A and indirectly by improving anemia and reducing transfusion burden.

Collectively, these exploratory data suggest that KER-050 has the potential to provide benefit to patients with MDS beyond treatment of anemia, such as reestablishing hematopoiesis across multiple cell lineages, restoring homeostasis within the osteohematopoietic niche and ameliorating myocardial strain.

- *Modulation of TGF-β Superfamily Signaling by KER-050 Demonstrated Potential to Treat Myelofibrosis and Mitigate Ruxolitinib-Associated Cytopenias*

This ongoing, open-label, two-part Phase 2 clinical trial is evaluating KER-050 administered with or without ruxolitinib in patients with MF who have anemia and were either currently on, failed, or ineligible for ruxolitinib at baseline. Safety data are presented for all patients that received at least one dose of KER-050 in Part 1 (n=41) as of September 14, 2023. Evaluations of markers of hematopoiesis and anemia over 12 weeks, along with measurements of spleen volume and symptom scores (by the MF-symptom assessment form-Total Symptom Score, or "MF-SAF-TSS") over 24 weeks, were presented for dose levels 1 through 3, ranging from 0.75 mg/kg to 3.0 mg/kg (collectively, the "efficacy evaluable patients"). Data for dose level 4 (4.5 mg/kg), the highest dose level being evaluated in Part 1, are not included due to limited exposure as of the data cutoff date. All data presented from this trial is as of the September 14, 2023 data cut-off date.

KER-050 was generally well tolerated by the safety population. There was one dose-limiting toxicity reported from a patient in the 1.5mg/kg dose level of the monotherapy arm. The patient had an increase in hemoglobin of at least 2 g/dL, which met protocol criteria for dose reduction at the end of cycle 1. There were no adverse events associated with this event, and the maximum observed hemoglobin remained within normal limits. There were three cases of fatal TEAEs in the trial that were each deemed unrelated to treatment. The most commonly reported TEAEs (in ≥10% of patients) were diarrhea, thrombocytopenia, asthenia (weakness), fatigue and pyrexia (fever). Treatment-related TEAEs were relatively infrequent, most of which were mild to moderate, with two patients experiencing Grade 3 or higher worsening cytopenias.

Additional data from the efficacy evaluable patients include:

- Increases in hemoglobin were observed in non-transfusion dependent patients in both arms, suggesting that KER-050 has the potential to address anemia due to MF and ruxolitinib-associated anemia.
  - Additionally, most patients had reductions in transfusion burden, including patients receiving up to 15 RBC units per 12 weeks at baseline.
- Non-transfusion dependent patients, who received a median of three RBC units per 12 weeks at baseline, experienced sustained increases in hemoglobin within the first 12 weeks of treatment in both the monotherapy and combination arms (pooled across dose cohorts).
  - Additionally, observed increases in soluble transferrin receptor, reticulocytes and hemoglobin were generally higher with increasing dose levels between 0.75 mg/kg to 3.0 mg/kg (pooled across both monotherapy and combination arms at each dose level).
- At week 24, reduction in spleen size was observed in 57.1% (n=4/7) of patients with baseline spleen size ≥ 450 $cm^3$ and a week 24 spleen assessment, including one of three patients in the monotherapy arm and three of four patients in the combination arm.
- At week 24, decrease in disease symptoms was observed in 66.7% (n=8/12) of patients with at least two symptoms with an average score ≥ 3 or an average total score of ≥ 10 on the MF-SAF-TSS questionnaire at baseline and a week 24 MF-SAF-TSS assessment.

The data support the potential of KER-050 to ameliorate ineffective hematopoiesis and address cytopenias due to MF and associated with ruxolitinib, and provide broader clinical benefit in patients as observed by the reduction in spleen size and improvement in symptoms.

**Conference Call and Webcast Information**

Keros will host a conference call and webcast today, December 11, 2023, at 8:00 a.m. Eastern time, to discuss the additional data from its two ongoing Phase 2 clinical trials of KER-050, one in patients with MDS and one in patients with MF, which was presented at the 65th ASH Annual Meeting and Exposition.

The conference call will be webcast live at: https://event.webcasts.com/starthere.jsp?ei=1645187&tp_key=cad9574144. The live teleconference may be accessed by dialing (877) 407-0309 (domestic) or (201) 389-0853 (international). An archived version of the call will be available in the Investors section of the Keros website at https://ir.kerostx.com/ for 90 days following the conclusion of the call.

**About the Ongoing Phase 2 Clinical Trial of KER-050 in Patients with MDS (NCT04419649)**

Keros is conducting an open label, two-part, multiple ascending dose Phase 2 clinical trial to evaluate KER-050 in patients with very low-, low-, or intermediate-risk MDS who either have or have not previously received treatment with an erythroid stimulating agent.

The primary objective of this trial is to assess the safety and tolerability of KER-050 in patients with MDS that are RS positive or non-RS. The primary objective of Part 2 of this trial is confirmation of the safety and tolerability of the RP2D (3.75 mg/kg and 5.0 mg/kg). The secondary objectives of this trial are to evaluate the pharmacokinetics, pharmacodynamics and efficacy of KER-050.

**About the Ongoing Phase 2 Clinical Trial of KER-050 in Patients with MF-Associated Cytopenias (RESTORE trial)**

Keros is conducting an open label, two-part, multiple ascending dose Phase 2 clinical trial to evaluate KER-050 as a monotherapy and in combination with ruxolitinib in patients with MF-associated cytopenias.

The primary objective of this trial is to assess the safety and tolerability of KER-050 in patients with MF-associated cytopenias. The primary objective of Part 2 of this trial is confirmation of the safety and tolerability of the RP2D (3.75 mg/kg and 5.0 mg/kg). The secondary objectives of this trial are to evaluate the pharmacokinetics, pharmacodynamics and efficacy of KER-050 administered with or without ruxolitinib.

**About KER-050**

Keros' lead protein therapeutic product candidate, KER-050, is an engineered ligand trap comprised of a modified ligand-binding domain of the TGF-ß receptor known as activin receptor type IIA that is fused to the portion of the human antibody known as the Fc domain. KER-050 is being developed for the treatment of low blood cell counts, or cytopenias, including anemia and thrombocytopenia, in patients with MDS and in patients with MF.

**About Keros Therapeutics, Inc.**

Keros is a clinical-stage biopharmaceutical company focused on developing and commercializing novel therapeutics to treat a wide range of patients with disorders that are linked to dysfunctional signaling of the TGF-ß family of proteins. We are a leader in understanding the role of the TGF-ß family of proteins, which are master regulators of the growth, repair and maintenance of blood cells and a number of tissues, including bone, skeletal muscle, adipose and heart tissue. By leveraging this understanding, we have discovered and are developing large and small molecules that have the potential to provide meaningful and potentially disease-modifying benefit to patients. Keros' lead protein therapeutic product candidate, KER-050 (elritercept), is being developed for the treatment of low blood cell counts, or cytopenias, including anemia and thrombocytopenia, in patients with MDS and in patients with MF. Keros' second product candidate, KER-012, is being developed for the treatment of pulmonary arterial hypertension and for the treatment of cardiovascular disorders. Keros' third product candidate, KER-065, is being developed for the treatment of neuromuscular diseases, with an initial focus on Duchenne muscular dystrophy.

