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): June 9, 2023

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

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

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 June 9, 2023, 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 showing the potential of a research form of KER-050 ("RKER-050") to restore erythropoiesis in an animal model of myelofibrosis, at the 28th Annual Congress of the European Hematology Association, held in person and virtually June 8 through 15, 2023. In addition, the Company announced preclinical data evaluating activin receptor-like kinase-2 inhibition, as well as its combination with RKER-050, as potential treatment options 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 8:00 a.m. Eastern time on June 9, 2023, the Company's management will discuss updates to and additional data from its hematology franchise, including the additional data from its ongoing 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 June 9, 2023.
99.2	Investor Presentation dated June 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: June 9, 2023

Keros Therapeutics Presents Clinical Trial and Preclinical Study Results from its KER-050 Program and Preclinical Data from its ALK2 Inhibitor Program at the 28th Annual Congress of the European Hematology Association

- *Keros Therapeutics will be hosting a conference call and webcast today, June 9, 2023, at 8:00 a.m. Eastern time, to provide an update on its hematology franchise.*

Lexington, Mass. – June 9, 2023 – Keros Therapeutics, Inc. ("Keros" or the "Company") (Nasdaq: KROS), a clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of novel treatments for patients suffering from hematological, pulmonary and cardiovascular 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 showing the potential of a research form of KER-050 ("RKER-050") to restore erythropoiesis in an animal model of myelofibrosis ("MF"), at the 28th Annual Congress of the European Hematology Association ("EHA"), held in person and virtually June 8 through 15, 2023. In addition, Keros announced preclinical data evaluating activin receptor-like kinase-2 ("ALK2") inhibition, as well as its combination with RKER-050, as potential treatment options for anemia of inflammation.

"We are pleased to present additional data from our ongoing Phase 2 clinical trial of KER-050 in MDS patients at EHA this year, which demonstrated durable hematological responses with longer-term treatment in a broad, lower-risk MDS patient population, including those with high transfusion burden," said Jasbir S. Seehra, Ph.D., President and Chief Executive Officer of Keros. "Additionally, we are excited to announce that we have recently expanded this trial to include two cohorts of MDS patients with iron overload, which will enable us to further explore the potential of KER-050 to reduce iron overload and improve iron utilization in MDS patients. Separately, we believe that we will have sufficient data from this trial at the end of this year that will allow us to begin the process of engaging with regulators on the design of a Phase 3 clinical trial."

Clinical Presentation

- *KER-050 treatment improved markers of erythropoietic activity and hematopoiesis over six months which resulted in hematological responses across a broad, lower-risk MDS population*

This ongoing, open-label, two-part, Phase 2 clinical trial is evaluating KER-050 in participants with very low-, low-, or intermediate-risk MDS. In Part 1, the dose escalation portion of the trial, 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 in Part 1 received KER-050 subcutaneously every 28 days for up to four cycles at the following dose levels: Cohort 1, 0.75 mg/kg; Cohort 2, 1.5 mg/kg; Cohort 3, 2.5 mg/kg; Cohort 4, 3.75 mg/kg; and Cohort 5, 5.0 mg/kg. In Part 2, the dose confirmation portion of the trial, an identical dosing schedule was followed, and patients initiated treatment at a starting dose of 3.75 mg/kg, the recommended Part 2 dose ("RP2D"), with the opportunity to dose escalate to 5.0 mg/kg or to down-titrate based on individual titration rules. Following completion of Part 1, eligible patients were given the opportunity to escalate up to the RP2D and receive long-term treatment with KER-050 for up to an additional 20 cycles ("Part 1 Extension").

As of April 3, 2023 (the "data cut-off date"), 25 patients from Part 1, including the Part 1 Extension, and 34 patients from Part 2, had received at least one dose of KER-050 at RP2D (collectively, the "safety population"). Of these patients, 37 had completed at least 24 weeks of treatment or discontinued as of the data cut-off date (the "evaluated RP2D patients"). Data for hematological response and markers of hematopoiesis were presented from exploratory analyses of these evaluated RP2D patients.

