Keros Therapeutics Presents Clinical Data from its KER-050 and KER-047 Programs and Preclinical Data from its KER-050 and ALK2 Inhibitor Programs at the 64th American Society of Hematology Annual Meeting and Exposition

December 12, 2022 3:00 PM EST

Keros Therapeutics will be hosting a conference call and webcast today, December 12, 2022, at 4:01 p.m. ET.

LEXINGTON, Mass., Dec. 12, 2022 (GLOBE NEWSWIRE) -- 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, 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 initial data from its ongoing Phase 2 clinical trial of KER-050 in patients with myelofibrosis ("MF") and from its ongoing Phase 2 clinical trial of KER-047 in patients with iron-refractory iron deficiency anemia ("IRIDA"), at the 64th American Society of Hematology ("ASH") Annual Meeting and Exposition, held in person and virtually December 10 through 13, 2022. In addition, Keros presented preclinical data showing the potential of a research form of KER-050 ("RKER-050") to treat anemia and bone loss in an animal model of MDS, as well as preclinical data evaluating the treatment effect of activin receptor-like kinase 2 ("ALK2") inhibition combined with RKER-050 in a mouse model of anemia of inflammation.

"We are pleased to present clinical and preclinical data from our lead hematological programs at ASH this year. In our ongoing Phase 2 clinical trial in MDS, we observed a sustained response with longer-term treatment with KER-050 across all transfusion burdens. Data from our ongoing Phase 2 trial in MF support the potential for KER-050 to treat multiple cytopenias as either a monotherapy or in combination with ruxolitinib," said Jasbir S. Seehra, Ph.D., President and Chief Executive Officer of Keros. "In addition, clinical data from one IRIDA patient in our Phase 2 clinical trial of KER-047 was suggestive of iron redistribution consistent with KER-047's mechanism of action."

Clinical Presentations

- *Effects of KER-050 on Iron Metabolism: Exploratory Analyses from an Ongoing Phase 2 Study in Patients with Myelodysplastic Syndromes*

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 October 1, 2022 (the "data cut-off date"), 25 patients from Part 1, including the Part 1 Extension, and 11 patients from Part 2, had received at least one dose of KER-050 at RP2D (collectively, the "safety population"). 29 of these patients had completed eight weeks of treatment and the applicable assessments as of the data cut-off date (the "evaluable RP2D patients").

Of the 36 patients in the safety population, 63.9% (n=23/36) were RS positive while 36.1% (n=13/36) were non-RS. The safety population was comprised of 10 non-transfused ("NT"), six low transfusion burden ("LTB") and 20 high transfusion burden ("HTB") patients.

As of the data cut-off date, 51.7% (n=15/29) of the evaluable RP2D patients 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 of ≥ 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 transfusion-dependent patients who required ≥ 2 RBC units transfused at baseline.

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

- 51.7% (n=15/29) of the evaluable RP2D population achieved HI-E over an eight-week period.
- 50.0% (n=9/18) of the transfused RP2D patients receiving ≥ 2 RBC units at baseline achieved TI for at least eight weeks. Of these 18 patients, 12 were RS positive and six were non-RS.

    - 50.0% (n=6/12) of these RS positive patients achieved TI for at least eight weeks.
    - 50.0% (n=3/6) of these non-RS patients achieved TI for at least eight weeks.
- Of the transfused RP2D patients, 50.0% (n=8/16) of those who are HTB achieved TI for at least 8 weeks. Of these 16 patients, 11 were RS positive and five were non-RS.
    - 45.5% (n=5/11) 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.
- 53.3% (n=8/15) of the transfused RP2D patients receiving ≥ 2 RBC units at baseline, with the opportunity to extend treatment beyond four cycles, achieved TI for at least 12 weeks, demonstrating a sustained TI benefit with continued treatment.
    - Of these transfused RP2D patients, 50.0% (n=7/14) of those who are HTB achieved TI for at least 12 weeks.

As of the data cut-off data, sustained increases in platelet counts were observed for patients achieving HI-E or TI over a 24-week treatment period, supporting a potentially differentiated mechanism of KER-050 to promote hematopoiesis across multiple cell lineages.