**Cautionary Note Regarding Forward-Looking Statements**

Statements contained in this press release 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 "believes," "expects," "intends," "plans," "potential," "projects," "would" and "future" or similar expressions such as "look forward" 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 clinical trials for KER-050, including its regulatory plans; the potential of KER-050 to treat beyond MF- and MDS-associated cytopenias to have a direct effect on the pathogenesis of MF and MDS, respectively; the potential of KER-050 to ameliorate ineffective hematopoiesis across multiple lineages in patients with MDS and to improve quality of life in patients with lower-risk MDS; and the potential of KER-050 to address anemia due to MF and ruxolitinib-associated anemia. 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-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 November 6, 2023, and its other documents subsequently filed with or furnished to the SEC. All forward-looking statements contained in this press release 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.

**Investor Contact:**
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KEROS
THERAPEUTICS
Hematology Franchise:
Update at 65th Annual Congress of the
American Society of Hematology
December 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-012 and KER-065, including its regulatory plans; 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-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.

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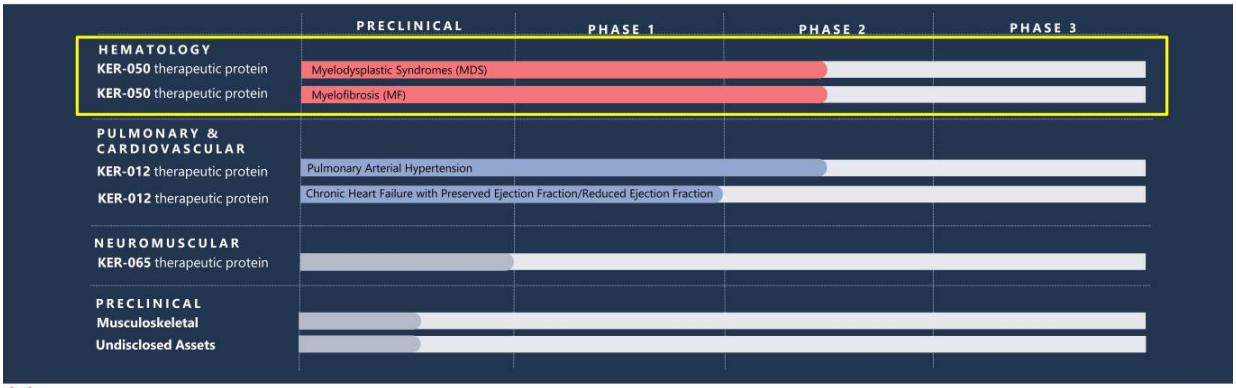
Certain information contained in this presentation relates to or is based on studies, publications, surveys and other data obtained from third-party sources and the Company's own internal estimates and research. While we believe these third-party sources to be reliable as of the date of this presentation, 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 a 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**



# 65th American Society of Hematology Annual Meeting and Exposition

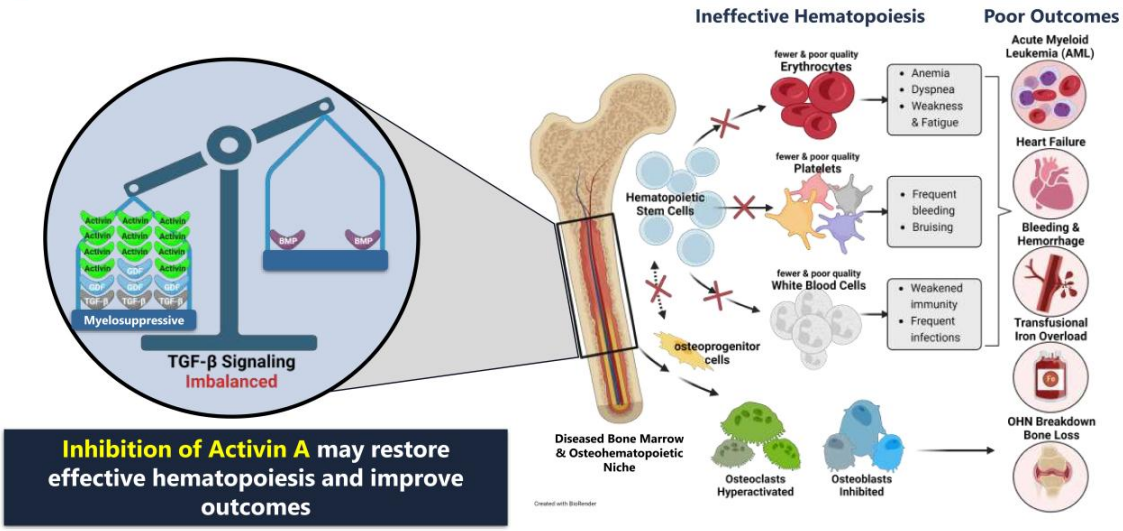
## Clinical Presentations

- "*Durable Clinical Benefit with KER-050 treatment: Findings From an Ongoing Phase 2 Study in participants with Lower-Risk MDS*" – Publication Number: 196
- *"KER-050 Treatment Reduced Iron Overload and Increased Bone Specific Alkaline Phosphatase in participants with Lower-Risk MDS Supporting Potential to Restore Balance to the Osteohematopoietic Niche"* – Publication Number: 1089
- *"Modulation of TGF-β Superfamily Signaling By KER-050 Demonstrated Potential to Treat Myelofibrosis and Mitigate Ruxolitinib-Associated Cytopenia"* – Publication Number: 3185

## Preclinical Presentations

- *"RKER-050, A Modified Activin Receptor Type IIA Ligand Trap, Promoted Erythropoiesis in a Murine Model of Myelofibrosis"* – Publication Number: 4524
- *"RKER-216 Reversed Microcytic Anemia in a Mouse Model of Iron Refractory Iron Deficiency Anemia"* – Publication Number: 2466

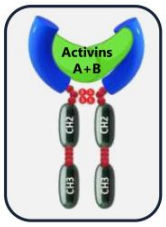
# Imbalanced TGF-β Signaling in Bone Marrow Results in Ineffective Hematopoiesis and Poor Outcomes in Both MDS and MF[1,2,3]




**Inhibition of Activin A may restore effective hematopoiesis and improve outcomes**

1. Verma A, et al. J Clin Inv 2020; 2. Portale F, et al., Haematologica. 2019, 3. Rambaldi B., et al, Ann Hematol. 2021
BMP = bone morphogenetic protein; GDF = growth differentiation factor; TGF-β = transforming growth factor-β

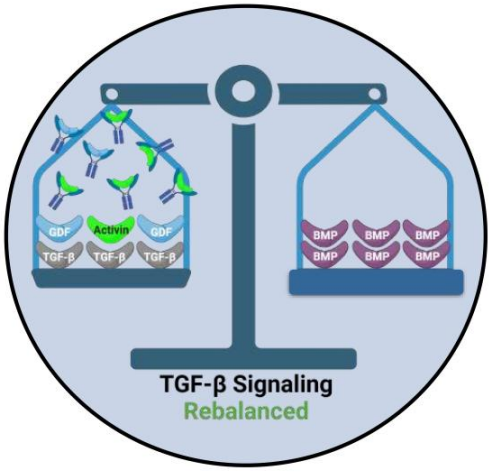
# KER-050 is Designed to Target Bone Marrow Disorders of Ineffective Hematopoiesis Including MDS and MF