Of the 59 patients in the safety population, 71.2% (n=42/59) were RS positive while 28.8% (n=17/59) were non-RS. The safety population included 12 non-transfused ("NT"), 16 low transfusion burden ("LTB") and 31 high transfusion burden ("HTB") patients.

As of the data cut-off date, KER-050 was generally well tolerated by the 59 patients in the safety population. No patients had progressed to acute myeloid leukemia. There were two cases of fatal treatment-emergent adverse events ("TEAEs") in the trial (cardiac failure and myocardial infarction), each of which were determined to be unrelated to treatment. Four additional patients experienced TEAEs that led to discontinuation of treatment. One case was deemed treatment related (injection site reaction), and in three patients, the events were determined to be unrelated to treatment (dyspnea, chronic obstructive pulmonary disease and cardiac failure congestive (in one patient), and nodular melanoma). The most commonly reported TEAEs (in ≥15% of patients) were COVID-19, diarrhea, dyspnea, fatigue, nausea and nosebleeds (epistaxis).

As of the data cut-off date, 51.4% (n=19/37) of the evaluated RP2D patients achieved an overall erythroid response over the first 24 weeks of treatment, which is defined as meeting one of the following two endpoints:

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

Additional data from the evaluated RP2D patients, as of the data cut-off date, include:

- 51.4% (n=19/37) of the evaluated RP2D patients achieved HI-E over an eight-week period during the first 24 weeks of treatment.
- 42.3% (n=11/26) of the transfused RP2D patients receiving ≥ 2 RBC units at baseline achieved TI for at least eight weeks over the first 24 weeks of treatment. Of these 26 patients, 19 were RS positive and seven were non-RS.
  - 42.1% (n=8/19) of these RS positive patients achieved TI for at least eight weeks over the first 24 weeks of treatment.
  - 42.9% (n=3/7) of these non-RS patients achieved TI for at least eight weeks over the first 24 weeks of treatment.
- Of the transfused RP2D patients, 40.9% (n=9/22) of those who are HTB achieved TI for at least eight weeks during the first 24 weeks of treatment. Of these 22 patients, 17 were RS positive and five were non-RS.
  - 35.3% (n=6/17) of these RS positive HTB patients achieved TI for at least eight weeks.
  - 60.0% (n=3/5) of these non-RS HTB patients achieved TI for at least eight weeks.
- Of the 19 patients who achieved HI-E or TI during the first 24 weeks of treatment (the "HI-E or TI Responders"), 10 of them (52.6%) had ongoing response as of the data cutoff date.
  - The median duration of response for the HI-E or TI Responders was 42.4 weeks.

As of the data cut-off date, 44.1% (n=15/34) of the evaluated RP2D patients who had at least eight weeks of post-baseline platelet measurements exhibited sustained increases in platelet counts from baseline over at least eight weeks. Additionally, sustained increases in hemoglobin were observed over six months of treatment with KER-050 in the LTB and NT HI-E responders.

Additional data from the exploratory analysis of biomarkers of erythropoiesis and iron overload ("IO") were also presented, with data from the evaluated RP2D patients. Key observations from this analysis, as of the data cut-off date, are as follows:

- Soluble transferrin receptor levels generally increased with KER-050 treatment in HI-E or TI Responders, while ferritin levels generally decreased.
- As of the data cut-off date, 18 patients had baseline ferritin of >500 ng/mL. Of those 18 patients, eight (44.4%) had a maximum mean decrease of ≥250 ng/mL over any 12-week period during the first six months of treatment with KER-050, suggesting potential for KER-050 to reduce IO in the most impacted patients.

Based on these additional data, this trial has been expanded to include two cohorts of MDS patients with iron overload either with or without iron chelation, which would allow Keros to further evaluate the potential of KER-050 to reduce serum ferritin, an indicator of iron overload, in that MDS patient population.

Preclinical Presentations

- *A modified activin receptor type II ligand trap RKER-050 restored erythropoiesis in a mouse model of myelofibrosis*

RKER-050 was tested in a mouse model of advanced MF. Male MF mice with established anemia were administered either vehicle or 10 mg/kg of RKER-050 twice weekly for 12 weeks. Healthy male mice received only vehicle.

