Krystal Biotech Announces FDA Clearance of Investigational New Drug Application for KB408 for the Treatment of Alpha-1 Antitrypsin Deficiency

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• Orphan Drug Designation Granted to KB408

PITTSBURGH, Sept. 21, 2023 (GLOBE NEWSWIRE) -- Krystal Biotech, Inc. (the "Company") (NASDAQ: KRYS), a commercial-stage biotechnology company focused on the discovery, development, and commercialization of genetic medicines to treat diseases with high unmet medical needs, announced today that the U.S. Food and Drug Administration (FDA) cleared the Investigational New Drug Application (IND) for KB408 for the treatment of alpha-1 antitrypsin deficiency (AATD).

KB408 is a modified, replication-defective, non-integrating HSV-1-derived vector carrying two full-length copies of the serpin family A member 1 (*SERPINA1*) gene to enable expression of alpha-1 antitrypsin (AAT). KB408 is formulated for inhaled delivery to the respiratory cells of the lungs via nebulization.

"We are excited to advance KB408, our investigational gene therapy for patients with alpha-1 antitrypsin deficiency, into the clinic in our Serpentine-1 study," said Hubert Chen, M.D., Senior Vice President of Clinical Development at Krystal Biotech. Dr. Chen continued, "This IND acceptance represents an important milestone for us as we work to address a serious lung disease with limited treatment options, and also allows us to demonstrate the potential of our platform to deliver genes repeatedly to epithelial cells of the lung."

On August 15th, the Company submitted an IND application to request FDA authorization to initiate a Phase 1 clinical trial of KB408. At the end of the 30-day review period, the Company received notification from the FDA that the IND has been cleared. The Company anticipates dosing the first patient in a Phase 1 clinical trial in Q1 2024. On September 5th, the FDA granted orphan-drug designation for KB408 for the treatment of AATD.

The Phase 1 clinical trial is a Phase 1, open-label, single dose escalation study in adult patients with AATD with a PI*ZZ genotype. Three planned dose levels of KB408 will be evaluated with three patients in each cohort to evaluate the safety, tolerability, and efficacy of KB408. Details about the Phase 1 study can be found at www.clinicaltrials.gov under NCT identifier: NCT06049082.

About KB408
KB408 is an inhaled (nebulized) formulation of the Company's novel replication-defective, non-integrating HSV-1-based vector designed to deliver two copies of the *SERPINA1* transgene, that encodes for human alpha-1 antitrypsin protein, for the treatment of AATD.

About Alpha-1 Antitrypsin Deficiency
AATD is a rare genetic disease caused by mutations in the *SERPINA1* gene that lead to decreased levels and/or decreased functionality of AAT protein. In the most common form of AATD, occurring in people with a PI*ZZ genotype, these mutations cause the body to produce misfolded AAT protein that gets trapped inside the liver, leading to low levels of AAT protein in the blood. Low blood levels of AAT can allow inflammation to proceed unchecked and damage the lungs. Over time, the deficiency can lead to progressive enzymatic destruction of the lung tissue, ultimately causing life-threatening pulmonary impairment and severe respiratory insufficiency. In severe cases, current disease management includes intravenous plasma-derived AAT augmentation therapy which requires weekly infusions, the clinical benefit of which remains to be established. There is currently no cure for AATD.

About Krystal Biotech, Inc.
Krystal Biotech, Inc. (NASDAQ: KRYS) is a commercial-stage biotechnology company focused on the discovery, development and commercialization of genetic medicines to treat diseases with high unmet medical needs. VYJUVEK™ is the Company's first commercial product, the first-ever redosable gene therapy, and the only medicine approved by the FDA for the treatment of dystrophic epidermolysis bullosa. The Company is rapidly advancing a robust preclinical and clinical pipeline of investigational genetic medicines in respiratory, oncology, dermatology, ophthalmology, and aesthetics. Krystal Biotech is headquartered in Pittsburgh, Pennsylvania. For more information, please visit http://www.krystalbio.com, and follow @KrystalBiotech on LinkedIn and Twitter.

Forward Looking Statements
Any statements in this press release about future expectations, plans and prospects for Krystal Biotech, Inc., including statements about the timing of the initiation and details of the planned Phase 1 clinical trial of KB408, and other statements containing the words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "likely," "will," "would," "could," "should," "continue," and similar expressions, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including: uncertainties associated with regulatory review of clinical trials and applications for marketing approvals, the availability or commercial potential of product candidates, the sufficiency of cash resources and need for additional financing and such other important factors as are set forth under the caption "Risk Factors" in the Company's annual and quarterly reports on file with the U.S. Securities and Exchange Commission. In addition, the forward-looking statements included in this press release represent the Company's views as of the date of this release. The Company anticipates that subsequent events and developments will cause its views to change. However, while the Company may elect to update these forward-looking statements at some point in the future, it specifically disclaims any obligation to do so. These forward-looking statements should not be relied upon as representing the Company's views as of any date subsequent to the date of this release.

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