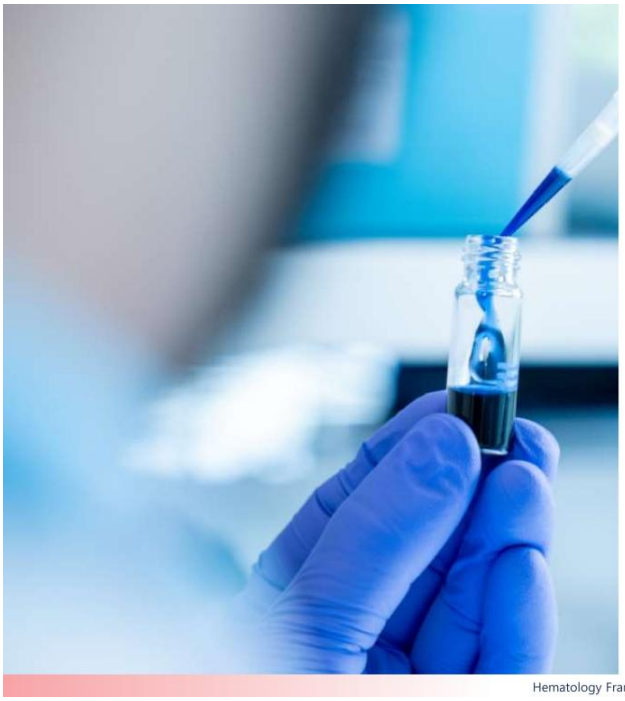



**KER-050 (elritercept)**

- **Designed to inhibit select TGF-beta ligands, including Activin A, which has been associated with driving disease pathogenesis and progression**

| Domain | Effect |
|---|---|
| Erythropoiesis | ALL stages of differentiation and maturation |
| Thrombopoiesis | ALL stages of differentiation and maturation |
| Bone | Increased bone formation |
| Iron Metabolism | Improved iron utilization |





# KER-050 (Elritercept)

## 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)

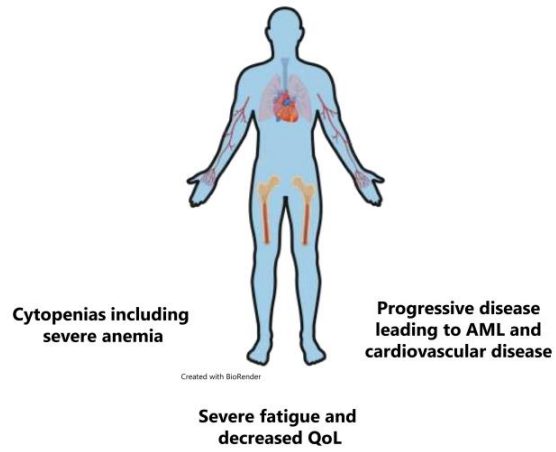
### MDS
MDS is a collection of bone marrow disorders characterized by ineffective hematopoiesis and peripheral cytopenias.

### 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.

**Impact of MDS**




QoL = quality of life

# Current Treatment Landscape for Treatment of Anemia in Lower Risk MDS

### RBC Transfusions

- RBC transfusions provide symptomatic relief of anemia
- Transfusion dependency is associated with iron overload, further exacerbating damage to the bone marrow and increasing risk of AML progression and cardiovascular disease
- Prolonged transfusion dependence is associated with shorter overall survival

### Erythroid Stimulating Agents

- ESAs are currently first line treatment of choice but response is limited in patients with endogenous erythropoietin levels (>200 U/L) and high transfusion burden (≥4 units of RBC/8 weeks)

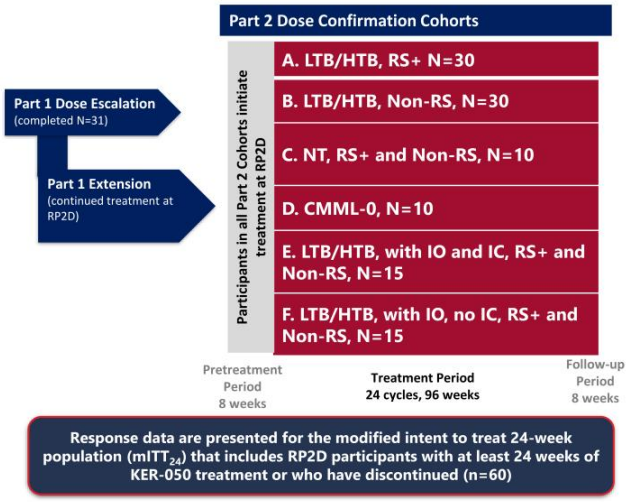
### Erythroid Maturation Agent

- Reblozyl approved in 1st and 2nd line MDS
- In second line treatment, only 20% of high transfusion burden (HTB) patients achieved 8-week transfusion independence with Reblozyl® versus 4% with placebo[1]
- In 2nd line setting, "patient reported outcome (PRO) data showed no improvement in quality of life for patients who received luspatercept or who responded to luspatercept." *(Medical reviewer from the luspatercept FDA review document Page 11 4/3/2020)*

**Unmet need remains for treatment that can address the multifaceted pathophysiology of MDS**

1. Fenaix P, et al. New Eng J Med 2020; 382:140-151

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




**Response data are presented for the modified intent to treat 24-week population ($mITT_{24}$) that includes RP2D participants with at least 24 weeks of KER-050 treatment or who have discontinued (n=60)**

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

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

**Key Eligibility Criteria:**
- MDS per 2016 WHO criteria, RS+ or non-RS, very-low, low, or intermediate risk disease (LR-MDS) by IPSS-R with anemia (NT, LTB, HTB)
  - CMML in Cohort D

**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 Data Cutoff Date:**
- Part 1 Extension Ongoing
- RP2D: 3.75 mg/kg with the ability to titrate to 5 mg/kg Q4W
- RP2D experienced patients: N=79
  - 7 (8.9%) patients received ≤3 doses
  - 50 (63%) patients were ongoing and remained on treatment
  - Median duration of treatment = Approx. 29 weeks (Range = Approx. 4 to 114 weeks)
  - Median doses received = 7 (range 1 to 28 doses)
  - 22 (27.8%) patients received ≥12 doses

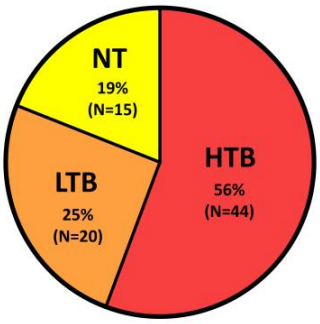
**Data are presented as of a data cutoff date of September 1, 2023.**

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; RS = ring sideroblasts.; IO = Iron Overload; IC = Iron Chelation

# Trial Enrolled Hard-to-Treat Patients with High Disease Burden

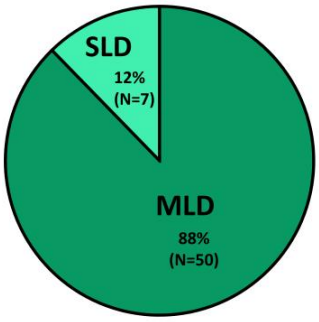
| Baseline Characteristic | RP2D (N=79) |
|---|---|
| Median age, years (range) | 75 (53, 89) |
| Sex, male, n (%) | 50 (63.3) |
| Hemoglobin, g/dL, median (range) | 8.37 (3.7, 10.5) |
| RS+, n (%)<br>Non-RS, n (%) | 57 (72.2)<br>22 (27.8) |
| Prior ESA, n (%) | 21 (26.6) |
| Median baseline EPO level, U/L (range)* | 127.8 (1, 4000) |
| Thrombocytopenia, n (%) (platelets < 150 x $10^9$/L) | 20 (25) |

**Baseline Transfusion Burden**




- 44 (56%) had high transfusion burden (HTB, ≥4 RBC units/8 weeks)
- 25 (32%) heavily transfused (≥ 6 RBC units/8 weeks)