As of the data cut-off date, KER-050 was generally well tolerated by the 36 patients in the safety population. No dose-limiting toxicities were reported, and no patients progressed to acute myeloid leukemia. There was one case of a fatal treatment-emergent adverse event ("TEAE") in the trial that was determined to be unrelated to treatment. There were three additional TEAEs that led to discontinuation of treatment, one of which was deemed treatment related (injection site reaction) and two of which were determined to be unrelated to treatment (dyspnea and chronic obstructive pulmonary disease). The most commonly reported TEAEs were diarrhea, fatigue, dyspnea and nausea.

An exploratory analysis of biomarkers of iron overload ("IO") was also presented, with data from the 31 participants who received up to four cycles of treatment in the completed Part 1. 58.1% (n=18/31) of these patients were classified as HTB. At baseline, transfusion-dependent patients exhibited biomarkers suggestive of a greater degree of ineffective hematopoiesis than NT patients, including lower levels of hemoglobin, reticulocytes and soluble transferrin receptor. In addition, lower levels of transferrin and elevated levels of serum ferritin at baseline, especially among HTB patients, suggest more severe IO in transfusion-dependent patients as compared to NT patients. Key observations from this analysis, as of the data cutoff date, are as follows:

- Soluble transferrin receptor levels generally increased with KER-050 treatment, particularly in HTB patients, while ferritin levels decreased.
- On an individual level, most patients who achieved HI-E or TI also showed decreases in serum ferritin. Such decreases were generally greater in patients with baseline ferritin of >500 ng/mL, suggesting potential for KER-050 to reduce IO in the most impacted patients.
- Reductions in transfusion burden, based on transfused RBCs over eight weeks, was generally associated with reductions in serum ferritin, especially for patients who achieved TI.

Taken together, the results from the trial and the exploratory analysis as of the data cut-off date suggest that KER-050 has the potential to improve hematopoiesis, reduce transfusion burden and reduce IO, particularly in patients receiving frequent RBC transfusions.

- *Modulation of TGF-β Superfamily Signaling to Treat Myelofibrosis and Mitigate JAK Inhibitor Toxicity: A Report on the Phase 2 Study of KER-050 in Participants with Myelofibrosis*

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. Part 1, the dose escalation portion of the trial, is designed to assess the safety and tolerability of KER-050 at dose levels of 0.75 mg/kg, 1.5 mg/kg, 3.0 mg/kg and 4.5 mg/kg, both in a monotherapy arm and in a combination therapy arm with ruxolitinib, to identify doses of KER-050 to be evaluated in Part 2, the dose expansion portion of the trial.

As of the data cut-off date of October 1, 2022, 12 patients were enrolled in Part 1, with six patients in each arm receiving 0.75 mg/kg dose of KER-050. For the patients in the combination therapy arm, the median ruxolitinib dose was 12.5 mg twice daily at baseline. As of the data cut-off date, in each of the arms, at least half of the enrolled patients had received three or more doses of KER-050. At baseline, 41.7% (n=5/12) were transfusion-dependent, with an average transfusion burden of 9.8 RBC units in the 12 weeks preceding Cycle 1, Day 1.

As of the data cut-off date, KER-050 was generally well tolerated, with no drug-related serious adverse events or dose-limiting toxicities reported. No participants had a treatment-related dose reduction of KER-050 or ruxolitinib as of the data cut-off date. The most commonly reported TEAEs were diarrhea, COVID-19, dyspnea and fatigue. One patient withdrew from the trial due to an unrelated adverse event.

Although variability was observed, as of the data cut-off date, treatment with KER-050 at the lowest dose in the trial (0.75 mg/kg) resulted in increased reticulocytes and platelets on aggregate across cycles 1 and 2. These increases were observed in both monotherapy and combination arms, as well as in both non-transfusion-dependent and transfusion-dependent patients. These data support the potential of KER-050 to potentially promote differentiation of erythroid and megakaryocytic precursors and treat anemia and thrombocytopenia in patients with MF.

