Keros Therapeutics Presents Preclinical Data from its KER-065 Program at the 28th International Annual Congress of the World Muscle Society

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LEXINGTON, Mass., Oct. 04, 2023 (GLOBE NEWSWIRE) -- Keros Therapeutics, Inc. (“Keros”) (Nasdaq: KROS), a clinical-stage biopharmaceutical company focused on developing and commercializing novel therapeutics to treat a wide range of patients with disorders that are linked to dysfunctional signaling of the transforming growth factor-beta (“TGF-ß”) family of proteins, today announced results from preclinical studies evaluating the treatment effect of a research form of KER-065 (“RKER-065”) in a mouse model of Duchenne muscular dystrophy (“DMD”) and in prednisolone-treated mice, which were presented at the 28th International Annual Congress of the World Muscle Society (“WMS”) on Wednesday, October 4, 2023.

“We are pleased to present promising preclinical data from our KER-065 program at WMS this year, showing that treatment with RKER-065 led to a robust increase in muscle mass, muscle function and bone mass in a mouse model of DMD and in prednisolone-treated mice,” said Jasbir S. Seehra, Ph.D., President and Chief Executive Officer of Keros. “We believe these data support the potential of KER-065 to treat multiple pathophysiologies of DMD and other neuromuscular diseases, and we look forward to commencing a Phase 1 clinical trial of KER-065 in healthy volunteers in the first quarter of 2024.”

RKER-065 treatment led to a robust increase in muscle mass, functional strength, and bone formation in a DMD mouse model

- *RKER-065 ameliorated muscle and bone loss in a progressive murine model of Duchenne muscular dystrophy*

Keros studied the effect of RKER-065 in a progressive and phenotypically severe DMD mouse model. DMD mice were dosed with vehicle or 10 mg/kg of RKER-065 once weekly for four or six weeks. A cohort of healthy mice received only vehicle.

In DMD mice, treatment with RKER-065 led to significant increases in body weight and lean mass by four weeks compared to vehicle-treated DMD mice. Additionally, an increase in forelimb grip strength was observed, which is supportive of improved muscle function. DMD mice treated with RKER-065 demonstrated significant increases in muscle mass in the pectoralis and tibialis anterior (“TA”) as compared to vehicle-treated DMD mice. In addition, expression of utrophin, a functional analog of dystrophin, was higher in the TA of DMD mice treated with RKER-065 compared to vehicle-treated DMD mice.

Concomitant with neuromuscular decline, vehicle-treated DMD mice had significant decreases in bone mineral density (“BMD”), while DMD mice treated with RKER-065 showed no significant difference compared to healthy adult mice. RKER-065 treatment led to a significant increase in trabecular bone volume fraction by six weeks as compared to vehicle-treated DMD mice and a significant increase in trabecular thickness as compared to healthy mice. The RKER-065-treated DMD mice also had a significant decrease in trabecular spacing and a significant increase in trabecular number compared to both healthy mice and vehicle-treated DMD mice.

Overall, treatment with RKER-065 led to a robust increase in muscle mass, functional strength and bone formation in the DMD mouse model. These studies suggest that KER-065 has the potential to benefit DMD patients who suffer from severe muscle loss and impaired muscle function and are at higher risk of fractures.

RKER-065 increased muscle mass, improved muscle function and prevented bone loss in prednisolone-treated mice

- *RKER-065, a novel ActRII ligand trap, counteracted the negative impact of glucocorticoid treatment on bone and muscle in mice*

In order to evaluate if RKER-065 can prevent the negative effect of glucocorticoids, the standard of care for DMD, on bone and muscle mass function, Keros treated healthy mice, divided into two groups matched by body weight, with 5.0 mg/kg prednisolone daily (“Pred”) and 10.0 mg/kg of RKER-065 weekly (“Pred-RKER-065”) or Pred daily and vehicle weekly (“Pred-vehicle”) for 9 weeks. A cohort of vehicle-treated mice were fed daily with cherry syrup.

The Pred-vehicle mice exhibited reduced weight gain relative to vehicle – which is consistent with the use of glucocorticoid treatment – while weight gain was maintained in Pred-RKER-065-treated mice. The Pred-vehicle mice also exhibited reduced lean mass gain relative to vehicle, while Pred-RKER-065-treated mice had a robust increase in lean mass compared to Pred-vehicle mice. The observed increase in lean mass in the Pred-RKER-065 mice was associated with an increase in forelimb grip strength compared to Pred-vehicle and vehicle, which was apparent by day 34.

At day 32, both right femoral and whole-body BMD in the Pred-vehicle mice were lower than vehicle. No difference in BMD reduction was observed between the Pred-RKER-065 and vehicle cohorts, suggesting that RKER-065 treatment prevented prednisolone-associated BMD reduction. A similar trend was observed at day 52. Additionally, Pred-RKER-065-treated mice showed increases in trabecular bone parameters relative to both vehicle and Pred-vehicle cohorts.

These data demonstrate that RKER-065 can increase muscle mass, improve muscle function, and prevent bone loss in prednisolone-treated mice. These data further support that targeting activin and myostatin can potentially increase muscle and bone strength in muscular dystrophic patients under glucocorticoid therapy.

About KER-065

KER-065, Keros’ fourth product candidate, is designed to bind to and inhibit select TGF-ß ligands, including myostatin and activin A, which are

negative regulators of muscle and bone mass and strength. Through inhibition of these TGF-ß ligands, we believe that KER-065 has the potential to induce muscle and bone anabolic effects, increase fat metabolism and reduce fibrosis. KER-065 is being developed for the treatment of neuromuscular diseases, with an initial focus on DMD.

About Keros Therapeutics, Inc.

Keros is a clinical-stage biopharmaceutical company focused on developing and commercializing novel therapeutics to treat a wide range of patients with disorders that are linked to dysfunctional signaling of the TGF-ß family of proteins. We are a leader in understanding the role of the TGF-ß family of proteins, which are master regulators of the growth, repair and maintenance of blood cells and a number of tissues, including bone, skeletal muscle, adipose and heart tissue. By leveraging this understanding, we have discovered and are developing large and small molecules that have the potential to provide meaningful and potentially disease-modifying benefit to patients. 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 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. Keros' fourth product candidate, KER-065, is being developed for the treatment of neuromuscular diseases, with an initial focus on DMD.

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 "believe," "can," "look forward," "potential" and/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 trial for KER-065; and the potential of KER-065 to treat DMD and other neuromuscular 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 product candidates, KER-050, KER-047, KER-012 and KER-065; 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 August 7, 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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