**Baseline Dysplasia Category****




- 50 (88%) had multi-lineage dysplasia (MLD)

**Data are presented as of a data cutoff date of September 1, 2023.**
*9 RP2D patients had missing baseline EPO; **Excludes 22 RP2D participants with unknown dysplasia category
EPO= erythropoietin, SLD = single lineage dysplasia; MLD = multi lineage dysplasia

# KER-050 was Generally Well-tolerated

- **Most frequent TEAEs (≥ in 15% of patients) regardless of causality were:**
  - Dyspnea or diarrhea (18; 22.8% each)
  - Fatigue (16; 20.3%)
  - Nausea (15; 19.0%)
  - Headache (12; 15.2%)
- **Most TEAEs were mild (Grade 1) to moderate (Grade 2)**
- **3 treatment-related TESAEs of injection site reaction (Grade 2), dyspnea (Grade 3), and syncope (Grade 3) occurred in 1 patient each**
  - Dyspnea and syncope were assessed as not related to study treatment by the Sponsor due to underlying co-morbidities
- **Fatal TESAEs (cardiac failure and myocardial infarction) occurred in 2 (2.5%) patients; both were assessed as unrelated by the PI and Keros**
- **No patients progressed to AML**

| Category | RP2D (N=79) n (%) |
|---|---|
| **Any TEAE** | **74 (93.7)** |
| **Any treatment-related TEAE** | **33 (41.8)** |
| **Any TESAE** | **28 (35.4)** |
| **Any treatment-related TESAE** | **3 (3.8)** |
| **Any TEAE leading to death** | **2 (2.5)** |
| **Any TEAE leading to KER-050 discontinuation*** | **11 (13.9)** |

***Treatment-related TEAEs leading to KER-050 discontinuation: injection site reaction, platelet count increased, and dyspnea**

**Unrelated TEAEs leading to KER-050 discontinuation: nodular melanoma, NSCLC, MI, dementia Alzheimer's type, dyspnea, cardiac failure, and COPD & cardiac failure congestive (both in 1 patient)**

Treatment-related = considered to be related to the study treatment by the treating investigator.
Number and percent of patients with events were summarized.

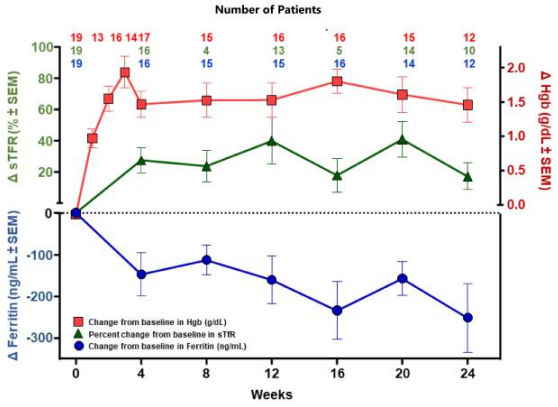
**Data are presented as of a data cutoff date of September 1, 2023.**
AML = acute myeloid leukemia; COPD = chronic obstructive pulmonary disease; MI = myocardial infarction; NSCLC = non-small cell lung cancer; TEAE = treatment emergent adverse event; TESAE = treatment emergent serious adverse event

# KER-050 Treatment Led to Sustained Increases in Hemoglobin

- Durable increases in hemoglobin were achieved in NT and LTB patients
- Increases in sTfR a marker of erythropoiesis and decreases in serum ferritin were also observed

**Collectively, suggests KER-050 resulted in durable restoration of erythropoiesis and improved iron metabolism**

Observed Change in HgB, sTfR, and Ferritin



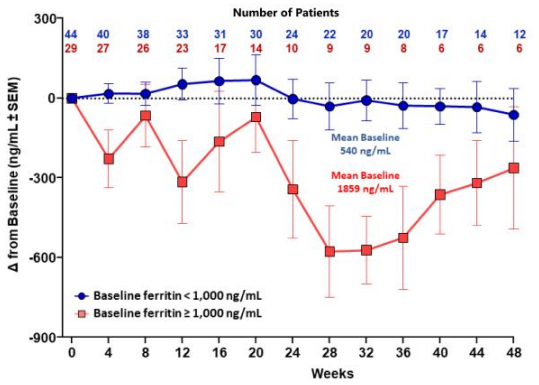

**Data are presented as of a data cutoff date of September 1, 2023.**
Hgb=hemoglobin; sTfR=soluble transferrin receptor

# Treatment of KER-050 Led to Decreased Iron Overload Regardless of Transfusion Burden in Exploratory Analysis

- **Among the 29 patients with baseline ferritin ≥ 1,000 and post-baseline measurements:**
  - 14 (48%) showed decreases of ferritin to <1000 ng/ml while on treatment
  - 20 (69%) showed a ≥20% reduction in ferritin while on treatment
  - 2 patients, including one who was NT, discontinued iron chelator therapy due to decreases in ferritin observed while on treatment

**Supports KER-050 potential to ameliorate iron overload in patients with MDS, regardless of baseline transfusion burden**

**Observed Change in Serum Ferritin by Baseline Ferritin**



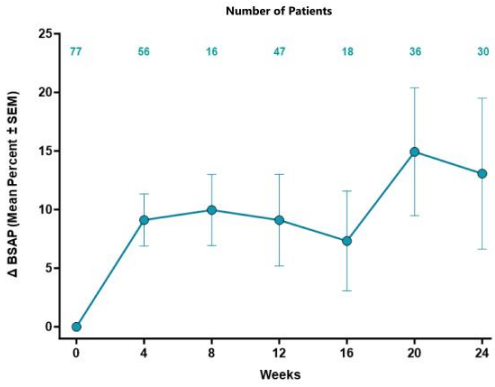

**Data are presented as of a data cutoff date of September 1, 2023.**
Hgb=hemoglobin; sTfR=soluble transferrin receptor

# Potential of KER-050 to Restore Osteohematopoietic Environment in Exploratory Analysis

- **In MDS, disrupted crosstalk between hematopoietic stem cells and osteoprogenitors within the OHN leads to suppression of bone formation (osteogenesis) and hematopoiesis[1]**
- **BSAP (bone-specific alkaline phosphatase) is a marker of osteoblast activity**
- **Sustained increase in BSAP observed with KER-050 treatment**
  - Seen regardless of hematologic response, baseline transfusion burden, or RS status

**Findings are consistent with preclinical studies and support KER-050's potential to act on multiple components of the OHN to restore a bone marrow microenvironment conducive to functional hematopoiesis**

**Observed Changes in BSAP**




**Data are presented as of a data cutoff date of September 1, 2023.**
1. Moses B, et al. ASH 2022;
OHN=osteohematopoietic niche

# Hematologic Responses Observed in Broad Array of Patients Treated with KER-050

| Responders/N (%) | $mITT_{24}$ | |
|---|---|---|
| | All (N=60) | HTB (N=33) |
| **Overall Response[a,b]** | **30/60 (50)** | **15/33 (45.5)** |
| **Modified IWG 2006 HI-E[c]** | **28/60 (47)** | **15/33 (45.5)** |
| **RS+** | 23/40 (58) | 12/23 (52.2) |
| **non-RS** | 5/20 (25) | 3/10 (30) |
| **TI ≥8 weeks[d]** | **18/46 (39.1)** | **11/33 (33.3)** |
| **RS+** | 15/32 (46.9) | 8/23 (34.8) |
| **non-RS** | 3/14 (21.4) | 3/10 (30) |