The following data from two patients enrolled in this trial were also presented:

- In a 60-year-old, non-transfusion-dependent female patient with primary MF in the monotherapy arm, an increase in reticulocytes was observed after a single 0.75 mg/kg dose of

KER-050, which was followed by a sustained increase in hemoglobin of ≥1.5 g/dL over baseline with continued dosing for ≥12 consecutive weeks in the first 24 weeks of the trial. The observed increases in erythropoietic markers corresponded with sustained decreases in ferritin and erythropoietin, which is consistent with upregulation of erythropoiesis. An overall increase in platelet count was also observed in this patient.

- In a 75-year-old, transfusion-dependent male patient with high-risk MF and severe thrombocytopenia in the combination arm, increases in reticulocytes and soluble transferrin receptor levels were observed following the first cycle of treatment. Though platelet counts fluctuated over the treatment period, improvements were observed following the second and third cycles. The patient experienced a reduction in RBC transfusion burden from nine units per 12 weeks pre-treatment to six units per 12 weeks post-treatment.

- *Preliminary Results of a Phase 2 Clinical Trial of the ALK-2 Inhibitor KER-047 for Treatment of Iron Refractory Iron Deficiency Anemia*

This ongoing, open-label, two-part Phase 2 clinical trial is evaluating KER-047 in patients with IRIDA, which is an inherited form of iron deficiency anemia in which matriptase-2, a cell surface protease, does not function properly, resulting in elevated ALK2 signaling and high hepcidin levels. In Part 1, the dose escalation portion of the trial, patients will receive KER-047 once daily for 14 days, starting at the lowest dose of 25 mg in Cohort 1, followed by a 14-day washout period.

This presentation reported observations from one patient enrolled in Cohort 1 of Part 1 who completed the 14-day treatment and washout periods. Treatment with KER-047 was generally well tolerated by this patient, with no serious adverse events or dose-limiting toxicities reported during treatment. There was one TEAE reported, which was determined to be unrelated to the treatment.

In this patient, hepcidin and serum ferritin levels decreased following administration of KER-047. Serum ferritin returned to baseline levels in the washout period, indicating that the effect was potentially treatment-associated. Reticulocyte hemoglobin also increased in this patient during the treatment period. Taken together, these data are suggestive of iron redistribution consistent with the mechanism of action of KER-047.

Preclinical Presentations

- *RKER-050, a Novel Activin Receptor Type II Ligand Trap, Rescued Anemia and Reduced Bone Loss in a Mouse Model of Myelodysplastic Syndromes*

RKER-050 was tested in a mouse model of MDS. Male MDS mice with established anemia were administered either vehicle or 7.5 mg/kg of RKER-050 once weekly for six weeks. Healthy male mice received only vehicle.

The vehicle-treated MDS mice showed reductions in RBCs, hemoglobin, hematocrit and reticulocytes compared with healthy controls. Relative to vehicle-treated MDS mice, RKER-050-treated MDS mice showed increases in those RBC parameters, demonstrating that RKER-050 can mitigate anemia in an MDS mouse model.

Additionally, analysis of bone microarchitecture showed significantly weaker bone in MDS mice compared to healthy controls. In contrast, bone parameters in RKER-050-treated MDS mice were significantly improved relative to the vehicle-treated MDS mice.

These results suggest that RKER-050 can mitigate anemia and bone loss in an MDS mouse model, potentially by rebalancing hematopoiesis and bone turnover. In particular, the ability of RKER-050 to improve bone microarchitecture within the trabecular region could be an important step in reestablishing healthy blood cell production. Accordingly, Keros believes that KER-050 has the potential to treat patients with MDS and other hematological diseases, including MF, where a disease-impacted bone marrow microenvironment contributes to ineffective hematopoiesis and bone loss.

