Krystal Biotech Announces First Patient Dosed in Phase 1 Clinical Trial of KB407 for the Treatment of Cystic Fibrosis

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PITTSBURGH, July 03, 2023 (GLOBE NEWSWIRE) -- Krystal Biotech, Inc. (the "Company") (NASDAQ: KRYS), a biotechnology company focused on developing and commercializing genetic medicines for patients with debilitating diseases, announced today that the first patient has been dosed at the Cystic Fibrosis Institute of Chicago in the Company's Phase 1 CORAL-1/US study evaluating KB407, an engineered HSV-1-based, aerosol-delivered, mutation agnostic, genetic medicine for the treatment of patients with cystic fibrosis (CF).

"By delivering full-length copies of *CFTR* directly to the lung via nebulization, KB407 has the potential to address the basic genetic defect present in cystic fibrosis," said Steven R. Boas, M.D., Director of the Cystic Fibrosis Institute and Professor of Pediatrics at Northwestern University Feinberg School of Medicine. "As this therapy does not depend on the type of *CFTR* mutation present, KB407 may potentially benefit all individuals affected by cystic fibrosis."

"Dosing our first patient in the KB407 Phase 1 clinical trial is an exciting step forward for the company and for the patients we aim to benefit," said Hubert Chen, M.D., Senior Vice President of Clinical Development at Krystal Biotech. "Not only is the Phase 1 study designed to provide key insights into the safety and efficacy of KB407, it is also a critical step in expanding our vector platform to tissues beyond the skin. We look forward to continued enrollment into the Phase 1 study with anticipated data in 2024."

CORAL-1/US Study Overview

The CORAL-1/US study is a multicenter, dose-escalation trial of KB407 in patients (n~20) with CF regardless of their underlying genotype. Each administration of KB407 will be nebulized in under 30 minutes. This study will include three cohorts and enroll five subjects each in the first two cohorts and ten subjects in the last cohort.

Cohort 1 participants will receive a single administration of KB407 on Day 0, and Cohort 2 participants will receive administrations of KB407 on Day 0 and Day 1. Cohorts 1 and 2 will be conducted on an open-label basis and up to 3 subjects in each of the first two cohorts may receive concurrent CFTR modulator therapy. Cohort 3 participants will be randomized 4:1 to receive administrations of KB407 or placebo on Day 0, Day 1, Day 2, and Day 3. Cohort 3 will follow a randomized, placebo-controlled, and double-blind design and will enroll only subjects who are not otherwise eligible for CFTR modulators. A Data Monitoring Committee will conduct a safety review after each cohort before proceeding to the next one.

The primary endpoint of the trial will be the safety and tolerability of nebulized KB407. Changes in lung function from baseline will be assessed by the percent predicted forced expiratory volume in one second ($ppFEV_1$). Vector shedding and biodistribution will also be assessed in blood, urine, buccal, and sputum samples. The CORAL-1/US study also includes a bronchoscopy sub-study for assessment of *CFTR* transgene expression in the airways at both the nucleic acid and protein levels. At select sites, subjects may undergo an optional bronchoscopy 24 to 96 hours after the last dose of KB407. The bronchoscopy will include bronchial brushings and endobronchial biopsies.

Details about the Phase 1 study can be found at www.clinicaltrials.gov under NCT identifier NCT05504837.

About KB407
KB407 is an investigational, redosable gene therapy designed to molecularly correct the underlying cause of CF by delivering two copies of the *CFTR* gene directly to the airways via nebulization. By enabling the expression of full-length, healthy CFTR protein in the lung, treatment with KB407 has the potential to restore proper anion transport within transduced cells to correct the lung manifestations of the disease. Because KB407 is engineered to enable expression of wild-type CFTR protein, treatment is agnostic to patients' underlying *CFTR* mutations. The US Food and Drug Administration and the European Commission have granted orphan drug designation for KB407 to treat patients with CF.

About Cystic Fibrosis

CF is a genetic disease caused by mutations in the *CFTR* gene which result in dysfunctional or absent CFTR protein, and buildup of mucus in the lungs that leads to persistent lung infections and progressive pulmonary disease. The Cystic Fibrosis Foundation estimates that there are close to 40,000 children and adults living with CF in the US, and an estimated 105,000 people diagnosed with CF across 94 countries. People of every racial and ethnic group are affected by this debilitating disease.

Although CFTR modulators are effective in patients with certain *CFTR* mutations, patients may still experience pulmonary symptoms requiring treatment. Importantly, approximately 10-15% of CF patients harbor genetic mutations that are not expected to be responsive to approved therapies and currently have no available disease-modifying treatment options, representing a significant unmet need.

About Krystal Biotech, Inc.
Krystal Biotech, Inc. (NASDAQ: KRYS) is a commercial-stage fully integrated company focused on developing genetic medicines for patients with debilitating diseases. 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 presently has three candidates in clinical development and a wide-ranging pipeline that is powered by its proprietary, redosable HSV-1 gene delivery platform. 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 clinical utility of KB407, the expansion of the Company's platform to tissues beyond the skin, the potential of KB407 to treat all patients with cystic fibrosis, the timing of reporting results from the Phase I clinical trial of KB407, 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 including KB407, 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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