**HI-E and TI response rates in $mITT_{24}$ patients with HTB were similar to those observed in the overall $mITT_{24}$ population, supporting the potential for KER-050 to treat a broad array of patients with MDS including those with greater transfusion burden and bone marrow dysfunction**

**Data are presented as of a data cutoff date of September 1, 2023.**
a. Includes data for weeks 0-24 in $mITT_{24}$ patients; b. Defined as achieving modified IWG 2006 HI-E and/or TI; c. Modified HI-E = mean increase in hemoglobin ≥1.5 g/dL (NT+LTB) or reduction in transfusion of ≥4 RBC units (HTB) over 8 weeks on treatment compared to 8-week pre-treatment period; d. TI-evaluable patients received at least 2 RBC units in the 8-week pre-treatment period;
$mITT_{24}$ = modified intent to treat 24-week population; TI = transfusion independence

# Higher Hematologic Response Rates Observed in Patients with Baseline EPO <500 U/L

| Responders/N (%) | $mITT_{24}$ EPO<500 U/L[a] | |
|---|---|---|
| | All (N=50) | HTB (N=26) |
| **Overall Response[a,b]** | **28/50 (56.0)** | **14/26 (53.8)** |
| **Modified IWG 2006 HI-E[c]** | **26/50 (52.0)** | **14/26 (53.8)** |
| **RS+** | 21/36 (58.3) | 11/20 (55) |
| **non-RS** | 5/14 (35.7) | 3/6 (50) |
| **TI ≥8 weeks[d]** | **17/38 (44.7)** | **10/26 (38.5)** |
| **RS+** | 14/29 (48.3) | 7/20 (35) |
| **non-RS** | 3/9 (33.3) | 3/6 (50) |

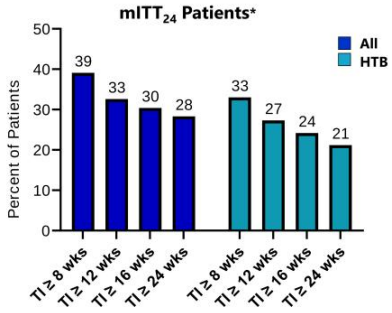
- **Studies in mainly LR-MDS patients suggest that the majority (~90%) of patients have serum EPO levels < 500 U/L[1]**
- **EPO levels ≥500 U/L are associated with lower erythroid response rates across multiple treatments[1]**
- **9 patients in the $mITT_{24}$ population had baseline EPO levels ≥ 500 U/L:**
  - 6/9 had non-RS MDS
  - 3/9 were reclassified by IPSS-M as having high or very-high risk disease

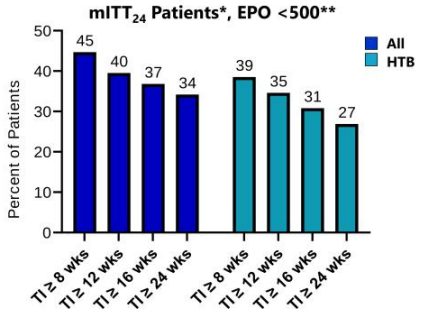
**Data are presented as of a data cutoff date of September 1, 2023.**

a. Includes data for weeks 0-24 in $mITT_{24}$ patients, excluding one patient with del5q MDS although their baseline EPO was <500 U/L; b. Defined as achieving modified IWG 2006 HI-E and/or TI; c. Modified HI-E = mean increase in hemoglobin ≥1.5 g/dL (NT+LTB) or reduction in transfusion of ≥4 RBC units (HTB) over 8 weeks on treatment compared to 8-week pre-treatment period; d. TI-evaluable patients received at least 2 RBC units in the 8-week pre-treatment period

1. Park, S et al. Annals of Hematology. 2020.

# Observed Rates of TI for ≥24 Weeks Support Durability of Response with KER-050 Treatment

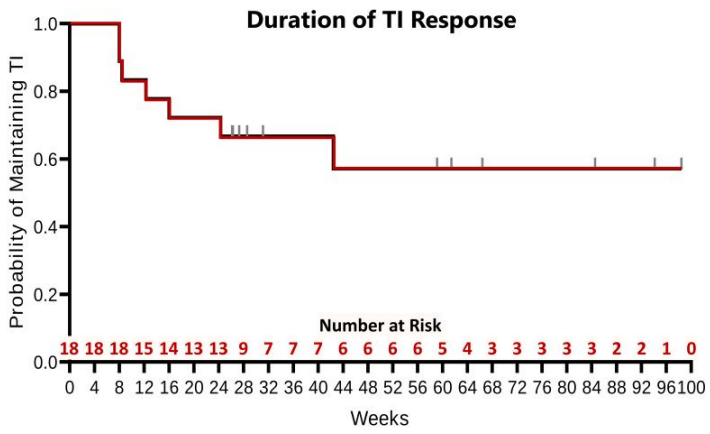



**Durable TI was observed including in patients with HTB, and response rates were relatively higher in patients with baseline EPO < 500 U/L**

**Data are presented as of a data cutoff date of September 1, 2023.**
*During Weeks 0-48; **Excludes 1 patient with del5q MDS

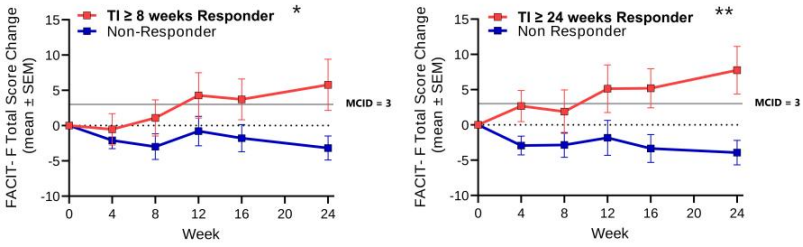
# Durable TI Responses Observed with KER-050 Treatment




- **18 participants in the mITT$_{24}$ population had TI ≥ 8 weeks**
  - 11/18 (61.1%) had HTB
  - 13/18 (72%) had TI ≥ 24 weeks
- **11/18 (61.1%) had ongoing TI at time of data cut-off**
  - Median baseline transfusion burden: 4 RBC units/8 weeks (range 2 to 11)
  - 6/11 (54.5%) had ongoing TI for > 52 weeks including participants who had received up to 11 RBC units/8 weeks at baseline
- **Median duration of response not reached (range: 8 to 98 weeks)**

**Data are presented as of a data cutoff date of September 1, 2023.**
Longest TI interval through KER-050 treatment for mITT$_{24}$ patients who achieved TI≥8 weeks during weeks 0-24; Patients with ongoing response censored at time of cutoff (denoted by vertical lines)

# Durable and Clinically Meaningful Improvements in FACIT-Fatigue Scores were Observed in TI Responders to KER-050



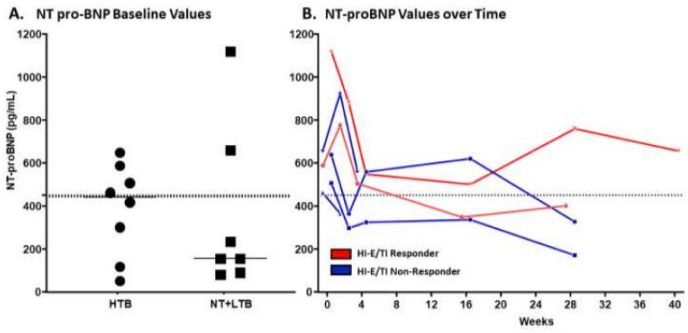

- **Health-related quality of life (HRQOL) is negatively impacted by MDS[1,2] with fatigue identified as a critically important domain to assess in patients with MDS[3]**
  - Prolonged transfusion dependence is associated with significantly worse HRQOL and shorter overall survival[3]
  - Evidence suggests that worse fatigue is associated with reduced survival in MDS[4]
  - The FACIT-Fatigue scale is a validated measure of self-reported fatigue and its impact upon daily activities and function that has been widely used in MDS studies[4,5]

