Keros Therapeutics Presents Results from Preclinical Study of KER-012 in Pulmonary Arterial Hypertension at the American Thoracic Society International Conference

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LEXINGTON, Mass., May 14, 2021 (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 results from a preclinical study of KER-012 on pulmonary and cardiac dysfunction in an established rodent model of pulmonary arterial hypertension (“PAH”) at the virtual American Thoracic Society International Conference held May 14 through 19, 2021. Additional data from a previously conducted nonclinical study in cynomolgus monkeys was also included in the presentation.

KER-012 prevented markers of inflammation and fibrosis, and vascular remodeling in a rodent PAH model and did not alter red blood cell number in rats or non-human primates.

- *RKER-012, a Novel Activin Receptor Type IIB (ActRIIB) Ligand Trap, Reduced Cardiopulmonary Pathology in a Rodent Model of Pulmonary Arterial Hypertension*

Keros combined administration of SUGEN5416, a tyrosine kinase inhibitor of vascular endothelial growth factor receptors 1/2, with exposure to chronic hypoxia to recapitulate the biology in PAH. A research form of KER-012 (“RKER-012”) was tested in this SUGEN/hypoxia (“SH”) rat model of PAH. Adult male rats were subjected to SH and received either vehicle or 10 mg/kg RKER-012 twice weekly for four weeks. Rats maintained under normal oxygen conditions (“normoxic controls”) received only vehicle.

Consistent with enhanced pulmonary vascular remodeling and cardiac fibrosis, vehicle-treated SH rats showed significantly greater right ventricle plasminogen activator inhibitor-1 (“PAI-1”) expression (+236.7%; $p<0.05$), α-smooth muscle actin (“α-SMA”) expression (+255.4%; $p<0.05$) and increased arterial wall thickness (+43.8%, $p<0.001$), relative to normoxic controls. Treatment with RKER-012 reduced heart PAI-1 expression and lung α-SMA to levels equivalent to normoxic controls and reduced arterial wall thickness, which Keros believes suggests that KER-012 could potentially prevent the progression of PAH.

Additionally, vehicle-treated SH rats had significantly greater neutrophil number (+139.2%; $p<0.01$) relative to normoxic controls. Treatment with RKER-012 reduced neutrophils to levels of normoxic controls, indicating a reduction in PAH-associated inflammation. There was no effect of SH or RKER-012 on either white blood cells or lymphocytes.

Finally, vehicle-treated SH rats had significantly greater Fulton index, which measures enlargement of the right ventricle (+21.7; $p<0.0001$), as well as trends for increased atrial natriuretic peptide (“ANP”) (+172.8%; $p=0.18$) and B-type natriuretic peptide (“BNP”) (+38.7%; $p=0.057$), relative to normoxic controls. Treatment with RKER-012 reduced Fulton Index to control levels, and reduced ANP and BNP expression to levels below controls, which Keros believes indicates that KER-012 could potentially reduce PAH-induced damage to the heart.

RKER-012 did not increase red blood cell number in the SH rats, relative to either vehicle-treated SH rats or normoxic controls. Similarly, KER-012 did not increase red blood cells in healthy naïve non-human primates, a model highly translatable to humans.

“The Keros team is presenting exciting data on our KER-012 program at ATS. PAH is associated with imbalanced signaling in the transforming growth factor-beta (“TGF-ß”) pathway, and the results of this study suggest that KER-012 prevented disease progression in this PAH model, which we believe supports our hypothesis that rebalancing signaling by inhibiting certain ligands may provide benefit in PAH,” said Jasbir S. Seehra, Ph.D., President and Chief Executive Officer of Keros. “Additionally, treatment with KER-012 did not increase red blood cells in both rats and nonhuman primates, which can result from inhibition of this pathway. We believe that the current study supports that KER-012 has the potential to treat PAH in patients without dose-limiting increases in red blood cells.”

About KER-012

KER-012 is designed to bind to and inhibit the signaling of TGF-ß ligands, including activin A and activin B, which are key regulators of bone remodeling that act to suppress bone growth. 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 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 disorders associated with bone loss, such as osteogenesis imperfecta and osteoporosis, and for the treatment of PAH.

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 pulmonary arterial hypertension.

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: the potential of KER-012 to treat diseases such as PAH without dose-limiting increases in red blood cells. 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 6, 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:

Julia Balanova
jbalanova@soleburytrout.com
646-378-2936