Fortress Biotech and Cyprium Therapeutics Announce $4.1 Million Grant from NINDS to Further Development of AAV-ATP7A Gene Therapy for Menkes Disease

Encouraging preclinical studies demonstrate potential to combine AAV-ATP7A gene therapy with CUTX-101, which could be the first FDA-approved treatment for Menkes disease

Cyprium Therapeutics, a majority-owned subsidiary of Fortress Biotech, is developing AAV-ATP7A gene therapy to be used in conjunction with CUTX-101 for the treatment of Menkes disease

Miami, FL, March 4, 2024 – Cyprium Therapeutics, Inc. ("Cyprium"), a majority-owned subsidiary of Fortress Biotech, Inc. (Nasdaq: FBIO) ("Fortress"), today announced that the National Institute of Neurological Disorders and Stroke ("NINDS") of the National Institutes of Health ("NIH") has awarded a three-year grant totaling approximately $4.1 million to the Research Institute at Nationwide Children's Hospital and Principal Investigator, Stephen G. Kaler, M.D., M.P.H., to fund completion of preclinical studies, manufacturing and preparation of an Investigational New Drug Application for a first-in-human clinical trial to advance adeno-associated virus ("AAV")-ATP7A gene therapy, also known as AAV-ATP7A, for the treatment of Menkes disease.

Often lethal if untreated, Menkes disease is an X-linked recessive disorder of copper metabolism caused by mutations in ATP7A, an evolutionarily conserved copper-transporting ATPase. The minimum birth prevalence for Menkes disease is believed to be 1 in 34,810 live male births, and potentially as high as 1 in 8,664 live male births, based on genome-driven ascertainment. In 2017, Cyprium entered into a worldwide, exclusive license agreement with the Eunice Kennedy Shriver National Institute of Child Health and Human Development ("NICHD") to develop and commercialize AAV-ATP7A gene therapy to deliver working copies of the copper transporter defective in patients with Menkes disease, and to be used in combination with CUTX-101 (Copper Histidinate), which is being developed by Sentynl Therapeutics, Inc. ("Sentynl"). AAV-ATP7A was previously granted Orphan Drug Designation by the U.S. Food and Drug Administration ("FDA").

"By combining CUTX-101 with working copies of ATP7A delivered by AAV, we hope to enhance clinical outcomes in Menkes disease, a fatal rare pediatric disease. This funding allows us to further evaluate the preclinical safety, tolerability and dosing of AAV9-codon-optimized, reduced-size ATP7A, which we propose to administer in a first-in-human clinical trial for Menkes disease. Advances in viral gene therapy and newborn screening make it feasible to envision changing the natural history of this difficult illness, in combination with CUTX-101, potentially the first FDA-approved treatment for Menkes disease," said Dr. Kaler, a physician-scientist in the Center for Gene Therapy in the Abigail Wexner Research Institute at Nationwide Children's Hospital, Principal Investigator of the preclinical and clinical studies, and professor of Pediatrics and Genetics at The Ohio State University College of Medicine.

Preclinical studies have demonstrated a synergistic effect of AAV-ATP7A and CUTX-101 in a reliable mouse model of Menkes disease. In early studies, cerebrospinal fluid ("CSF")-directed AAV gene therapy rescued 22-53% of mice with a mutation in the human Menkes disease homolog (mottled-brindled) when combined with CSF or subcutaneous copper. In addition, mutant mice treated with CSF-directed AAV9-reduced-size ATP7A in combination with CUTX-101 showed higher brain copper levels, normalized brain neurochemicals, improvement of brain mitochondrial abnormalities, and near-normal growth and neurobehavioral outcomes.

More recently, based on successful intravenous AAV9 gene therapy in mice and humans with spinal muscular atrophy at the Center for Gene Therapy, Nationwide Children's Hospital, the Kaler Laboratory evaluated intravenous administration of AAV9-codon-optimized, reduced-size ATP7A combined with subcutaneous administration of CUTX-101 in Menkes disease mouse models. This regimen led to 95% long-term rescue of *mottled-brindled* mutant mice (n=19/20), using an AAV9 dose of 2.6 x 10^{13} vg/kg body weight, the most successful long-term rescue of this mouse model to date.

Lindsay A. Rosenwald, M.D., Executive Chairman, President and Chief Executive Officer of Fortress, stated, "We are honored to have the NIH's support, and Dr. Kaler's and Nationwide Children's leadership, to progress the development of AAV-ATP7A gene therapy, to help provide a more effective therapeutic option to patients with Menkes disease. As we continue the research and development of AAV-ATP7A in combination with CUTX-101, there is great potential for this next generation approach to enhance the treatment of Menkes disease, which currently has no FDA-approved treatment. We look forward to continuing to advance AAV-ATP7A with Dr. Kaler and supporting Sentynl as they finalize and complete the NDA submission for CUTX-101."

The content and research reported in this release are solely the responsibility of the authors and do not necessarily represent the official views of the NIH.

About AAV-ATP7A Gene Therapy

AAV-ATP7A is an adeno-associated virus (AAV)-based gene therapy in preclinical development for the treatment of Menkes Disease. AAV-ATP7A is being developed to deliver working copies of the copper transporter that is defective in Menkes patients and to be used in combination with CUTX-101 (Copper Histidinate). AAV-ATP7A was developed in part under an Exclusive License Agreement with the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), and in conjunction with the Research Institute at Nationwide Children's Hospital and Principal Investigator, Dr. Stephen G. Kaler.

