# 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 13, 2021**

# 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 8.01 Other Events.**

On December 13, 2021, Keros Therapeutics, Inc. (the “Company”) issued a press release announcing additional data from its ongoing Phase 2 clinical trial of KER-050 in patients with very low-, low-, or intermediate-risk myelodysplastic syndromes ("MDS"), as well as preclinical data on the differentiated mechanism of action of KER-050 and its activity in cytopenia models, being presented at the 63rd American Society of Hematology Annual Meeting and Exposition held December 11 through 14, 2021. In addition, the Company announced preclinical data evaluating ALK2 inhibition as a potential treatment option for anemia of inflammation. 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 4:01 p.m. Eastern Time on December 13, 2021, the Company’s management will discuss the additional data from its Phase 2 clinical trial of KER-050 in patients with MDS. 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 13, 2021. |
| 99.2 | Investor Presentation dated December 2021. |
| 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 13, 2021

**Keros Therapeutics Presents Clinical Trial and Preclinical Study Results from its KER-050 Program and Preclinical Data from its ALK2 Inhibitor Program at the 63rd American Society of Hematology Annual Meeting and Exposition**

- *Keros Therapeutics will be hosting a conference call and webcast today, December 13, 2021, at 4:01 p.m. ET.*

**Lexington, Mass. – December 13, 2021 –** Keros Therapeutics, Inc. (“Keros”) (Nasdaq: KROS), a clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of novel treatments for patients suffering from hematological and musculoskeletal disorders with high unmet medical need, today announced that it presented additional data from its ongoing Phase 2 clinical trial of KER-050 in patients with very low-, low-, or intermediate-risk myelodysplastic syndromes (“MDS”), as well as preclinical data on the differentiated mechanism of action of KER-050 and its activity in cytopenia models, at the 63rd American Society of Hematology (“ASH”) Annual Meeting and Exposition, held in person and virtually December 11 through 14, 2021. In addition, Keros announced preclinical data evaluating ALK2 inhibition as a potential treatment option for anemia of inflammation.

“We were pleased to present additional data from our ongoing Phase 2 clinical trial of KER-050 in MDS patients at this year’s ASH annual meeting,” said Jasbir S. Seehra, Ph.D., President and Chief Executive Officer of Keros. “We believe these data support the potential of KER-050 as a treatment for multilineage cytopenias in MDS by potentially targeting multiple stages of hematopoiesis. We are also pleased to have recently initiated dosing for Cohort 5 of the trial at 5.0 mg/kg of KER-050, to be administered once every four weeks for 12 weeks, following the Safety Review Committee recommendation for this trial.”

Clinical Presentation

- *A Phase 2, Open-Label, Ascending Dose Study of KER-050 for the Treatment of Anemia in Patients with Very Low, Low, or Intermediate Risk Myelodysplastic Syndromes*

This ongoing, open-label, two-part, multiple ascending dose Phase 2 clinical trial is evaluating KER-050 in participants with very low-, low-, or intermediate-risk MDS who either have or have not previously received treatment with an erythroid stimulating agent (“ESA”). Enrollment was balanced approximately one-to-one between patients that did not have ring sideroblasts (“non-RS”) and patients that have ring sideroblasts (“RS positive”). Patients received KER-050 subcutaneously every 28 days for up to four cycles during Part 1 of the trial, at the following dose levels: Cohort 1, 0.75 mg/kg; Cohort 2, 1.5 mg/kg; Cohort 3, 2.5 mg/kg; and Cohort 4, 3.75 mg/kg.

As of October 25, 2021 (the “data cut-off date”), 24 patients in Cohorts 1, 2, 3 and 4 had received at least one dose of KER-050. KER-050 was observed to be generally well-tolerated as of the data cut-off date. No drug-related serious adverse events or dose-limiting toxicities were reported. The most commonly reported treatment-emergent adverse events were nausea, fatigue, diarrhea and dyspnea, none of which were deemed related to study drug. Treatment-related adverse events were reported in four patients, which were mild or moderate in severity, and did not lead to dose modification or treatment discontinuation. No patients developed high-risk MDS or acute myeloid leukemia. Two patients withdrew from the trial prior to completing eight weeks of treatment with KER-050, one due to death deemed unrelated to study drug and one due to withdrawn patient consent.

16 patients in Cohorts 1, 2 and 3 had completed at least eight weeks of treatment and evaluation as of the data cut-off date (which we refer to as the “evaluable patients”). The 16 evaluable patients were comprised of four non-transfused (“NT”), three low transfusion burden (“LTB”) and nine high transfusion burden (“HTB”) patients. Of the 12 LTB and HTB patients, six were non-RS and six were RS positive.

