Keros Therapeutics Presents Clinical Trial and Preclinical Study Results from its KER-050 Program and Preclinical Data from its ALK2 Inhibitor Program at the 27th Annual Congress of the European Hematology Association

June 10, 2022 10:00 AM EDT

- *Keros Therapeutics will be hosting a conference call and webcast today, June 10, 2022, at 8:00 a.m. Eastern time.*

LEXINGTON, Mass., June 10, 2022 (GLOBE NEWSWIRE) -- 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 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 on multiple stages of thrombopoiesis, at the 27th Annual Congress of the European Hematology Association ("EHA"), held in person and virtually June 9 through 17, 2022. In addition, Keros announced preclinical data evaluating ALK2 inhibition as a potential treatment option for anemia of inflammation.

"We believe the additional data from our ongoing Phase 2 clinical trial of KER-050 in MDS patients continues to support the potential of KER-050 as a treatment for multilineage cytopenias, and are pleased to present at EHA this year," said Jasbir S. Seehra, Ph.D., President and Chief Executive Officer of Keros. "Additionally, we are excited to announce that we have recently initiated dosing for Part 2 of the trial, at a starting dose of 3.75 mg/kg, with an opportunity for patients to dose escalate to 5.0 mg/kg based on individual titration rules, 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 for Part 1 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; Cohort 4, 3.75 mg/kg; and Cohort 5, 5.0 mg/kg.

As of April 3, 2022 (the "data cut-off date"), 31 patients in Cohorts 1 through 5 had received at least one dose of KER-050. Of these, 27 patients in Cohorts 1 through 5 had completed eight weeks of treatment and evaluation as of the data cut-off date (the "evaluable patients"). The 27 evaluable patients were comprised of five non-transfused ("NT"), six low transfusion burden ("LTB"), and 16 high transfusion burden ("HTB") patients. Two of the transfused LTB patients required <2 red blood cell ("RBC") units at baseline. Of the 20 LTB and HTB patients that required ≥2 RBC units at baseline, eight were non-RS and 12 were RS positive.

As of the data cut-off date, 51.9% (n=14/27) of the evaluable 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 by ≥ 4 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 patients in Cohorts 1 through 5 of the trial, as of the data cut-off date, include:

- 46.2% (n=12/26) of the evaluable population achieved HI-E over an eight-week period.
- 45.0% (n=9/20) of the transfused patients receiving ≥ 2 RBC units at baseline achieved TI for at least eight weeks. Of these 20 patients, 12 were RS positive and eight were non-RS.
  - 50.0% (n=6/12) of these RS positive patients achieved TI for at least eight weeks.
  - 37.5% (n=3/8) of these non-RS patients achieved TI for at least eight weeks.
- 43.8% (n=7/16) of the HTB patients achieved TI for at least 8 weeks.

In addition, sustained increases in platelets were observed in HTB patients achieving HI-E or TI, which supports the potential of KER-050 as a treatment for multilineage cytopenias in difficult-to-treat HTB patients. Increases in reticulocytes and serum soluble transferrin receptor levels, as well as decreases in serum ferritin, were also observed in HTB patients. Together, these exploratory pharmacodynamic data suggest an improvement in erythropoiesis.

As of the data cut-off date, KER-050 was observed to be generally well-tolerated in the 31 patients in Cohorts 1 through 5 who had received at least one dose of KER-050. No drug-related serious adverse events or dose-limiting toxicities were reported. The most commonly reported treatment-emergent adverse events were dyspnea, fatigue, anemia, diarrhea, headache and nausea. Treatment-related adverse events were reported in five patients, which were mild or moderate in severity. No patients developed acute myeloid leukemia. Four patients withdrew from the trial prior to completing treatment with KER-050, one due to death deemed unrelated to study drug, one due to withdrawn consent and two due to unrelated treatment-emergent adverse events.

Following recommendation by the Safety Review Committee, dosing for Part 2 of the trial was initiated at a starting dose of 3.75 mg/kg, with an opportunity for patients to dose escalate to 5.0 mg/kg based on individual titration rules.

Preclinical Presentations

- *RKER-050, a novel inhibitor of TGF-β superfamily signaling, induced platelet production in healthy mouse megakaryocytes*

