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

December 13, 2021 2:01 PM EST

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

LEXINGTON, Mass., Dec. 13, 2021 (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 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 C57Bl/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