- *ALK2 Inhibition and a Modified Activin Receptor Type IIA Ligand Trap Co-therapy Maximized Hematologic Improvements in a Mouse Model of Anemia of Inflammation*

This preclinical study evaluated whether RKER-050 combined with KTI-m216, 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 KTI-m216 or vehicle twice a week for four weeks. In a separate study, CKD mice received biweekly KTI-m216 or vehicle with a weekly dose of vehicle or 7.5 mg/kg RKER-050 intraperitoneally for four weeks.

- KTI-m216-treated CKD mice exhibited a decrease in serum hepcidin by >95% and an increase in circulating iron levels compared to vehicle-treated CKD mice. KTI-m216-treated CKD mice also showed similar improvements in hematological parameters compared to vehicle-treated CKD mice, suggesting that KTI-m216-mediated suppression of hepcidin levels improved erythropoiesis and subsequently increased serum iron levels.
- While KTI-m216 monotherapy improved hemoglobin levels in CKD mice relative to vehicle-

treated CKD mice, combination treatment with RKER-050 resulted in a greater magnitude of increase in hemoglobin levels. RBC counts were also observed to significantly increase in CKD mice receiving combination therapy compared to monotherapy. No significant differences in serum hepcidin or iron were observed between CKD mice receiving combination therapy or monotherapy.

By suppressing hepcidin through ALK2 inhibition, KTI-m216 increased circulating iron for erythropoiesis and improved, but did not fully rescue, anemia in the CKD mice. However, combining RKER-050 with KTI-m216 increased RBC production and provided a greater degree of benefit in treating anemia in CKD mice compared to KTI-m216 monotherapy, which supports the potential benefits of this combination therapy.

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 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.

About the Ongoing Phase 2 Clinical Trial of KER-050 in Patients with MF-Associated Cytopenias

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 participants with MF-associated cytopenias.

The primary objective of this trial is to assess the safety and tolerability of KER-050 in participants with MF-associated cytopenias. 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 administered with or without ruxolitinib.

About the Ongoing Phase 2 Clinical Trial of KER-047 in Patients with IRIDA

Keros has initiated an open-label, two-part Phase 2 clinical trial to evaluate KER-047 in participants with IRIDA. Part 1 is the 14-day dose-escalation portion of the trial consisting of up to four ascending dose cohorts starting at 25 mg once daily. Part 2 is the 28- to 56-day dose-expansion portion of the trial, with treatment dose and duration to be selected based on Part 1 results.

The primary objective of this trial is to assess the safety of KER-047. The secondary objectives of this trial are to evaluate the pharmacokinetics and pharmacodynamics of KER-047.

Conference Call and Webcast Information

The Company will host a conference call and webcast today, December 12, 2022, at 4:01 p.m. Eastern time, to discuss the additional results from its ongoing Phase 2 clinical trial of KER-050 in patients with MDS, as well as initial data from its ongoing Phase 2 clinical trial of KER-050 in patients with MF and from its ongoing Phase 2 clinical trial of KER-047 in patients with IRIDA, which was presented at the 2022 ASH Annual Meeting and Exposition.

The conference call will be webcast live at https://event.webcasts.com/starthere.jsp?ei=1583755&tp_key=6cc8555aa4. 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 TGF-β 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 KER-047

Keros' lead small molecule product candidate, KER-047, is designed to selectively and potently inhibit ALK2, a TGF-β receptor. KER-047 is being developed for the treatment of functional iron deficiency which is a consequence of elevated ALK2 signaling, including the Company's initial target, IRIDA.

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 TGF-β family of proteins, which are master regulators of RBC 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 associated with cardiac hypertrophy.

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 and KER-047; the potential of KER-050 to improve hematopoiesis across multiple cell lineages, and to reduce transfusion burden and reduce IO, particularly in patients receiving frequent RBC transfusions; the potential of KER-050 to treat multiple cytopenias in patients with MF as either a monotherapy or in combination with ruxolitinib; the potential of KER-050 to treat hematological diseases where a disease-impacted bone marrow microenvironment contributes to ineffective hematopoiesis and bone loss; and the potential benefits of combining RKER-050 with ALK2

inhibition 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 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 3, 2022, 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:

Deepankar Roy
droy@kerostx.com
(213) 268-1878