As of the data cut-off date, 50% (n=8/16) of the evaluable patients, three of whom were non-RS and five of whom were RS positive, achieved an overall erythroid response, which is defined as meeting one of the following two endpoints:

- IWG 2006 Hematological improvement-erythroid ("HI-E"), which is defined as either:
  - a ≥ 1.5 g/dL increase in hemoglobin for eight weeks in LTB and NT patients; or
  - a reduction by ≥ 4 red blood cell ("RBC") units transfused during any eight-week period during the trial, compared with the eight-week period prior to Cycle 1, Day 1 in HTB patients.
- Transfusion independence ("TI") for at least eight weeks in patients who require ≥ 2 RBC units transfused at baseline.

Additional data from the evaluable patients in Cohorts 1, 2 and 3 of the trial, as of the data cut-off date, include:

- 43.8% (n=7/16) of the evaluable patients achieved HI-E over an eight-week period.
- 45.5% (n=5/11) of the transfused patients receiving ≥ 2 RBC units at baseline achieved TI for at least eight weeks.

In addition, the following pharmacodynamic data were observed:

- Reticulocyte increases observed in patients achieving HI-E or TI endpoints.
- Increases in serum soluble transferrin receptor and decreases in serum ferritin observed in patients achieving HI-E or TI endpoints.
- Increases in platelets observed in patients achieving HI-E or TI.

Together, these data demonstrate the effects of KER-050 on both erythropoiesis and thrombopoiesis and support the continued development of KER-050 as a potential treatment option for ineffective hematopoiesis in MDS.

Preclinical Presentations

- *KER-050, an Inhibitor of TGF-β Superfamily Signaling, Promoted Thrombopoiesis and Reversed Immune Thrombocytopenia in a Mouse Model of Disease*

Administration of a mouse research form of KER-050 ("RKER-050") increased differentiation of early- and late-stage megakaryocyte precursors and increased platelet count:

- Healthy mice treated with a single 10 mg/kg dose of a research form of KER-050 ("RKER-050") had a 100% increase in platelets 12 hours after administration compared to vehicle-treated mice ($p<0.001$), which suggests that RKER-050 acted, at least in part, as a terminal maturation agent of proplatelets.
  - Keros also analyzed CD41+ cells, which are megakaryocyte precursors, from the bone marrow of healthy mice at 24 hours post-treatment in order to investigate the potential effects of RKER-050 on early stages of thrombopoiesis. An overall increase in the CD41+ cells was observed, as well as an increase in higher levels of ploidy, indicating that RKER-050 increased differentiation of megakaryocyte precursors towards the later stages of maturation.
- In mice with an established model of immune thrombocytopenia, treatment with a single 7.5 mg/kg dose of RKER-050 led to increased recovery in platelet levels post-platelet depletion compared to untreated mice. On Day 10, the final study day, an increase in the CD41+ cell

population and an increase in the number of these cells with a higher degree of ploidy was observed in the RKER-050-treated group.

- To understand the potential contribution that inhibiting activin A has on KER-050's potential effect on the thrombopoiesis pathway, Keros compared the effects of RKER-050 and an activin A neutralizing antibody on platelet levels after 24 hours. Treatment with either RKER-or an activin A antibody both led to an increase in platelet count. These results suggest that inhibition of activin A may be partially responsible for the platelet effects observed in mice treated with RKER-050.
    - Separately, bone marrow cells from mice were isolated and administered activin A (5 mg/kg), RKER-050 (10 mg/kg) or a combination of both for six days. Keros observed an increase in lower ploidy levels upon activin A treatment that shifted back to higher ploidy levels in cells treated with both activin A and RKER-050.

Overall, we believe these data show a potentially novel effect of KER-050 on thrombopoiesis in several preclinical models. Our results also suggest that the effect of RKER-050 on megakaryocyte populations could be partially due to the inhibition of activin A. Additionally, our data support the potential of KER-050 to accelerate the rate of platelet recovery due to acute depletion and, if approved, could represent a potential novel treatment approach for thrombocytopenia in patients with MDS, myelofibrosis and immune thrombocytopenia.

- *RKER-050 Rescued Ruxolitinib (Rux)-Associated Reductions in Red Blood Cell Volume*

After first establishing anemia in C57BI/6 mice by dosing with ruxolitinib ("rux"), a JAK2 inhibitor, the mice were dosed with vehicle ("control group") or 120 mg/kg rux twice daily for 37 days, which led to significant reductions in red blood cells, hemoglobin and hematocrit on Day 37 in the rux-treated mice compared to the control group. On Day 41, rux-treated mice received either vehicle ("rux-vehicle mice") or RKER-050 (7.5 mg/kg) ("rux-RKER-050 mice") twice weekly for a total of five doses, in addition to the twice daily treatment with rux.

