Keros Therapeutics Presents Results from a Preclinical Study of RKER-012 in Pulmonary Arterial Hypertension at the Pulmonary Hypertension Association International Conference and Scientific Sessions

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LEXINGTON, Mass., June 13, 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 results from a preclinical study of RKER-012 on cardiac and pulmonary pathology in an established rodent model of pulmonary arterial hypertension (“PAH”), which were presented at the Pulmonary Hypertension Association International Conference and Scientific Sessions held on June 10 through 12, 2022.

RKER-012 reduced cardiac and pulmonary pathology in a rodent PAH model.

- *RKER-012, a Novel Activin Receptor Type IIB (“ActRIIB”) Ligand Trap, Reduced Cardiac and Pulmonary Pathology in a Sugen/Hypoxia Model of PAH*

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, 10 mg/kg of activin receptor type IIA-Fc (“ActRIIA-Fc”) or 10 mg/kg RKER-012 twice weekly for three weeks. Rats maintained under normal oxygen conditions (“normoxic controls”) received only vehicle.

Consistent with the development of cardiac and pulmonary impairment, vehicle-treated SH rats exhibited increases in Fulton index, which measures enlargement of the right ventricle ($p<0.0001$) and systolic pulmonary arterial pressure (“sPAP”) ($p<0.0001$) relative to normoxic controls. Treatment of the SH rats with ActRIIA-Fc did not significantly attenuate increased Fulton index ($p>0.05$) and sPAP ($p>0.05$) relative to the vehicle-treated SH rats. However, relative to the vehicle-treated SH rats, treatment of the SH rats with RKER-012 significantly attenuated increased Fulton index ($p<0.01$) and prevented an increase in sPAP ($p<0.001$).

Additionally, vehicle-treated SH rats exhibited increased lung inflammation/fibrosis ($p<0.0001$), smooth muscle hypertrophy ($p<0.0001$), and arteriole muscularization ($p<0.0001$) relative to normoxic controls, while treatment with RKER-012 reduced these pathologies (all $p<0.0001$, relative to vehicle). Vehicle-treated SH rats also exhibited increased expression of atrial natriuretic peptide (“ANP”) and brain natriuretic peptide (“BNP”; both $p<0.05$) relative to normoxic controls. Treatment with RKER-012 significantly reduced ANP expression ($p<0.05$) and trended to reduce BNP expression ($p=0.11$), which Keros believes indicates that RKER-012 could potentially reduce PAH-induced damage to the heart.

Vehicle-treated SH rats also exhibited elevated expression of genes associated with the development of PAH-associated pathology in the lung and right ventricle, both hallmarks of PAH pathology, which were reduced with RKER-012 treatment.

In a study evaluating the binding activity of KER-012, KER-012 was observed to inhibit ligands associated with endothelial dysfunction, including activins A and B, and had a reduced affinity for BMP-9 compared to activin receptor type IIA.

Finally, in an in vitro study, human pulmonary arterial endothelial cells (“HPAECs”) were treated with RKER-012 (10 µg/mL) and placed into either normoxic or hypoxic conditions. HPAECs exposed to hypoxic conditions for 48 hours had significantly elevated expression of activin A ($p<0.05$) and increased levels of free activin A ($p<0.01$) relative to cells in normoxic conditions. Treatment with RKER-012 reversed the observed hypoxia-mediated increases in activin expression.

Taken together, Keros believes these data provide early evidence that KER-012 has the potential to benefit the vasculature, lung and heart tissues in patients with PAH.

About KER-012

KER-012 is designed to bind to and inhibit the signaling of TGF-ß 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 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 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. 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: the potential of KER-012 to benefit lung and heart tissues in patients with PAH. 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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