**Data are presented as of a data cutoff date of September 1, 2023.**
*Includes data for mITT$_{24}$ patients with baseline FACIT-Fatigue scores (n = 1 missing) for TI ≥ 8 weeks Responder, assessed from Weeks 0 to 24; ** Includes data for mITT$_{24}$ patients with baseline FACIT-Fatigue scores (n = 1 missing) for TI ≥ 24 weeks Responder, assessed from Weeks 0 to 48;
1. Stauder, R et. al., Blood. 2018; 2. Pleyer, Lisa, et al., Cancers. 2023; 3. Santini V. Et al., Clin Lymphoma Myeloma Leuk. 2018; 4. Oliva EN et al., Blood. 2021; 5. Sekeres M. et al., HemaSphere. 2023;
MCID = minimally clinically important difference

# Potential of KER-050 to Reduce Cardiac Stress in Exploratory Analysis

- In patients with LR-MDS, cardiovascular (CV) events represent a major cause of death possibly due to myocardial stress exacerbated by chronic anemia and iron overload in MDS[1-3]; NT-proBNP is a biomarker of myocardial stress
- Activin A has been shown to play a pathophysiologic role in CVD[4,5], and has been associated with inflammation[6], vascular and myocardial remodeling[7,8], myocardial infarction[9] and severity of HF[10]
- Decreases in NT-proBNP were observed rapidly following initiation of dosing and were sustained for the majority of individuals regardless of erythropoietic response

**Observed Decreases in NT-proBNP**




**Suggests KER-050 may ameliorate cardiac strain directly via inhibition of activin A and indirectly by improving anemia and reducing transfusion burden**

**Data are presented as of a data cutoff date of September 1, 2023.**

1. Madry et al, Br J Haematol 2022; 2. Oliva E, et al. Am J Blood Res 2011; 3. Gatterman N Int J Hematol 2018; 4. Yndestad A J Appl Physiol. (2009) 106:1356–64; 5. Liu H et al Arteriosclerosis,Thrombosis, and Vascular Biology. 2023;43:330–349; 6. Phillips D, et al. Cytokine Growth Factor Reviews 2009; 20(2):153-164; 7. Ryanto G, et al. Int J Mol Sci 2023; 24(4), 3332; 8. Lin JF, et al. Acta Cardiol Sin 2016; 32(4):420-427; 9.Yndestad et al Circulation. 2004;109:1379–1385; 10. Roh et al Sci Trans Med 2019; CVD=cardiovascular disease; NT-proBNP=N-terminal prohormone brain natriuretic peptide

# Summary of KER-050 in MDS

- **In the ongoing Phase 2 clinical trial of KER-050 in LR-MDS, the majority of patients enrolled had HTB or MLD indicating a difficult-to-treat trial population**
- **KER-050 was generally well-tolerated as of the data cut-off date, with a safety profile consistent to that previously reported for this trial[1,2]**
- **Durable responses of transfusion independence were observed in a broad range of patients with LR-MDS, including those with HTB**
  - Analysis of patients with EPO < 500 U/L revealed improved erythroid responses across the trial population, including in patients with HTB or non-RS disease
  - Transfusion independence, increases in hemoglobin, and increases in platelets were observed, supporting the potential for KER-050 to ameliorate ineffective hematopoiesis across multiple lineages in patients with MDS
- **Patients who achieved transfusion independence showed clinically meaningful improvements in FACIT-Fatigue scores indicating potential for KER-050 to improve quality of life in patients with LR-MDS**
- **Observations from exploratory assessments of biomarkers:**
  - Sustained increases in bone specific alkaline phosphatase (BSAP) were observed with KER-050 treatment supportive of potential to improve the bone marrow microenvironment
  - Several patients presented with elevated NT-proBNP at baseline, suggestive of increased myocardial stress
    - Rapid decreases with NT-ProBNP were observed with KER-050 treatment in HI-E/TI responders and non-responders
- **Collectively, these results support advancing KER-050 into a Phase 3 registration trial in patients with LR-MDS**

[1] Giagounidis et al. EHA 2023; [2] Chee et al. ASH 2022


# KER-050 (Elritercept)

RESTORE

## 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 patients with Myelofibrosis***

# Myelofibrosis

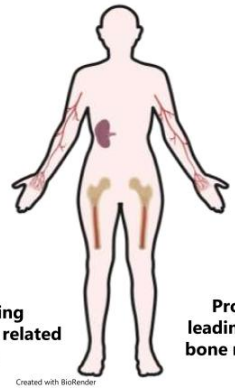
## MF
MF is a rare cancer of the bone marrow in which the marrow is replaced by scar tissue and is not able to produce healthy blood cells

## Clinical Consequences
MF is characterized by ineffective hematopoiesis, an enlarged spleen, bone marrow fibrosis and shortened survival. Both anemia and thrombocytopenia are negative prognostic indicators

## Current Treatments
Currently, there are limited therapeutic options to address the MF-associated cytopenias. Patients not only often experience multiple disease-associated, but also treatment-emergent, cytopenias, including anemia and thrombocytopenia

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

**Impact of MF**



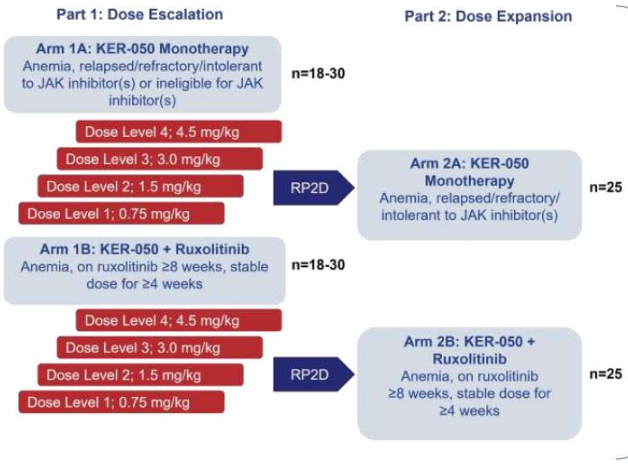

**Cytopenias including treatment and disease related severe anemia**

**Progressive disease leading to splenomegaly, bone marrow fibrosis and AML**

**Severe fatigue and Decreased QoL**

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

RESTORE




**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

**Following recommendation by the Safety Review Committee, dosing for Part 2 of this trial was initiated at a starting dose of 3.75 mg/kg, with an opportunity to dose escalate to 5.0 mg/kg based on individual titration rules, in both combination and monotherapy arms**