Red cell parameters continued to decline in rux-vehicle, and on Day 55, significant reductions in red blood cells, hemoglobin and hematocrit levels were observed compared to the control group. In contrast, administration of RKER-050 reversed the observed rux-associated reductions in these parameters, as evidenced by significant increases in red blood cells, hemoglobin and hematocrit in the rux-RKER-050 mice compared to the rux-vehicle mice. These results suggest that RKER-050 functions independently of the JAK-STAT signaling pathway, and could therefore be a potential treatment option for ineffective hematopoiesis resulting from defective JAK-STAT signaling in myelofibrosis patients. Keros also believes that KER-050 has the potential to mitigate the dose-limiting effects of rux and could potentially enhance duration of therapy in myelofibrosis patients.

- *A Monoclonal Antibody Targeting ALK2 as a Potential Therapeutic Agent for Anemia of Inflammation*

To induce disease in a model of chronic kidney disease ("CKD"), mice were dosed daily for six weeks with 50 mg/kg of adenine, resulting in changes associated with anemia of inflammation, including increased serum hepcidin, decreased iron and decreased hematologic parameters, that was confirmed on Day 42. After completing the six weeks of adenine-administration, mice received twice weekly treatment with 5 mg/kg of an investigational novel and selective neutralizing antibody to the ALK2 receptor ("KTI-018") or vehicle daily for 11 days in addition to continued adenine treatment. KTI-018-treated CKD mice exhibited a reversal of the CKD-related changes, including decreased serum hepcidin, increased in serum iron and improved hematologic parameters compared to vehicle-treated CKD mice.

These data show that, in a mouse model of CKD with anemia of inflammation, inhibition of ALK2 with KTI-018 decreased serum hepcidin, increased the bioavailability of iron for erythropoiesis, restored hematologic parameters to normal levels and appeared to ameliorate the anemia. Accordingly, Keros believes that targeting ALK2 inhibition could potentially treat anemia resulting from CKD and other chronic inflammatory diseases.

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

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

The primary objective of this trial is to assess the safety and tolerability of KER-050 in participants with MDS that are RS positive or non-RS. Patients in Cohorts 1, 2, 3, 4 and 5 of Part 1 of this trial received 0.75 mg/kg, 1.5 mg/kg, 2.5 mg/kg, 3.75 mg/kg and 5.0 mg/kg doses of KER-050, respectively, once every four weeks for 12 weeks. The primary objective of Part 2 of this trial is confirmation of the safety and tolerability of the selected dose levels. The secondary objectives of this trial are to evaluate the pharmacokinetics, pharmacodynamics and efficacy of KER-050. We expect to report additional data from this trial in mid-2022.

**Conference Call and Webcast Information**

The Company will host a conference call and webcast today, December 13, 2021, at 4:01 p.m. ET, to discuss the additional results from the ongoing Phase 2 clinical trial of KER-050 presented at the 2021 ASH Annual Meeting and Exposition.

The conference call will be webcast live at https://event.webcasts.com/starthere.jsp?ei=1518700&tp_key=27e9ef7be6. The live teleconference may be accessed by dialing (877) 405-1224 (domestic) or (201) 389-0848 (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 KER-050**

Keros' lead protein therapeutic product candidate, KER-050, is an engineered ligand trap comprised of a modified ligand-binding domain of the Transforming Growth Factor-Beta 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 myelodysplastic syndromes, or MDS, and in patients with myelofibrosis.

**About Keros Therapeutics, Inc.**

Keros is a clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of novel treatments for patients suffering from hematologic and musculoskeletal disorders with high unmet medical need. Keros is a leader in understanding the role of the transforming growth factor-Beta family of proteins, which are master regulators of red blood cell and platelet production as well as of the growth, repair and maintenance of muscle and bone. Keros' lead protein therapeutic product candidate, KER-050, is being developed for the treatment of low blood cell counts, or cytopenias, including anemia and thrombocytopenia, in patients with myelodysplastic syndromes and in patients with myelofibrosis. Keros' lead small molecule product candidate, KER-047, is being developed for the treatment of anemia resulting from iron imbalance, as well as for the treatment of fibrodysplasia ossificans progressiva. Keros' third product candidate, KER-012, is being developed for the

treatment of disorders associated with bone loss, such as osteoporosis and osteogenesis imperfecta, and for the treatment of PAH.