Administration of a 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 RKER-050 had an increase in platelet numbers at 12 hours, 37 days and 51 days after administration compared to vehicle-treated mice ($p \leq 0.001$, $p \leq 0.05$ and $p \leq 0.01$, respectively). At 14 days and 91 days after administration, counts normalized back to vehicle control levels, demonstrating a phasic response on thrombopoiesis. Taken together, these data suggest that RKER-050 may be affecting thrombopoiesis at multiple stages, including platelet formation and megakaryocyte progenitor renewal.
    - Keros also analyzed CD41+ cells, which are megakaryocyte precursors, from the bone marrow of healthy mice at 12 hours post-treatment in order to investigate the potential effects of RKER-050 on early stages of thrombopoiesis. An increase in the CD41+ cells was observed compared to vehicle-treated mice ($p \leq 0.01$), as well as an increase in higher levels of ploidy at 24 hours post-treatment, indicating that RKER-050 increased differentiation of megakaryocyte precursors towards the later stages of maturation.
- Keros also demonstrated that inhibition of activin A with a neutralizing antibody increased production of platelets. Similarly, treatment with RKER-050 increased platelet production. These data are consistent with these treatments acting to inhibit negative regulators of thrombopoiesis and shift the balance towards increased bone morphogenic protein ("BMP") signaling which promotes thrombopoiesis. These data support that RKER-050 promoted megakaryocyte maturation potentially by blocking inhibitory transforming growth factor-beta ("TGF-β") ligands, such as activin A, in this preclinical model.

Overall, these data support that KER-050 has the potential to treat thrombocytopenia, including in patients with MDS and myelofibrosis.

- *ALK2 inhibition lowered hepcidin and liberated spleen iron for erythropoiesis in anemia of inflammation*

Hepcidin, the key regulator of iron absorption and recycling, can be regulated by the BMP-SMAD and IL-6-STAT3 signaling pathways in normal and inflammatory conditions. To understand whether and how ALK2 inhibition decreases hepcidin in inflammation, healthy mice were dosed with 3 mg/kg KTI-m216, an investigational neutralizing antibody to the ALK2 receptor, or vehicle for one hour, followed by a 1 mg/kg dose of lipopolysaccharide ("LPS") or phosphate buffered saline ("PBS") for six hours. Serum IL-6 was induced in the vehicle-LPS and KTI-m216-LPS mice, compared to respective PBS controls, indicating that a model of acute inflammation was induced.

Serum hepcidin was increased by LPS to a similar extent in the vehicle- and KTI-m216-treated mice, compared to the respective vehicle-PBS and KTI-m216-PBS controls. However, KTI-m216-LPS mice had a 69% reduction in absolute serum hepcidin compared to vehicle-LPS controls. These data indicate that KTI-m216 inhibited the BMP-SMAD signaling in this preclinical model and is potentially sufficient for hepcidin reduction in inflammation.

To induce a model of chronic kidney disease ("CKD"), mice were fed a diet containing 0.2% adenine and 40 ppm iron for six to seven weeks. CKD mice developed characteristics of anemia of inflammation ("AI"), including decreased hemoglobin, increased serum IL-6 and hepcidin, decreased serum iron and increased tissue iron retention, compared to mice on a control diet. After AI was confirmed, CKD mice received twice weekly treatment

with 3 mg/kg of KTI-m218, an investigational neutralizing antibody to the ALK2 receptor, or vehicle for three weeks, while continuing the adenine diet. In a separate experiment, the CKD mice received twice weekly treatment with 3 mg/kg of KTI-m218 or vehicle for nine days, while on an adenine diet with 3 ppm iron.

KTI-m218-treated CKD mice on the continued adenine and 40 ppm iron diet exhibited a reversal of the CKD-related changes, including decreased serum hepcidin, increased serum iron, reduction in spleen iron and increased hemoglobin compared to vehicle-treated CKD mice. Similar responses were observed in the KTI-m218-treated CKD mice on the adenine and 3 ppm iron diet, which supports that the increased iron in KTI-m218-treated CKD mice was mostly from the spleen, rather than diet.

These data suggest that ALK2 inhibition-mediated hepcidin suppression was sufficient to improve erythropoiesis by liberating iron from the recycling pathway in a mouse model of AI. Accordingly, Keros believes that targeting ALK2 inhibition could potentially treat anemia resulting from CKD and other acute and 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. Confirmation of the safety and tolerability of the selected dose levels is the primary objective of Part 2 of this trial. The secondary objectives of this trial are to evaluate the pharmacokinetics, pharmacodynamics and efficacy of KER-050. Keros expects to report additional data from this trial by the end of 2022.

Conference Call and Webcast Information

The Company will host a conference call and webcast today, June 10, 2022, at 8:00 a.m. Eastern time, to discuss the additional results from the ongoing Phase 2 clinical trial of KER-050 presented at the 27th Annual Congress of EHA.

The conference call will be webcast live at https://event.webcasts.com/starthere.jsp?ei=1552417&tp_key=c785623d12. 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 MDS 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. Keros' third product candidate, KER-012, is being developed for the treatment of pulmonary arterial hypertension and for the treatment of disorders associated with bone loss, such as osteoporosis and osteogenesis imperfecta.

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 as a treatment for multilineage cytopenias, including patients with MDS and myelofibrosis, and potentially promote erythropoiesis in patients with ineffective hematopoiesis; the potential of KER-050 to treat thrombocytopenia in patients with MDS and myelofibrosis; and the potential of ALK2 inhibition to treat anemia resulting from CKD and other acute and 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 May 5, 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.

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