The vehicle-treated MF mice continued to exhibit a significant or trending decrease in RBC parameters, including RBCs, hemoglobin and hematocrit, compared to healthy controls. Relative to vehicle-treated MF mice, RKER-050-treated MF mice had a significant recovery of those RBC parameters, demonstrating that RKER-050 fully reversed anemia in this MF mouse model.

In the bone marrow, vehicle-treated MF mice showed a significant reduction in erythroid progenitors compared to healthy controls. Treatment with RKER-050 significantly increased certain erythroid progenitors in MF mice compared to vehicle-treated MF mice, suggesting bone marrow erythropoiesis was increased with RKER-050 treatment. Additionally, RKER-050-treated MF mice also had increased erythroid progenitors in the spleen compared to vehicle-treated MF mice, which may be due to the severe state of the disease-impacted bone marrow microenvironment in this MF mouse model.

Additionally, RKER-050 significantly reduced megakaryocyte progenitors in the bone marrow compared to the elevated levels observed in vehicle-treated MF mice, suggesting RKER-050 may positively influence the megakaryocyte lineage. However, platelets in the RKER-050-treated MF mice were not significantly increased compared to vehicle-treated MF mice at this advanced stage of disease.

These results suggest that RKER-050 can promote erythropoiesis and reduce aberrant megakaryocyte progenitor proliferation in the bone marrow in this MF mouse model. Keros believes that KER-050 has the potential to treat patients with MF and other hematological diseases where ineffective hematopoiesis occurs.

- *Combining ALK2 inhibition with a modified activin receptor IIA ligand trap provided additive benefits in resolving anemia in a mouse model of anemia of inflammation*

This preclinical study evaluated whether RKER-050 combined with RKER-216, an investigational neutralizing antibody to ALK2, could ameliorate anemia in a mouse model of induced chronic kidney disease ("CKD") representative of anemia of inflammation ("AI").

To induce a model of CKD, mice were fed a diet containing 0.2% adenine and 40 ppm iron for five weeks. After AI was confirmed, CKD mice were treated with 3 mg/kg of RKER-216 or vehicle twice a week for four weeks. In a separate study, CKD mice received twice weekly treatment of 3 mg/kg of RKER-216 or vehicle in combination with once weekly treatment of 7.5 mg/kg of RKER-050 or vehicle for four weeks.

- RKER-216-treated CKD mice exhibited a >95% decrease in serum hepcidin, decreases in spleen iron retention and an increase in transferrin saturation compared to vehicle-treated CKD mice. RKER-216-treated CKD mice also showed improvements in hemoglobin and RBC production compared to vehicle-treated CKD mice. Taken together, these data suggest that the observed increase in iron availability resulting from the administration of RKER-216 may be sufficient for improving iron-restricted erythropoiesis in this AI model.
- While RKER-216 monotherapy improved hemoglobin and RBC levels in CKD mice relative to vehicle-treated CKD mice, combination treatment with RKER-050 resulted in a greater magnitude of increase in both hematological parameters. No significant differences in serum hepcidin, spleen iron, or transferrin saturation were observed between CKD mice receiving combination therapy or monotherapy.

By targeting ALK2 inhibition to suppress hepcidin, RKER-216 increased iron availability for erythropoiesis and partially rescued anemia in CKD mice. Separately, the combination of RKER-216 and RKER-050 maximized the hematologic recovery in this AI model, which supports the potential benefits of this combination therapy.

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 participants 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 participants 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.

Conference Call and Webcast Information

The Company will host a conference call and webcast today, June 9, 2023, at 8:00 a.m. Eastern time, to discuss updates to and additional data from its hematology franchise, including the additional results from the ongoing Phase 2 clinical trial of KER-050 presented at the 28th Annual Congress of EHA.

The conference call will be webcast live at https://event.webcasts.com/starthere.jsp?ei=1615749&tp_key=a5c7667d07. 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 MF.

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 hematological, pulmonary and cardiovascular 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 a number of tissues, including blood vessels and heart tissue. 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 MDS and in patients with MF. Keros' lead small molecule product candidate, KER-047, is being developed for the treatment of functional iron deficiency. Keros' third product candidate, KER-012, is being developed for the treatment of pulmonary arterial hypertension and for the treatment of cardiovascular disorders.