**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 "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 clinical trials for KER-050; the potential of KER-050 to treat patients with MDS and myelofibrosis, and potentially promote erythropoiesis and thrombopoiesis in patients with ineffective hematopoiesis; the potential of KER-050 to accelerate the rate of platelet recovery due to acute depletion and to treat thrombocytopenia in patients with MDS, myelofibrosis and immune thrombocytopenia; the potential of KER-050 to mitigate the dose-limiting effects of rux and enhance duration of therapy in myelofibrosis patients; and the potential of ALK2 inhibition to treat anemia resulting from CKD and other chronic inflammatory diseases. 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; Keros’ ability to enter into new collaborations; 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 the Company’s Quarterly Report on Form 10-Q, filed with the SEC on November 4, 2021, 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:**

Mike Biega
mbiega@soleburytrout.com
(617) 221-9660

KEROS THERAPEUTICS

# KER-050 Update

13 December 2021| CONFIDENTIAL

# 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.

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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.

- Jasbir Seehra, President and Chief Executive Officer
- Keith Regnante, Chief Financial Officer
- Simon Cooper, Chief Medical Officer

# Harnessing the Powerful Biology of the TGF-β Superfamily

- Clinical-stage biopharmaceutical company developing novel therapeutics that target the TGF-β superfamily
- Leveraging our extensive experience in TGF-β superfamily protein structure, function and protein engineering to generate a clinical pipeline of differentiated therapeutics:

***Hematology***

**KER-050**: Modified activin receptor IIA (ActRIIA) ligand trap
- Designed to address ineffective hematopoiesis by modulating TGF-β superfamily signaling
- Potential to correct multiple cytopenias in patients with MDS and myelofibrosis (MF)

**KER-047**: Activin receptor-like kinase-2 (ALK2) inhibitor
- Designed to address anemias resulting from iron imbalance
- Potential to treat iron-refractory iron deficiency anemia (IRIDA), iron deficiency anemia and other diseases

***Pulmonary and Musculoskeletal***

**KER-012**: Modified activin receptor IIB ligand trap
- Designed to inhibit vascular remodeling and bone loss
- Potential to treat pulmonary arterial hypertension (PAH) and bone loss in osteogenesis imperfecta and osteoporosis

# Keros is Developing Differentiated Clinical Assets in Hematological and Musculoskeletal Disorders

| Program | Asset | Phase of Development | Status | Next Milestones* |
|---|---|---|---|---|
| Hematology | KER-050 (therapeutic protein) | Myelodysplastic syndromes (MDS) | Phase 2 clinical trial ongoing | Announce additional data from Part 1 of Phase 2 clinical trial: end of 2021 |
| | | Myelofibrosis | Completed Phase 1 clinical trial | Initiate Phase 2 clinical trial: Q4 2021 Initial data: 2022 |
| | KER-047 (small molecule) | Iron deficiency anemia | Completed expanded Phase 1 clinical trial | Initiate Phase 2 clinical trial: Q1 2022 Initial data: 2022 |
| | | Anemia from high hepcidin | | Initiate Phase 2 clinical trial: Q1 2022 Initial data: 2022 |
| Musculoskeletal | | Fibrodysplasia ossificans progressiva (FOP) | | |
| Pulmonary | KER-012 (therapeutic protein) | Bone disorders | Phase 1 clinical trial in healthy volunteers ongoing | Initial data: H1 2022 |
| | | Pulmonary arterial hypertension | | |
| Preclinical Pipeline | | Musculoskeletal and hematology | | |

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

# KER-050

A novel product candidate designed to address diseases arising from ineffective hematopoiesis

- Myelodysplastic syndromes
- Myelofibrosis

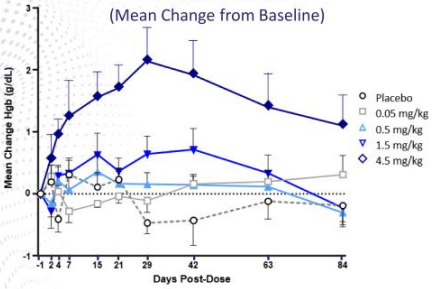
# KER-050 is a Modified ActRII Fusion Protein

- Activin receptors are expressed on hematopoietic cells and modulate differentiation of precursor cells
- KER-050 is a ligand trap composed of a modified extracellular domain of ActRIIA fused to the Fc region of a human IgG
- KER-050 is designed to increase red blood cell (RBC) and platelet production by inhibiting the signaling of ligands through activin receptors

# KER-050 Increased RBC Parameters and Platelets Following Single Doses in a Phase 1 Clinical Trial in Healthy Volunteers

**HEMOGLOBIN**

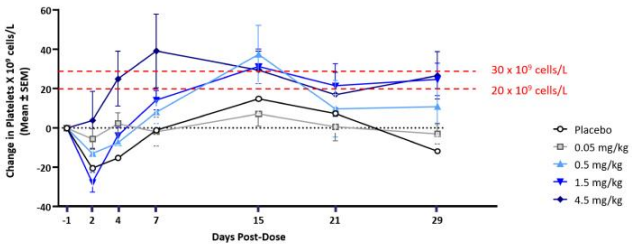
(Mean Change from Baseline)




