Keros Therapeutics Presents Additional Clinical Data from its KER-012 Program and Preclinical Data from its KER-050 Program at the American Society of Bone and Mineral Research 2022 Annual Meeting

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LEXINGTON, Mass., Sept. 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 musculoskeletal disorders with high unmet medical need, today announced that it presented preliminary clinical data from the Part 2 multiple ascending dose (“MAD”) portion of its Phase 1 clinical trial of KER-012 in healthy postmenopausal women at the American Society of Bone and Mineral Research 2022 Annual Meeting on Sunday, September 11, 2022. In addition, Keros also announced preclinical data evaluating the bone anabolic activity of RKER-050, a research form of KER-050, in a mouse model of myelodysplastic syndromes (“MDS”).

“We reported data from Part 2 of our Phase 1 clinical trial of KER-012, which continues to support the potential of KER-012 to correct dysfunctional activin signaling in multiple diseases,” said Jasbir S. Seehra, Ph.D., President and Chief Executive Officer of Keros. “We observed evidence of maximal inhibition of activin signaling as demonstrated by the reduction in follicle-stimulating hormone as well as increases in bone-specific alkaline phosphatase levels, which is a marker of osteoblast activity. Importantly, no clinically meaningful changes were seen in hemoglobin or red blood cells. We believe these results are supportive of the potential of KER-012 to treat diseases like pulmonary arterial hypertension and bone disorders characterized by increased activin signaling. With the completion of this Phase 1 clinical trial, we are preparing to initiate a Phase 2 clinical trial in early 2023 evaluating KER-012 in patients with pulmonary arterial hypertension.”

Clinical Presentation

- *KER-012, a Modified ActRIIB Ligand Trap, Administered to Healthy Postmenopausal Women was Generally Well Tolerated and Increased Biomarkers of Bone Formation, Supportive of a Bone Anabolic Mechanism*

This Phase 1 clinical trial was a randomized, double-blind, placebo-controlled, two-part trial to assess the safety, tolerability and pharmacokinetics of KER-012. Preliminary topline data from the Part 1 single ascending dose (“SAD”) portion of the trial was reported in May 2022. In Part 2 of the trial, subjects received three subcutaneous doses of either 0.75, 1.5 or 4.5 mg/kg of KER-012 or placebo administered 28 days apart with a 16-week safety follow-up. A total of 26 subjects were enrolled in three sequential multiple-ascending dose escalation cohorts, with eight subjects in the 0.75 mg/kg cohort and six subjects in each of the 1.5 mg/kg and 4.5 mg/kg cohorts receiving KER-012. Six subjects enrolled in Part 2 of this trial received placebo doses.

As of the data cut-off date of August 4, 2022, KER-012 was generally well tolerated at all dose levels tested. One subject discontinued after receiving two doses of placebo due to a serious adverse event unrelated to treatment. Another subject withdrew consent after receiving two 1.5 mg/kg doses of KER-012. There were no discontinuations due to treatment-related adverse events, and the majority of the adverse events that were observed were mild in severity and resolved.

Preliminary results from Part 2 of this trial include the following:

- Maximal target engagement was observed in the 4.5 mg/kg dose cohort, with a mean (standard deviation, “SD”) 52.0 (19.32)% reduction in follicle-stimulating hormone (“FSH”). Five out of six subjects who received a 4.5 mg/kg dose of KER-012 achieved a ≥40% reduction in serum FSH levels from baseline.
- Robust dose-dependent and sustained increases in markers of bone formation were observed:
    - Dose-dependent increases in serum levels of bone specific alkaline phosphatase (“BSAP”), a marker of osteoblast activity, were observed starting at the lowest dose of 0.75 mg/kg. The highest increase in BSAP was observed in the 4.5 mg/kg dose cohort, with mean (SD) maximum increases from baseline of 76.5 (20.33)%.
    - Repeat administration of KER-012 at 28-day intervals resulted in increases in BSAP after each dose, which is supportive of activation of osteoblasts after each dose potentially due to increased bone morphogenic protein signaling.
- Treatment with three doses of KER-012 at 28-day intervals did not elicit changes in hemoglobin or red blood cells in any of the multiple-dose cohorts evaluated in Part 2 of this trial.

Preclinical Presentation

- *RKER-050, a Novel Activin Receptor Type II Ligand Trap, Improved Bone Loss in a Myelodysplastic Syndrome Mouse Model*

A research form of KER-050 (“RKER-050”) was tested in a mouse model of MDS. Male MDS mice were administered either vehicle or 7.5 mg/kg of RKER-050 once weekly for six weeks. Healthy male mice received only vehicle.

Vehicle-treated MDS mice had reduced bone volume, lower bone volume fraction, increased trabecular separation and reduced trabecular number relative to healthy controls. However, treatment with RKER-050 prevented loss of bone volume, bone volume fraction and trabecular number and reduced trabecular separation in MDS mice relative to vehicle-treated MDS mice.

These data suggest that KER-050 has the potential to restore hematopoiesis and bone health, which may lead to the regeneration of a healthier bone marrow microenvironment in patients with MDS.

About KER-012
KER-012 is designed to bind to and inhibit the signaling of transforming growth factor-beta (“TGF-β”) ligands that suppress bone growth, including activin A and activin B. Keros believes that KER-012 has the potential to increase the signaling of bone morphogenic protein (“BMP”) pathways through this inhibition of activin A and activin B signaling, and consequently treat diseases such as pulmonary arterial hypertension (“PAH”) that are associated with reduced BMP signaling due to inactivating mutations in the BMP receptors. KER-012 is being developed for the treatment of PAH and for the treatment of disorders associated with bone loss, such as osteogenesis imperfecta and osteoporosis.

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 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 hematological, pulmonary, and musculoskeletal 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 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 PAH 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-012; the potential of KER-012 to correct dysfunctional activin signaling in multiple diseases; the potential of KER-012 to treat diseases like PAH and bone disorders characterized by increased activin signaling; and the potential of KER-050 to restore hematopoiesis and bone health, leading to the regeneration of a healthier bone marrow microenvironment in patients with MDS. 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, KER-012 and KER-047; that Keros may be delayed in initiating, enrolling or completing any clinical trials; competition from third parties that are developing products for similar uses; Keros’ ability to obtain, maintain and protect its intellectual property; Keros’ dependence on third parties in connection with manufacturing, clinical trials and pre-clinical studies; and risks relating to the impact on our business of the COVID-19 pandemic or similar public health crises.

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 August 4, 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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