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Fortress Biotech Announces Publication of Preclinical Data on AAV-ATP7A Gene Therapy Combined with CUTX-101 (Copper Histidinate) for Menkes Disease in Molecular Therapy: Methods & Clinical Development

NEW YORK, Sept. 12, 2018 (GLOBE NEWSWIRE) -- Fortress Biotech, Inc. (NASDAQ: FBIO) ("Fortress"), a biopharmaceutical company dedicated to acquiring, developing and commercializing novel pharmaceutical and biotechnology products, today announced the publication of preclinical data on adeno-associated virus (AAV)-based gene therapy combined with subcutaneous CUTX-101 (Copper Histidinate) in a mouse model of Menkes disease, a fatal infantile disorder of human copper metabolism. In March 2017, Fortress' subsidiary Cyprium Therapeutics, Inc. ("Cyprium") licensed preclinical AAV-ATP7A gene therapy from the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) to develop in combination with CUTX-101. The data were published online and will be included in the September 21, 2018 edition of the journal *Molecular Therapy: Methods & Clinical Development.*

The preclinical study was conducted by the NICHD laboratory of Stephen G. Kaler, M.D., and evaluated low-, intermediate- and high-dose recombinant AAV serotype 9 (rAAV9)-ATP7A delivered to the cerebrospinal fluid (CSF) in combination with subcutaneous CUTX-101 in a *mottled-brindled (mo-br)* mouse model that closely mimics the biochemical and clinical phenotypes of Menkes disease. The rAAV9 construct carried the genetic instructions for a compact, reduced-size (rs) version of the Menkes copper transporter, ATP7A. Mutant mice that received high-dose CSF-directed rAAV9-rsATP7A in combination with CUTX-101 demonstrated improved long-term survival (53%) compared to mice that did not receive treatment (0%) or were administered either treatment by itself (0%, 0%). This synergistic treatment effect represents the most successful rescue to date of the *mo-br* mouse model. In addition, mutant mice treated with the high-dose CSF-directed rAAV9-rsATP7A in combination with CUTX-101 showed higher brain copper levels, normalized brain neurochemicals, improvement of brain mitochondrial abnormalities, and normal growth and neurobehavioral outcomes.

"We are highly encouraged by these preclinical data, which provide new insights on a

potentially effective therapeutic approach for this difficult pediatric disease that currently has no FDA-approved treatment options," said Lung S. Yam, M.D., Ph.D., President and Chief Executive Officer of Cyprium. "We have made excellent progress toward new drug approval of subcutaneous CUTX-101 for Menkes disease based on Dr. Kaler's clinical trials and were granted FDA Fast Track Designation earlier this summer. We look forward to continuing to work with Dr. Kaler and NICHD to also advance the AAV-ATP7A gene therapy program toward the clinic and nominating a viral gene therapy candidate for drug development."

The study "Cerebrospinal fluid-directed rAAV9-rsATP7A plus subcutaneous Copper Histidinate advance survival and outcomes in a Menkes disease mouse model" can be accessed online at: https://doi.org/10.1016/j.omtm.2018.07.002.

About Menkes Disease and Related Copper Metabolism Disorders

Menkes disease is a rare X-linked pediatric disease caused by gene mutations of the copper transporter ATP7A, which affects approximately one in 100,000 newborns per year. Biochemically, Menkes patients have low levels of copper in their blood and brain, as well as abnormal levels of certain neurochemicals. Definitive diagnosis is typically made by sequencing the ATP7A gene. The condition is characterized by distinctive clinical features, including sparse and depigmented hair ("kinky hair"), failure to thrive, connective tissue problems, and severe neurological symptoms such as seizures. Mortality is high, with many patients dying before the age of three. Milder versions of ATP7A mutations are associated with other conditions, including Occipital Horn Syndrome and ATP7A-related Distal Motor Neuropathy. Currently, there is no FDA-approved treatment for Menkes disease and its variants.

About CUTX-101 (Copper Histidinate)

CUTX-101 is in clinical development to supplement blood and brain copper levels in patients diagnosed with classic Menkes disease who have not demonstrated significant clinical progression. CUTX-101 is a subcutaneous injectable formulation of Copper Histidinate manufactured under cGMP that is intended to improve tolerability due to physiological pH and to bypass the oral absorption of copper, which is impaired in patients with Menkes disease. In a Phase 1/2 clinical trial conducted at the National Institutes of Health (NIH), early treatment of Menkes patients with CUTX-101 led to an improvement in neurodevelopmental outcomes and survival. A Phase 3 trial of CUTX-101 in Menkes disease is ongoing at the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD).

About Cyprium Therapeutics

Cyprium Therapeutics, Inc. (Cyprium), a Fortress Biotech company, is focused on the development of novel therapies for the treatment of Menkes disease and related copper metabolism disorders. In March 2017, Cyprium entered into a Cooperative Research and Development Agreement (CRADA) with the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), part of the National Institutes of Health (NIH), to advance the clinical development of CUTX-101 (Copper Histidinate injection) for the treatment of Menkes disease. In addition, Cyprium and NICHD entered into a worldwide, exclusive license agreement to develop and commercialize adeno-associated virus (AAV)-based gene therapy, called AAV-ATP7A, to deliver working copies of the copper transporter

that is defective in Menkes patients, and to be used in combination with CUTX-101. CUTX-101 was granted U.S. Food and Drug Administration (FDA) Fast Track Designation, and both CUTX-101 and AAV-ATP7A have received FDA orphan drug designation previously. Cyprium is a majority-owned subsidiary of Fortress Biotech (NASDAQ: FBIO) and is based in New York City.

About Fortress Biotech

Fortress Biotech, Inc. ("Fortress") is a biopharmaceutical company dedicated to acquiring, developing and commercializing novel pharmaceutical and biotechnology products. Fortress develops and commercializes products both within Fortress and through certain subsidiary companies, also known as Fortress Companies. In addition to its internal development programs, Fortress leverages its biopharmaceutical business expertise and drug development capabilities and provides funding and management services to help the Fortress Companies achieve their goals. Fortress and the Fortress Companies may seek licensings, acquisitions, partnerships, joint ventures and/or public and private financings to accelerate and provide additional funding to support their research and development programs. For more information, visit www.fortressbiotech.com.

Forward-Looking Statements

This press release may contain "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934, as amended. Such statements include, but are not limited to, any statements relating to our growth strategy and product development programs and any other statements that are not historical facts. Forward-looking statements are based on management's current expectations and are subject to risks and uncertainties that could negatively affect our business, operating results, financial condition and stock price. Factors that could cause actual results to differ materially from those currently anticipated include: risks relating to our growth strategy; our ability to obtain, perform under and maintain financing and strategic agreements and relationships; risks relating to the results of research and development activities; uncertainties relating to preclinical and clinical testing; risks relating to the timing of starting and completing clinical trials; our dependence on third-party suppliers; our ability to attract, integrate and retain key personnel; the early stage of products under development; our need for substantial additional funds; government regulation; patent and intellectual property matters; competition; as well as other risks described in our SEC filings. We expressly disclaim any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in our expectations or any changes in events, conditions or circumstances on which any such statement is based, except as required by law.

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