- Observed increase in RBC parameters continued to build through day 29 which we believe is supportive of KER-050 acting on multiple stages of erythropoiesis
- Observed sustained increase in hemoglobin through day 84 after a single dose supports monthly or less frequent dosing

**PLATELETS**

(Mean Change from Baseline in Platelets at Each Dose)




- Single doses of KER-050 observed to lead to clinically meaningful changes in platelets through day 29
- Maximum changes observed between 7-15 days post-dosing

# American Society of Hematology Annual Meeting and Exposition

*KER-050 Presentations:*

*Preclinical*

- KER-050, an Inhibitor of TGF-β Superfamily Signaling, Promoted Thrombopoiesis and Reversed Immune Thrombocytopenia in a Mouse Model of Disease (Abstract #2068)
- RKER-050 Rescued Ruxolitinib (Rux)-Induced Reduction in Red Blood Cell Parameters (Abstract #934)

*Clinical*

- A Phase 2, Open-Label, Ascending Dose Study of KER-050 for the Treatment of Anemia in Patients with Very Low, Low, or Intermediate Risk Myelodysplastic Syndromes (Abstract #3675)

*Preclinical*

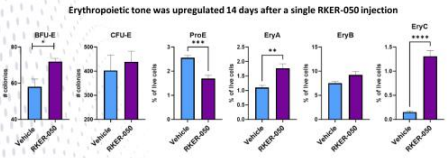
ALK2/Iron homeostasis

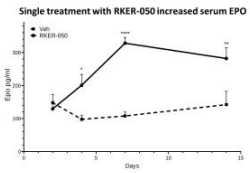
- A Monoclonal Antibody Targeting ALK2 As a Potential Therapeutic Agent for Anemia of Inflammation (Abstract #2007)

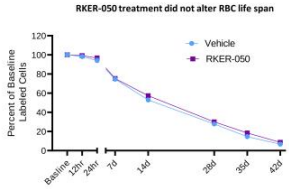
# KER-050 Preclinical Data Support Potential to Promote All Stages of Erythropoiesis

In a preclinical study of healthy mice, treatment with a mouse research form of KER-050 (RKER-050):

- Stimulated terminal maturation of late-stage erythroid precursors and increased the outflux of late-stage reticulocytes into circulation
- Expanded the early-stage precursor population that differentiate to replenish the late-stage erythroblast pools
- Increased erythropoietin levels
- Unaltered life span of RBCs

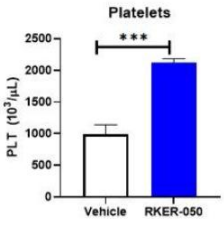



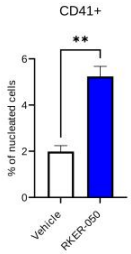



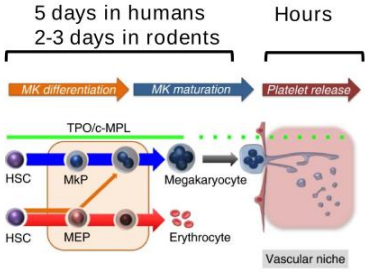

**EHA 2021: Abstract # 2736**

# RKER-050 Preclinical Data Support Potential to Promote All Stages of Thrombopoiesis

- Observed rapid onset of platelet increase in mouse models is consistent with terminal maturation of proplatelets
- Observed increase in the number of CD41+ cells and the polyploid in mouse models is consistent with increase in early stages of thrombopoiesis



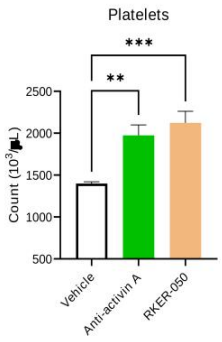




*** p < 0.05; **** p < 0.0001

# RKER-050 Increased Platelets Potentially Through Activin A Inhibition

- In a preclinical study in mice, RKER-050 administration resulted in rapid and sustained increases in platelets
- Activin A inhibited differentiation of platelet production in the preclinical study
  - Decreased number of polyploid CD41+ cells (megakaryocytes)
- Treatment with an activin A neutralizing antibody in the preclinical study increased platelet count
- KE-050 (and RKER-050) is designed to inhibit a subset of TGF-β superfamily ligands, including activin A, activin B, GDF8 and GDF11