About CUTX-101 (Copper Histidinate)

CUTX-101 is a subcutaneous injectable formulation of Copper Histidinate in clinical development by Sentynl Therapeutics to treat patients with Menkes Disease. In a Phase 1/2 clinical trial conducted by Stephen G. Kaler, M.D., M.P.H., at the National Institutes of Health ("NIH"), early treatment of patients with Menkes disease with CUTX-101 led to an improvement in neurodevelopmental outcomes and survival. Cyprium previously reported positive topline clinical efficacy results for CUTX-101, demonstrating statistically significant improvement in overall survival for Menkes disease subjects who received early treatment (ET) with CUTX-101, compared to an untreated historical control cohort, with a nearly 80% reduction in the risk of death. Median overall survival (OS) was 177.1 months for CUTX-101 ET cohort compared to 16.1 months for the untreated historical control cohort. CUTX-101 has been granted FDA Breakthrough Therapy, Fast Track, Rare Pediatric Disease and FDA Orphan Drug Designations. Additionally, the European Medicines Agency granted Orphan Drug Designation for CUTX-101. An expanded access protocol, administered by Sentynl Therapeutics, for patients with Menkes disease is ongoing at multiple U.S. medical centers. Sentynl acquired the CUTX-101 program via asset purchase in December 2023 and will owe Cyprium milestone and royalty payments in connection with the development and commercialization of the product.

About Menkes Disease

Menkes disease is a rare X-linked recessive pediatric disease caused by gene mutations of copper transporter *ATP7A*. The minimum birth prevalence for Menkes disease is believed to be 1 in 34,810 live male births, and potentially as high as 1 in 8,664 live male births, based on recent genome-driven ascertainment (Kaler SG, Ferreira CR, Yam LS. Estimated birth prevalence of Menkes disease and *ATP7A*-related disorders based on the Genome Aggregation Database (gnomAD). *Molecular Genetics and*

Metabolism Reports 2020 June 5;24:100602). The condition is characterized by distinctive clinical features, including sparse and depigmented hair ("kinky hair"), connective tissue problems, and severe neurological symptoms such as seizures, hypotonia, failure to thrive, and neurodevelopmental delays. Mortality is high in untreated Menkes disease, with many patients dying before the age of two years old. 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 Cyprium Therapeutics

Cyprium Therapeutics, Inc. ("Cyprium") 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 with the Eunice Kennedy Shriver National Institute of Child Health and Human Development ("NICHD"), part of the NIH, to advance the clinical development of CUTX-101 (Copper Histidinate injection) for the treatment of Menkes disease. In 2023, Cyprium completed the transfer of its proprietary rights and assigned its FDA documents pertaining to CUTX-101 Copper Histidinate product candidate for the treatment of Menkes disease, to Sentynl Therapeutics, Inc. Cyprium and NICHD also previously 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 patients with Menkes disease, and to be used in combination with CUTX-101; AAV-ATP7A is currently in pre-clinical development and has been granted FDA Orphan Drug Designation. Cyprium was founded by Fortress Biotech, Inc. (Nasdaq: FBIO) and is based in Miami. For more information, visit www.cypriumtx.com.

About Fortress Biotech

Fortress Biotech, Inc. ("Fortress") is an innovative biopharmaceutical company focused on efficiently acquiring, developing and commercializing or monetizing promising therapeutic products and product candidates. The company has eight marketed prescription pharmaceutical products and over 25 programs in development at Fortress, at its majority-owned and majority-controlled partners and subsidiaries and at partners and subsidiaries it founded and in which it holds significant minority ownership positions. Such product candidates span six large-market areas, including oncology, rare diseases and gene therapy, which allow it to create value for shareholders. Fortress advances its diversified pipeline through a streamlined operating structure that fosters efficient drug development. The Fortress model is focused on leveraging its significant biopharmaceutical industry expertise and network to further expand the company's portfolio of product opportunities. Fortress has established partnerships with some of the world's leading academic research institutions and biopharmaceutical companies to maximize each opportunity to its full potential, including AstraZeneca, City of Hope, Fred Hutchinson Cancer Center, St. Jude Children's Research Hospital, Nationwide Children's Hospital and Sentynl. 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. As used below and throughout this press release, the words "we", "us" and "our" may refer to Fortress individually or together with one or more partner companies, as dictated by context. Such statements include, but are not limited to, any statements relating to our growth strategy and product development programs, ability to generate shareholder value, ability of our products to receive necessary approvals, including FDA approval, ability of our products and therapies to help patients 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; financing and strategic agreements and relationships; our need for substantial additional funds and uncertainty relating to financings; our ability

to identify, acquire, close and integrate product candidates successfully and on a timely basis; our ability to attract, integrate and retain key personnel; the early stage of products under development; 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; the ability to secure and maintain third-party manufacturing, marketing and distribution of our and our partner companies' products and product candidates; 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 may be required by law, and we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995. The information contained herein is intended to be reviewed in its totality, and any stipulations, conditions or provisos that apply to a given piece of information in one part of this press release should be read as applying *mutatis mutandis* to every other instance of such information appearing herein.

Company Contacts:
Jaclyn Jaffe and Nicole McCloskey

Cyprium Therapeutics, Inc.
ir@cypriumtx.com

Fortress Biotech, Inc.
(781) 652-4500
ir@fortressbiotech.com

Media Relations Contact:
Tony Plohoros
6 Degrees
(908) 591-2839
tplohoros@6degreespr.com