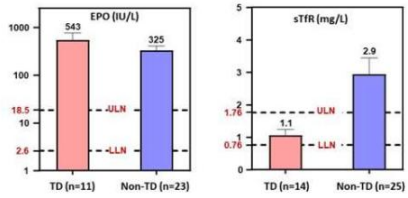
# Baseline Characteristics

RESTORE

## RESTORE Baseline Demographics

| Characteristic | Monotherapy (N=21) | Combination (N=20) | Total (N=41) |
|---|---|---|---|
| Age, years, median (range) | 72.0 (60, 85) | 74.5 (45, 86) | 73.0 (45, 86) |
| Male (%) | 14 (66.7) | 12 (60) | 26 (63.4) |
| DIPSS risk category, n (%) | | | |
| Intermediate -1 | 4 (19.0) | 1(5.0) | 5 (12.2) |
| Intermediate-2 | 13 (61.9) | 13 (65.0) | 26 (63.4) |
| High | 4 (19.0) | 6 (30.0) | 10 (24.4) |
| Mutation | | | |
| JAK2 | 10 (47.6) | 10 (50.0) | 20 (48.8) |
| CALR | 2 (9.5) | 5 (25.0) | 7 (17.1) |
| MPL | 3 (14.3) | 2 (10.0) | 5 (12.2) |
| Triple-negative | 5 (23.8) | 0 | 5 (12.2) |
| RBC U/12 wks, median (range) | 4 (0, 25) | 4.5 (0, 15) | 4 (0, 25) |
| TD (≥6 RBC U/12 wks)* | 10 (6, 25) [n=6] | 9 (6, 15) [n=9] | 10 (6, 25) [n=15] |
| Non-TD (<6 RBC U/12wks) | 3 (0, 9) [n=15] | 3 (0, 5) [n=11] | 3 (0, 9) [n=26] |
| Hgb (g/dL), median (range) | 8.18 (7.2, 10.1) | 8.03 (5.4, 9.4) | 8.08 (5.4, 10.1) |
| Reticulocytes, x10$^9$/L, median (range) | 50.4 (9, 328) | 70.7 (7, 173) | 62.1 (7, 328) |
| Platelets, x10$^9$/L, median (range) | 112.0 (27, 561) | 158.1 (42, 243) | 142.3 (27, 561) |
| Spleen volume, cm$^3$, median (range) | 587.4 (138,2650) [n=16] | 920.6 (357,2195) [n=17] | 867.7 (138,2650) [n=33] |
| ≥ 450 cm$^3$, n(%) | 11 (68.8) | 12 (70.6) | 23 (69.7) |
| MF-SAF-TSS, total, median (range) | 16 (0, 56) | 10 (0, 36) | 11 (0, 56) |
| ≥ 10, n(%) | 18 (85.7) | 11 (55.0) | 29 (70.7) |

## RESTORE Baseline Biomarkers of Erythropoiesis




- **Patients with high disease burden and severe erythropoietic dysfunction**
- **Most receiving transfusions**
  - 37% TD (IWG 2013 criteria; ≥6 RBC units/12 weeks)
  - Transfusions prevalent even among NTD (median: 3 RBC units/12 weeks)
- **Most had splenomegaly**
  - Marked splenomegaly observed in the KER-050+RUX arm, indicative of inadequate control of disease
- **TD and NTD had anemia with ↑ EPO ≈ erythropoietic dysfunction**
  - In TD, mean serum EPO was 543 IU/L and in NTD, mean EPO was 325 IU/L

**Data are presented as of a data cutoff date of September 14, 2023.**
IWG=International Working Group; LLN=lower limit of normal; RUX=ruxolitinib; ULN=upper limit of normal

# KER-050 Was Generally Well-Tolerated in Patients with Significant Disease Burden

RESTORE

- **TEAEs mild to moderate**
- **Treatment-related TEAEs relatively infrequent**
  - Two had Grade 3 or higher worsening cytopenias
- **One Dose Limiting Toxicity in Part 1**
  - Increased Hgb ≥2 g/dL in dose Level 2 cohort of monotherapy arm
  - No associated AE, Hgb within normal limits
- **Three TEAEs* leading to death, all deemed unrelated to study therapy**

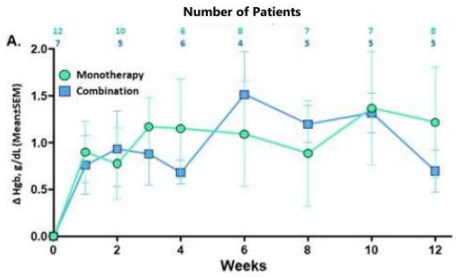
| Category, n (%) | Monotherapy (N=21) | Combination (N=20) | Total (N=41) |
|---|---|---|---|
| **Any TEAE** | **20 (95.2)** | **19 (95.0)** | **39 (95.1)** |
| **Most frequent TEAEs (≥10%* of participants)** | | | |
| Diarrhea | 3 (14.3) | 6 (30.0) | 9 (22.0) |
| Thrombocytopenia | 5 (23.8) | 2 (10.0) | 7 (17.1) |
| Asthenia | 5 (23.8) | 1 (5.0) | 6 (14.6) |
| Fatigue | 3 (14.3) | 3 (15.0) | 6 (14.6) |
| Pyrexia | 5 (23.8) | 1 (5.0) | 6 (14.6) |
| **DLTs** | **1 (4.8)** | **0** | **1 (2.4)** |
| **SAEs** | **7 (33.3)** | **8 (40.0)** | **15 (36.6)** |
| **KER-050-related TEAE** | **6 (28.6)** | **4 (20.0)** | **10 (24.4)** |
| **Ruxolitinib-related TEAE** | **N/A** | **6 (30.0)** | **6 (14.6)** |
| **KER-050-related TEAE of Grade ≥ 3** | **1 (4.8)** | **0** | **1 (2.4)** |
| **Ruxolitinib-related TEAE of Grade ≥ 3** | **N/A** | **1 (5.0)** | **1 (2.4)** |
| **TEAE leading to KER-050 discontinuation** | **4 (19.0)** | **3 (15.0)** | **7 (17.1)** |
| **TEAE leading to ruxolitinib discontinuation** | **N/A** | **2 (10.0)** | **2 (4.9)** |
| **TEAE Leading to Death** | **1 (4.8)** | **2 (10.0)** | **3 (7.3)** |

**Data are presented as of a data cutoff date of September 14, 2023.**
*Transformation to AML, cerebrovascular accident and pneumonia
DLT=dose limiting toxicity

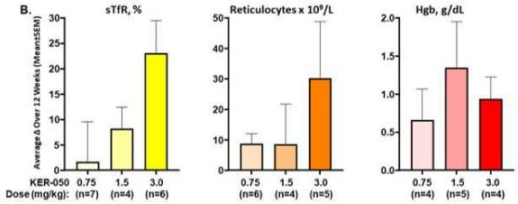
# KER-050 Treatment Led to Sustained Increases in Hemoglobin

- **Biomarkers of erythropoiesis assessed in NTD RESTORE patients**
  - Sustained increases in Hgb observed over first 12 weeks of KER-050 treatment in both monotherapy and combination arms
  - Observed increases in sTfR, reticulocytes and Hgb generally higher with increasing dose levels between 0.75 to 3 mg/kg

**Observed Change in Hgb**




**Biomarkers of Erythropoiesis**

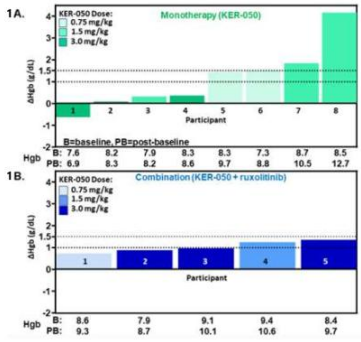



**Data are presented as of a data cutoff date of September 14, 2023.**

# Treatment with KER-050 Led to Robust Increases in Hemoglobin and Reduction in Transfusion Burden in MF Patients

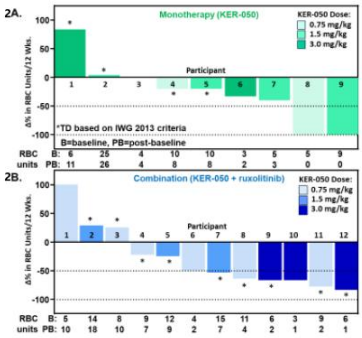
RESTORE

### Observed Maximum Change in Hgb: NTD Patients




- **Hemoglobin assessed in NTD RESTORE patients:**
  - Observed increases in Hgb in monotherapy arm suggests potential for KER-050 to address anemia due to underlying MF
  - Observed increases in Hgb in combination arm suggests potential to mitigate RUX-associated anemia