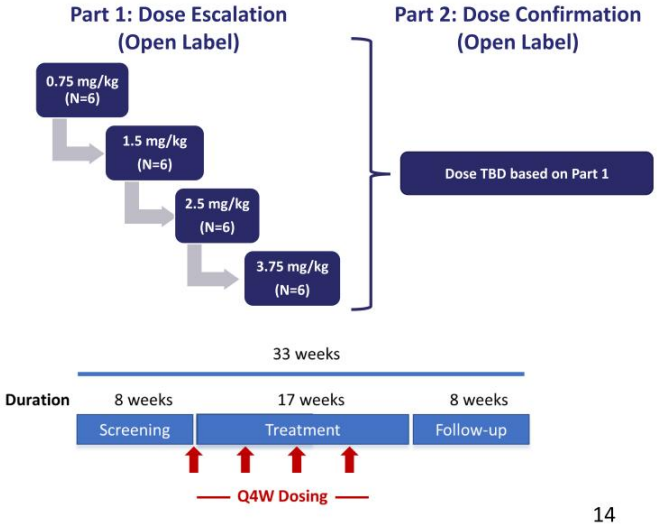

** p < 0.01, *** p < 0.001.

# KER050-MD-201

## A Phase 2 Clinical Trial Of KER-050 For The Treatment Of Anemia In Patients With Very Low, Low Or Intermediate Risk Myelodysplastic Syndromes (MDS)

# Phase 2 Clinical Trial of KER-050 in MDS

- Phase 2, multicenter, open-label clinical trial in very low-, low- and intermediate-risk MDS patients
- KER-050 administered once every four weeks (Q4W) for 12 weeks
- Trial objectives:
  - Evaluate safety, tolerability and pharmacokinetics
  - Evaluate pharmacodynamic effects and efficacy of KER-050
- Protocol was amended to allow patients in Part 1 and Part 2 to remain on treatment up to 24 cycles (2 years)



# Phase 2 Clinical Trial of KER-050 in MDS

**Key Eligibility Criteria**:

- MDS with very low-, low-, or intermediate-risk disease, as classified by the International Prognostic Scoring System-Revised, including both patients that did not have ring sideroblasts (non-RS) and patients that have ring sideroblasts (RS+)
- ESA naïve and experienced patients are eligible
- No prior treatment with azacitidine, decitabine, lenalidomide, luspatercept or sotatercept
- Anemia, categorized in one of the following three groups:
  - Non-transfused (NT): hemoglobin (Hgb) <10 g/dL
  - Low transfusion burden (LTB): 1-3 units of RBC/8 weeks, Hgb <10 g/dL
  - High transfusion burden (HTB): ≥4 units of RBC/8 weeks

**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

# Trial Status and Baseline Characteristics

- Abstract announcing additional data from our ongoing Phase 2 clinical trial of KER-050 in MDS was presented at the 63rd American Society of Hematology (ASH) Annual Meeting and Exposition
- Data cut-off date: October 25, 2021
- Safety and efficacy data presented from Cohorts 1, 2 and 3:
  - Cohort 1: 0.75 mg/kg Q4W
  - Cohort 2: 1.5 mg/kg Q4W
  - Cohort 3: 2.5 mg/kg Q4W
- Safety data presented from Cohorts 1, 2, 3 and 4 (3.75 mg/kg)
- 24 patients in Cohorts 1, 2, 3 and 4 received at least one dose of KER-050 as of the data cut-off date
  - 16 patients in Cohorts 1, 2 and 3 completed 8 weeks of evaluation and treatment with KER-050 as of the data cut-off date (which we refer to as the “evaluable patients”), comprised of:
    - 4 NT patients; 3 LTB patients; and 9 HTB patients
    - 8 were non-RS and 8 were RS+
  - 2 patients in Cohort 2 were not efficacy-evaluable due to withdrawal of consent (n=1) and death (n=1)
  - 6 patients in Cohort 4 were not efficacy-evaluable as they had not completed 8 weeks of evaluation and treatment as of the data cut-off date

# Biomarkers of Ineffective Hematopoiesis in Very Low-, Low- and Intermediate-Risk MDS Patients

| Biomarker | RS Status Mean (SD) | |
|---|---|---|
| | RS+ (N=13) | Non-RS (N=11) |
| EPO (IU/L) | 326.0 (826.2) | 490.2 (855.7) |
| Reticulocytes ($10^9$/L) | 39.1 (28.0) | 29.8 (24.8) |
| Platelets ($10^9$/L) | 228.4 (67.8) | 134.6 (55.5) |
| TPO (pg/mL) | 74.2 (69.3) | 42.8 (60.1) |
| sTfR (mg/L) | 1.9 (1.0) | 1.2 (0.6) |

- MDS is characterized by ineffective hematopoiesis due to dysregulated differentiation of myeloid, erythroid and/or megakaryocytic lineages which results in multilineage cytopenias
- Non-RS patients had lower reticulocyte and platelet counts, higher endogenous EPO levels and lower sTFR than RS+ patients at baseline, which suggsted a greater degree of ineffective hematopoiesis