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, including its regulatory plans; the potential of KER-050 to reduce serum ferritin in MDS patients with iron overload; the potential of KER-050 to treat patients with MF and other hematological diseases where ineffective hematopoiesis occurs; the potential of RKER-050 to promote erythropoiesis and reduce aberrant megakaryocyte proliferation in the bone marrow; and the potential benefits of combining RKER-050 with RKER-216 to treat anemia resulting from CKD. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. These risks and uncertainties include, among others: Keros' limited operating history and historical losses; Keros' ability to raise additional funding to complete the development and any commercialization of its product candidates; Keros' dependence on the success of its product candidates, KER-050, KER-047 and KER-012; 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 May 4, 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.

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KEROS THERAPEUTICS

Hematology Franchise: Program Updates and Summary of Data Presented at 28th Annual Congress of the European Hematology Association

June 9, 2023

Disclaimer

Statements contained in this presentation regarding matters that are not historical facts are “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995, as amended. Words such as "anticipates," "believes," "expects," "intends," “plans,” “potential,” "projects," “would” and "future" or similar expressions are intended to identify forward-looking statements. Examples of these forward-looking statements include statements concerning: Keros’ expectations regarding its growth, strategy, progress and the design, objectives and timing of its preclinical studies and clinical trials for KER-050, KER-047 and KER-012; 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 public health crises, such as the COVID-19 pandemic.

These and other risks are described more fully in Keros’ filings with the Securities and Exchange Commission (SEC), including the “Risk Factors” section of Keros’ Quarterly Report on Form 10-Q, filed with the SEC on May 4, 2023, and its other documents subsequently filed with or furnished to the SEC. All forward-looking statements contained in this presentation speak only as of the date on which they were made. Except to the extent required by law, Keros undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

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

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

Keros Hematology Franchise

- Keros is harnessing the powerful biology of the TGF-β superfamily to develop product candidates with the potential to address the multiple mechanisms leading to ineffective erythropoiesis
  - KER-050: Designed to inhibit signaling by activin A, activin B, GDF8 and GDF11 to promote growth and differentiation of erythroid precursors and increase platelets
  - KER-047: Designed to inhibit activin receptor-like kinase-2 (ALK2) to inhibit hepcidin and mobilize iron for incorporation into hemoglobin

KER-050 clinical data are presented as of a data cutoff date of April 3, 2023.

28th Annual Congress of the European Hematology Association

Clinical Presentation

"KER-050 treatment improved markers of erythropoietic activity and hematopoiesis over six months which resulted in hematological responses across a broad, lower-risk MDS population"

- Abstract Code: S166

Preclinical Presentations

"A modified activin receptor type II ligand trap RKER-050 restored erythropoiesis in a mouse model of myelofibrosis"

- Abstract Code: P992

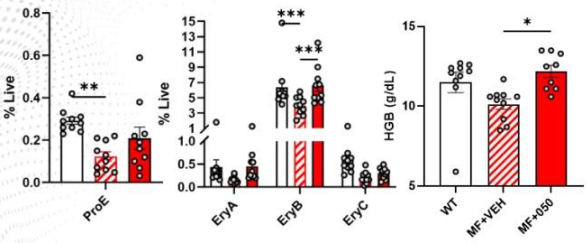
"Combining ALK2 inhibition with a modified activin receptor IIA ligand trap provided additive benefits in resolving anemia in a mouse model of anemia of inflammation"

- Abstract Code: P1488

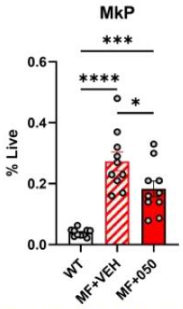
Myelofibrosis is Characterized by Ineffective Hematopoiesis