### Observed Reductions in Transfusion Burden




- **Changes in transfusion burden over 12 weeks assessed in patients receiving ≥ 3 units RBC/12 weeks at baseline**
- **Decreased transfusion burden occurred in most patients, notably:**
  - At 3 lowest KER-050 dose levels
  - In patients receiving up to 15 RBC units/12 weeks at baseline
- **Data support potential of KER-050 to improve anemia due to MF and RUX-associated anemia**

**Data are presented as of a data cutoff date of September 14, 2023.**

# Preliminary Data Support Potential for KER-050 to Address Multiple Aspects of MF

RESTORE

| Hematopoiesis | Spleen Size | Symptoms |
|---|---|---|
| • Observed increases in markers of erythropoiesis<br>• Mean increases in hemoglobin and reduction in transfusion burden observed over 12 weeks<br>• Maintenance or improvement in platelet counts observed | • Observed reduction in spleen size in 4/7 (57%) evaluable* patients (1/3 mono, 3/4 combo) at Week 24<br>• Median reduction (n=4) = -27.1% (range -47.5% to -11.2%)<br>• Median change (n=7) = -11.2% (range: -47.5% to 30%) | • Observed reduction in disease symptoms in 8/12 (67%) evaluable# patients at Week 24<br>• Median reduction (n=8) = -16.8% (range -55.6% to -6.7%)<br>• Median change (n=12) = -13.2% (range -55.6% to 54.5%) |

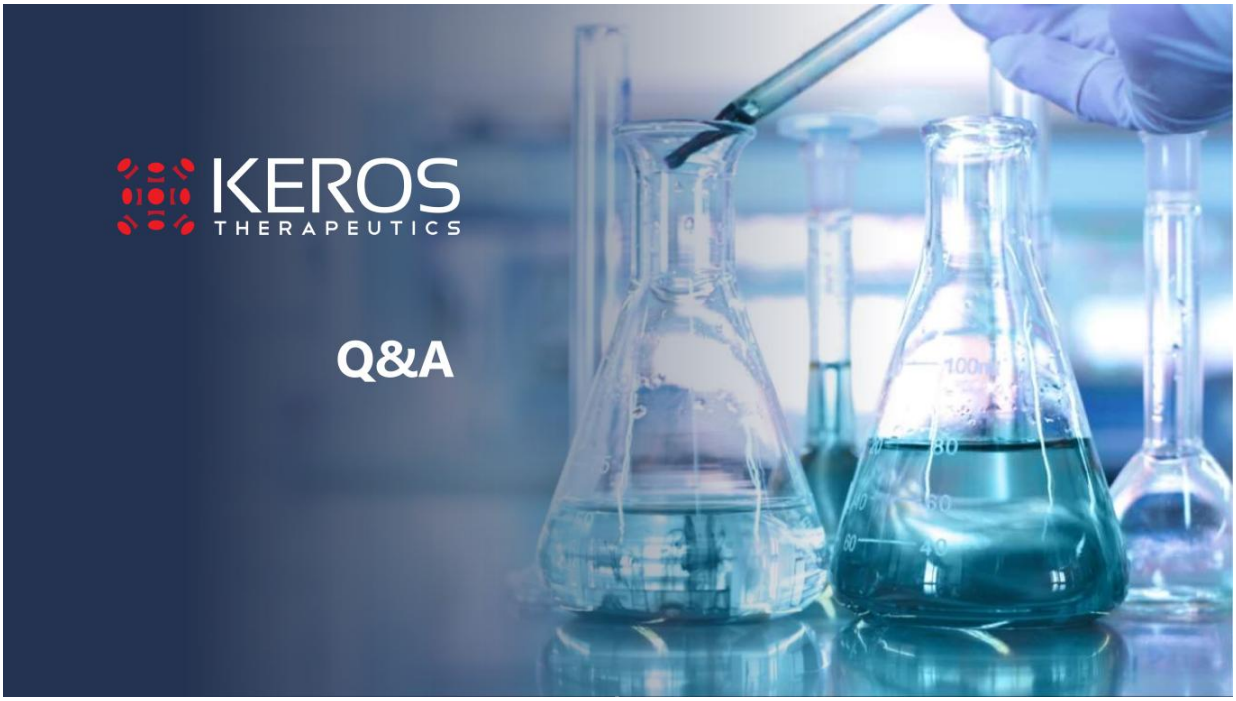
**Data are presented as of a data cutoff date of September 14, 2023.**
*Evaluable defined as patients with baseline spleen size ≥ 450 $cm^3$ and a Week 24 spleen assessment
# Evaluable defined as patients with at least 2 symptoms with an average score ≥ 3 or an average total score of ≥ 10 on the MF-SAF-TSS questionnaire at baseline and with a Week 24 MF-SAF-TSS assessment

# Summary of KER-050 in Myelofibrosis

- **KER-050 was generally well-tolerated in RESTORE Part 1 as of the data cutoff date, including patients with high disease burden and complex comorbidities**
  - Safety review committee approved RP2D of KER-050 consistent with dose selected for Part 2 of the ongoing Phase 2 clinical trial of KER-050 in patients with lower-risk MDS
- **RESTORE data presented here support potential for KER-050 to:**
  - **Ameliorate ineffective hematopoiesis and address cytopenias (anemia and thrombocytopenia) due to MF and associated with RUX**
    - Based on observed increased markers of erythropoiesis, increased Hgb, decreased transfusion burden, maintained or increased platelets even at doses <RP2D
  - **Provide broader clinical benefit in patients with MF (decreased spleen size and improved symptoms)**

# Key Takeaways

- **KER-050 is a novel ligand trap designed to inhibit select TGF-beta ligands, including Activin A, which has been associated with driving disease pathogenesis and progression**
- **Data presented at ASH from the Phase 2 trials in MDS and MF support the potential of KER-050 to ameliorate ineffective hematopoiesis, improve bone health and reduce cardiac stress**
- **In LR-MDS patients:**
  - KER-050 demonstrated durable transfusion independence, including in patients with high transfusion burden
  - Durable clinical responses were associated with improvements in patient-reported measures of fatigue
  - Exploratory biomarker data demonstrate the potential of KER-050 to reduce NT-proBNP, a measure of cardiac stress/strain, and other key biomarker data, supporting its broad potential
- **Collectively, these results support advancing KER-050 into a Phase 3 registration trial in patients with LR-MDS**
  - Keros plans to engage with regulators in H1 2024 on the design of the Phase 3 clinical trial of KER-050 in patients with LR-MDS
- **In MF:**
  - Preliminary findings from Phase 2 clinical trial in myelofibrosis demonstrate that KER-050 can ameliorate ineffective hematopoiesis and address cytopenias
  - KER-050 has the potential broader clinical benefit seen through reduction of spleen size and overall reduction in symptom score


KEROS
THERAPEUTICS
Q&A