# Safety Data as of the Data Cut-off Date (October 25, 2021)

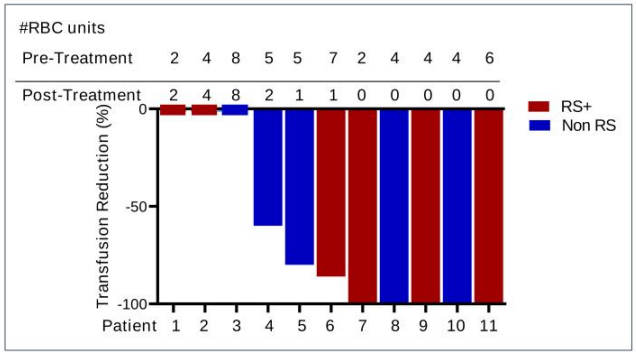
- Safety Review Committee has reviewed data from 0.75 mg/kg (Cohort 1), 1.5 mg/kg (Cohort 2), 2.5 mg/kg (Cohort 3) and Cohort 4 (3.75 mg/kg)
- Summary of safety data as of the data cut-off date (Cohorts 1-4, n=24)
  - No drug-related serious adverse events (SAEs), dose-limiting toxicities or drug-related dose modifications reported
  - 6 treatment-emergent SAEs in 5 patients, all of which were deemed unrelated to study drug:
    - Grade 2 (pyrexia, cardiac failure congestive)
    - Grade 3 (anaemia, pneumonia, pneumothorax)
    - Grade 5 (death – obesity-related heart disease)
  - Most frequent treatment-emergent adverse events (AEs):
    - Diarrhea, dyspnea, fatigue and nausea
  - Treatment-related AEs, reported in 4 patients, by maximum grade:
    - Grade 1 (headache, pain in extremity, abdominal pain)
    - Grade 2 (rash, diarrhea, nausea, peripheral edema)
      - The treatment-related AE of maculopapular rash was reported in one patient, after the patient's first dose, and resolved without recurrence following subsequent doses
- 2 withdrawals (death deemed unrelated to study drug; patient decision)
- No patients developed high-risk MDS or acute myeloid leukemia

# Preliminary Results from Phase 2 Clinical Trial

**Preliminary results***:

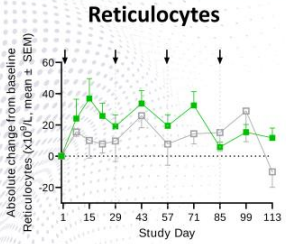
- **n=8/16 (50%)** of the evaluable patients met at least one of the following endpoints:
  - 2006 IWG HI-E criteria: **n=7/16 (43.8%)**
    - Hemoglobin increase of ≥1.5 g/dL for 8 weeks (in NT and LTB patients)
    - Reduction of ≥4 RBC units transfused over 8 weeks compared to baseline (in HTB patients)
  - Transfusion independence for at least 8 weeks in patients who require ≥ 2 RBC units transfused at baseline: **n=5/11 (45.5%)**
    - RS+ 3/6
    - Non-RS 2/5

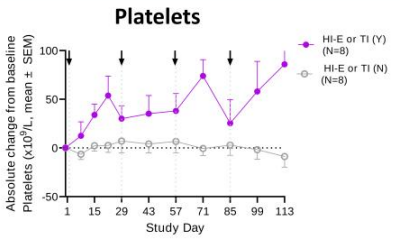
**Maximum Reduction in Transfusions Over 8 Weeks***

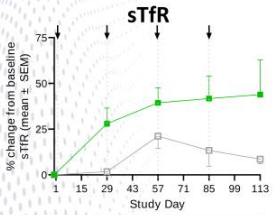



*Data cut-off date: October 25, 2021

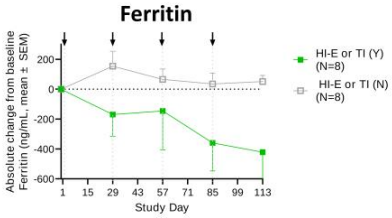
# KER-050 Demonstrated Improvement in Erythropoiesis and Thrombopoiesis




Baseline sTfR mg/L:
HI-E or TI (Y): 1.97 ± 1.06
HI-E or TI (N): 1.42 ± 0.62




Baseline Ferritin 867±748 ng/mL
4/16 patients are on iron chelation
3/4 on iron chelation achieved HI-E or TI

### KER-050 upregulated erythropoiesis

- Reticulocyte increases observed in patients achieving HI-E or TI endpoints
- Increases in serum soluble transferrin receptor (sTfR) and decreases in serum ferritin observed in patients achieving HI-E or TI endpoints