- Myelofibrosis (MF) is a group of rare cancers of the bone marrow in which the marrow is replaced by scar tissue and is not able to produce healthy blood cells
- MF is characterized by ineffective hematopoiesis, an enlarged spleen, bone marrow fibrosis and shortened survival. Patients often experience multiple disease-associated and treatment-emergent cytopenias, including anemia and thrombocytopenia
- The ineffective hematopoiesis in MF is driven by molecular abnormalities in the JAK-STAT signaling pathway, which leads to proliferation of red blood cell progenitors and platelet progenitors, or megakaryocytes
  - Megakaryocyte accumulation and breakdown is implicated in the inducement of bone marrow fibrosis
- KER-050 was evaluated for its ability to promote hematopoiesis in the Gata1low mouse model of myelofibrosis
  - Gata1 is an essential driver of megakaryocyte and erythroid differentiation
  - In both mice and humans, insufficient levels of Gata1 result in accumulation of megakaryocyte-erythroid precursors, bone marrow disruption and ineffective hematopoiesis

RKER-050 Treatment Restored Hematopoiesis in the Bone Marrow, Reversing Anemia and Normalizing Megakaryocyte Precursor Number in the Mouse Model of MF



Treatment of GATA1low mice with RKER-050 restored erythropoiesis to the bone marrow and reversed anemia



RKER-050 also reduced the MK hyperproliferation in BM, supporting a less congested BM

These data support the potential of KER-050 to treat the cytopenias, restore hematopoiesis in the bone marrow and reduce spleen size in patients with MF

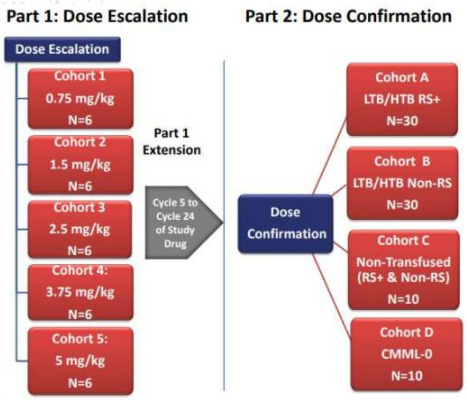
*p≤0.05,**p≤0.01,***p≤0.001,****p≤0.0001; WT = wild type; MF+VEH = MF mice with established anemia administered vehicle twice weekly for 12 weeks; MF+050 = MF mice with established anemia administered 10 mg/kg of RKER-050 twice weekly for 12 weeks; MkP = megakaryocyte progenitors

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)

MD-201: A Phase 2 Clinical Trial to Assess KER-050 in Low- to Intermediate-Risk MDS

Design and Dose Levels



- Primary Objective:
  - Assess safety and tolerability of KER-050
- Secondary Endpoints include:
  - Hematological Improvement- Erythroid (HI-E)
  - Transfusion Independence (TI) ≥8 weeks
- Ongoing Trial: Status as of April 3, 2023:
  - Part 1 Dose Escalation (N=31; completed)
  - RP2D: 3.75 mg/kg w/titration to 5 mg/kg/4 weeks
  - RP2D Experienced Patients: N=59
    - 25 patients from Part 1
    - 34 patients from Part 2

RP2D = Recommended Part 2 Dose

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

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

Parameter	RP2D (N=59)
Median Age, years (range)	74.0 (53-89)
Sex, n (%) Male	34 (57.6)
RBC Transfusion Status, units per 8 weeks, n (%)	
Non-transfused (NT), 0 units	12 (20.3)
Low Transfusion Burden (LTB), <4 units	16 (27.1)
High Transfusion Burden (HTB), ≥4 units	31 (52.5)
≥8 units	12 (20.3)
Ring Sideroblast Status, n (%)	
RS Positive	42 (71.2)
Non-RS	17 (28.8)
IPSS-R Risk Category, n (%)	
Very Low	8 (13.6)
Low	39 (66.1)
Intermediate	11 (18.6)
Missing	1 (1.7)
MDS WHO 2016 Classification, n (%)	
MDS	2 (3.4)
MDS-MLD	12 (20.3)
MDS-RS-MLD	29 (49.2)
MDS-RS-SLD	5 (8.5)
Missing	11 (18.6)
Prior ESA	13 (22.0)
Concurrent Iron Chelator	17 (28.8)

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

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

Opportunity to Evaluate Longer-Term Exposure to KER-050

Exposure of overall MDS RP2D Population as of the data cutoff date:

- 59 patients received ≥1 dose of KER-050 (included in safety population)
- Median duration of treatment = 225 days (≈32 weeks)
  - Range 6 to 649 days (≈1 to 93 weeks)
- Median doses received = 6
  - Range 1 to 22
    - 14 (23.7%) patients received ≥12 doses
    - 15 (25.4%) patients received <3 doses

Hematological response and markers of hematopoiesis are presented from exploratory analyses of RP2D patients with at least 6 months of KER-050 treatment or who have discontinued (n=37)

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

KER-050 Was Generally Well-Tolerated

- Most TEAEs were Grades 1 or 2 (51%)
- Most frequent TEAEs (in ≥15% of patients) regardless of causality were:
  - Fatigue, n=13 (22%)
  - Nausea, n=11 (18.6%)
  - Diarrhea, n=11 (18.6%)
  - Epistaxis, n=10 (16.9%)
  - COVID-19, n=9 (15.3%)
  - Dyspnea, n=9 (15.3%)
- Of the most frequent TEAEs, all were grade 1 or 2 except:
  - 1 Grade 3 (COVID-19)
  - 4 Grade 3 (Dyspnea)
- 1 treatment-related TESAE (Grade 2 Injection site reaction)
- 2 fatal TEAEs (cardiac failure and myocardial infarction); both determined to be unrelated to study treatment by the investigator
- No patients progressed to AML

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

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

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

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

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

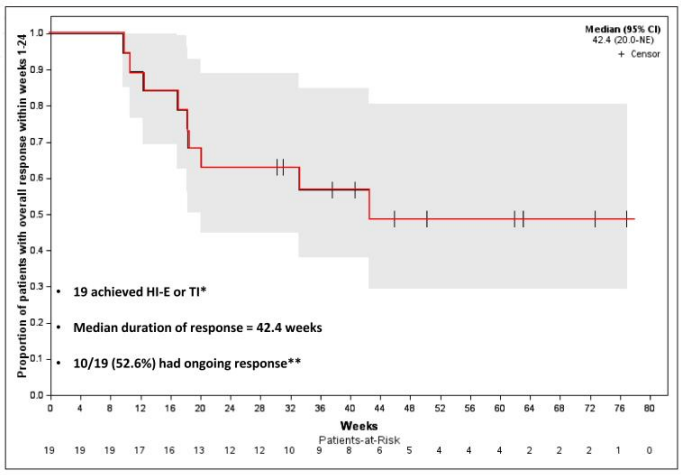
Response Endpoint	RP2D Patients[1]	
	All Evaluable	HTB Evaluable
Overall Erythroid Response (HI-E or TI)	19/37 (51.4)	11/22 (50)
IWG 2006 HI-E	19/37 (51.4)	11/22 (50)
TI ≥ 8 weeks[2] RS+ Non-RS	11/26 (42.3) 8/19 (42.1) 3/7 (42.9)	9/22 (40.9) 6/17 (35.3) 3/5 (60)

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

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

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

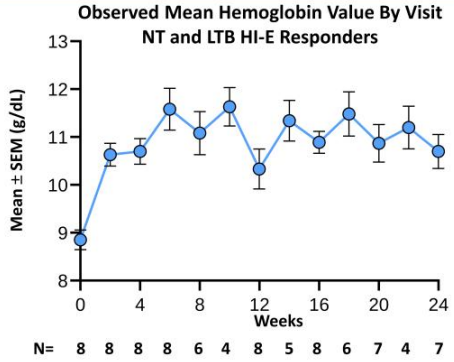
Data Suggest KER-050 Elicited a Durable Response



* During weeks 0-24 in RP2D patients with ≥24wk of treatment or who discontinued
**Patients with ongoing response censored at time of data cutoff, denoted by vertical lines