### KER-050 upregulated thrombopoiesis

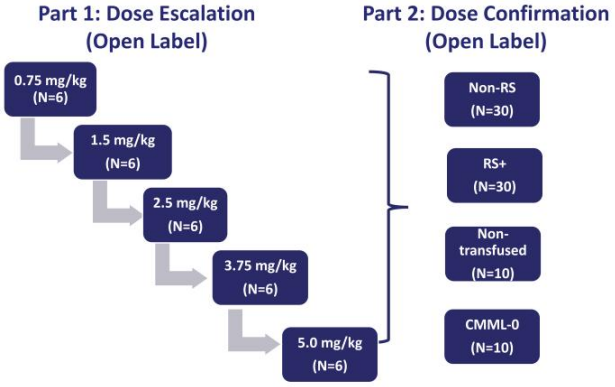
- Sustained increases in platelets observed in patients achieving HI-E or TI endpoints
- No patients required dose reduction due to thrombocytosis
- Preclinical data demonstrate this effect could potentially be mediated by KER-050 inhibition of activin A

# Summary of KER-050 Phase 2 Clinical Trial

- Keros believes the additional data from this 12-week treatment Phase 2 clinical trial demonstrate proof-of-concept of KER-050 in patients with very low-, low- or intermediate-risk MDS
  - Data consistent with observations from the Phase 1 clinical trial in healthy volunteers
- Dose levels as of the data cut-off date were generally well tolerated
- Increases in hematological parameters were observed in RS+ and non-RS patients that received doses of KER-050 Q4W
  - Increases in reticulocytes, hemoglobin and platelets were observed
- Observed increases in reticulocytes and soluble transferrin receptor and observed decreases in serum ferritin suggest that administration of KER-050 is potentially associated with increased erythropoiesis, with a broader effect on hematopoiesis being suggested by the increase in platelets
- Clinically meaningful reductions in transfusion burden as well as transfusion independence were observed in both RS+ and non-RS patients

# Updated Design of KER050-MD-201

- Cohort 4 Safety Review Committee permitted dosing of participants in Cohort 5 at 5.0 mg/kg, Q4W for 24 months
- Preparing to initiate Part 2 of this trial, with centers participating globally
- Data from Part 2 will inform our registration plans for KER-050
- Part 2 will explore KER-050 in larger cohorts of RS+ and non-RS patients
- A group of non-transfused patients and one of chronic myelomonocytic leukemia will also be included



# Keros Summary

## We Believe Keros is Positioned for Clinical and Commercial Success

- Keros is focused on the development of novel TGF-β therapeutics
  - Robust biology that has been validated in the clinic
- Keros is well-positioned to harness the potential of the TGF-β superfamily
  - ActRII program (KER-050) is in a Phase 2 trial in patients with MDS and we expect to initiate a Phase 2 trial in patients with MF in Q4 2021
  - Multiple Phase 2 trials for ALK2 program (KER-047) expected to commence in Q1 2022
  - KER-012 is a selective activin receptor ligand trap with an ongoing Phase 1 trial in healthy volunteers; initial data expected from Part 1 of this trial in the H1 2022
  - Clinical programs have potentially differentiated mechanism of action
- Our discovery approach has the potential to identify additional molecules with differentiated profiles from existing third-party products and product candidates
  - Pipeline of preclinical assets: bone, muscle and pulmonary

# Anticipated Key Milestones*

## KER-050

| | |
|---|---|
| • Initiate Part 2 of Phase 2 trial in MDS | Q1 2022 |
| • Initiate Phase 2 trial in myelofibrosis | Q4 2021 (initial data 2022) |

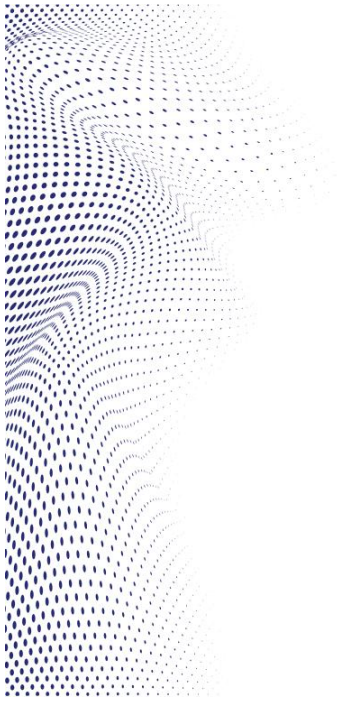
## KER-047

| | |
|---|---|
| • Initiate Phase 2 trial in IDA | Q1 2022 (initial data 2022) |
| • Initiate Phase 2 trial in IRIDA | Q1 2022 (initial data 2022) |

## KER-012

| | |
|---|---|
| • Announce initial data from Part 1 of Phase 1 trial | H1 2022 |
| • Announce additional data from Part 2 of Phase 1 trial | H2 2022 |

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



# Thank You