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

Sustained Increases in Hemoglobin Observed Over 6 Months of KER-050 Treatment

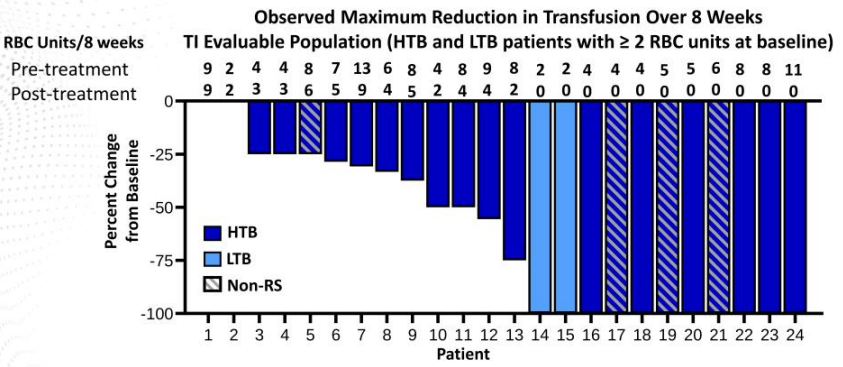


8/15 (53.3%) NT and LTB patients with ≥6 months of treatment (or discontinued) achieved HI-E response in first 24 weeks of treatment

Observed sustained increases in hemoglobin support durable response with KER-050

Data are presented as of a data cutoff date of April 3, 2023. Baseline hemoglobin calculated as average over 8-week pre-treatment period. Hemoglobin values within 14 days following a transfusion censored except for pre-transfusion values. Per protocol, KER-050 dose must be held at hemoglobin levels ≥12 g/dL.

Reductions in Transfusion Burden Observed with KER-050 Treatment

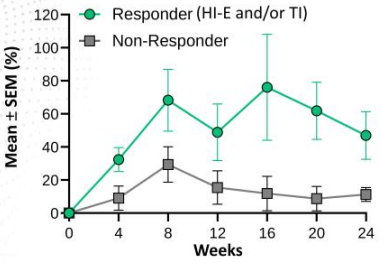


- Reduced transfusion burden observed in majority of LTB and HTB patients
- TI observed in both RS+ and non-RS patients
- TI achieved in patients with baseline transfusion burden ranging from 2 to 11 units/8 weeks

Data are presented as of a data cutoff date of April 3, 2023.
Note: 2 patients discontinued with insufficient data to determine 8-week transfusion reduction, and are not included in this plot

Data Suggest Enhanced Erythropoiesis and Potential to Reduce Iron Overload

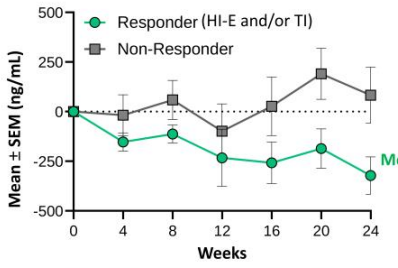
Observed Percent Change from Baseline In Soluble Transferrin Receptor (sTfR)



N=	19	16	10	16	11	17	15
	17*	15	7	11	7	9	7

*One patient was missing a baseline sTfR assessment.

Observed Change from Baseline In Ferritin



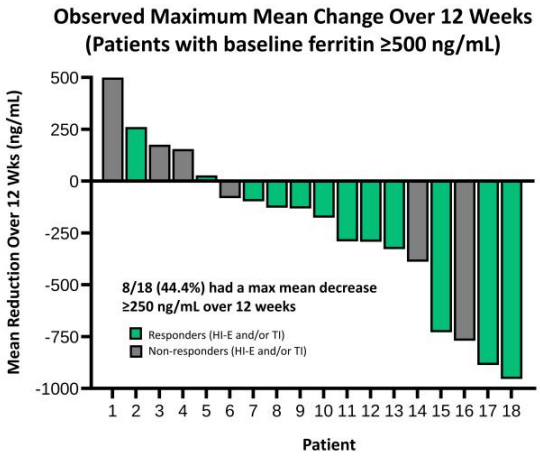
N=	19	17	17	17	18	17	16
	18	17	14	13	13	11	9

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

Observed Reductions in Serum Ferritin with KER-050 Treatment

Iron overload is a serious clinical complication in MDS

- A serum ferritin >1000 ng/mL is associated with 3x greater risk of death in MDS patients[1]
- Baseline ferritin in this analysis population (n=37):
  - Mean = 1026 ng/mL
  - Range = 86.3 to 5,829 ng/mL
  - 18 patients ≥500 ng/mL



[1]*A. Waszczuk-Gajda et al. 2016 Adv Clin Exp Med 25(4): 633-641*

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

Summary of KER-050 MDS Data

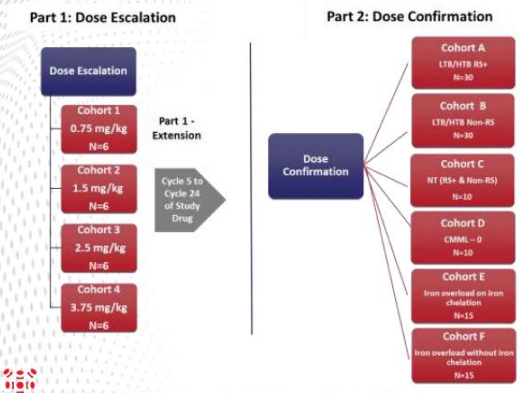
- KER-050 was generally well-tolerated; safety profile consistent to that previously reported for this trial
- Durable hematological responses were observed in a broad, lower-risk MDS population, including those with HTB and/or non-RS disease
- Observed decreases in serum ferritin, a marker of iron overload, may reflect:
  - Reduced iron overload due to reduced transfusion burden
  - Improved iron utilization with increased erythropoiesis

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

Phase 2 MDS Trial Amended to Evaluate KER-050 in Patients with Iron Overload

This trial has been expanded to include two cohorts of MDS patients with iron overload to further investigate the serum ferritin reductions observed as of the April 3, 2023 data cutoff date

Amended Phase 2 Clinical Trial Design and Dose Levels



- In lower-risk MDS patients, severe anemia and lack of effective treatment options leads to blood transfusions, often resulting in iron overload
  - This transfusional iron overload has negative consequences on hematopoiesis and cardiovascular health, and impacts progression to AML
- In MDS, patients that require 4 units of blood every 8 weeks will accumulate nearly 5 grams of iron in a year[1]
  - Typically, healthy adults have 3-4 grams of total body iron[2]
- Iron chelation therapy can reduce the degree of iron overload in patients, but its tolerability and safety profile limits its use in lower-risk MDS[3]

(1) 1 unit of RBC contains ~200 mg of iron; (2) Kohgo, 2008. International Journal of Hematology; and (3) Shah, 2016. J. Adv. Pract. Oncol.

Additional Hematology Program Updates

- **KER-050: Myelofibrosis**
  - This 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 myelofibrosis-associated cytopenias is ongoing
    - Following Safety Review Committee recommendation, dosing for Cohort 3 was initiated at 3.0 mg/kg in both combination and monotherapy arms
- **KER-047: Iron-refractory iron deficiency anemia (IRIDA)**
  - Our open label, two-part, dose-escalation and dose-expansion Phase 2 clinical trial to evaluate KER-047 in patients with IRIDA was originally planned to enroll 12 patients in a single center
    - In December 2022, we announced data from the one enrolled patient, which demonstrated the impact of KER-047 in reducing serum hepcidin and serum ferritin with observed increases in serum iron. This supports our hypothesized mechanism of action for KER-047 and will guide further development in this pathway
    - Difficulties with enrollment of this trial, given the small size of the patient population for this rare disease
    - We have decided to terminate this trial early, having observed data in the one patient enrolled that we believe is suggestive of proof of mechanism. The planned early termination is not on the basis of any safety concerns

Keros Anticipated Key Milestones

KER-050

• Complete enrollment in transfusion-dependent cohorts in Phase 2 MDS trial	H2 2023
• Announce additional data from Part 2 of Phase 2 MDS trial	H2 2023
• Announce dose escalation data from Phase 2 MF trial	H2 2023
• Initiate Part 2 of Phase 2 MF trial	H2 2023

KER-047

• Announce initial data from Phase 2 FID (MDS and MF) trial	H2 2023

KER-012

• Initiate Phase 2 PAH trial	H1 2023
• Initiate Phase 2 open-label biomarker trial	H2 2023

Q&A