Krystal Biotech Provides Updates from its Rare Genetic Lung Disease Pipeline

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- *New preclinical data from GLP toxicology and biodistribution study demonstrates in vivo safety of KB407 for cystic fibrosis*
- *Company expands rare genetic lung disease pipeline with KB408 for the treatment of alpha-1 antitrypsin deficiency*

PITTSBURGH, April 19, 2021 (GLOBE NEWSWIRE) -- Krystal Biotech Inc., ("Krystal") (NASDAQ: KRYS), the leader in redosable gene therapies for rare diseases, today announced positive results of its IND-enabling good laboratory practice (GLP) toxicology study of KB407, an inhaled gene therapy candidate for the treatment of cystic fibrosis (CF), in nonhuman primates (NHPs). In addition, the Company announced initial preclinical proof-of-concept for its second genetic pulmonary disease candidate, KB408, for the treatment of alpha-1 antitrypsin deficiency (AATD).

"Successful completion of this GLP toxicology and biodistribution study is an important milestone not only for KB407, but also for our emerging pulmonary portfolio," said Suma Krishnan, founder and chief operating officer of Krystal Biotech. "We are excited to expand our pulmonary pipeline with the addition of KB408 for the potential treatment of alpha-1 antitrypsin deficiency and look forward to continued progress with our additional discovery phase candidates."

KB407 for Cystic Fibrosis
KB407 is an inhaled (nebulized) formulation of an engineered HSV-1 based vector designed to deliver two copies of the full-length *CFTR* gene for the treatment of cystic fibrosis. Previously presented in vitro and in vivo data demonstrate robust transduction efficiency in patient-derived airway epithelial cells, correction of the CF phenotype in patient-derived organoids irrespective of the underlying CFTR mutation within 24 hours of infection, and distribution throughout the lungs of mice and a single nonhuman primate when dosed via nebulization.

To further characterize the safety profile of KB407, Krystal conducted a repeat-dose GLP toxicology and biodistribution study in 36 nonhuman primates (NHPs) who received three weekly doses of either KB407 high dose (n=10), KB407 low dose (n=10), vehicle (n=10), or air (n=6). Results of the study were positive and included:

- Repeat doses of KB407 in NHPs were well tolerated, and the No-Observed-Adverse-Effect Level (NOAEL) was at the highest dose tested;
- KB407 was distributed throughout the lung tissue, including the bronchioles and alveoli, with little-to-no vector detected in all other tissues and fluids tested;
- Tissue samples collected for immunofluorescent analysis show specific transduction of airway epithelia, with little-to-no vector detected in lung-resident macrophages; and
- Lung samples harvested 28 days after the last dose demonstrate persistence of the vector and CFTR expression to at least that timepoint.

Next Steps:
The Company intends to initiate a Phase 1 study of KB407 in 3Q21.

KB408 for Alpha-1 Antitrypsin Deficiency
KB408 is an inhaled (nebulized) formulation of our novel vector designed to deliver two copies of the *SERPINA1* gene, that encodes for normal human alpha-1 antitrypsin (AAT) protein, for the treatment of alpha-1 antitrypsin deficiency (AATD). AATD is a genetic condition caused by mutations that lead to decreased levels and/or decreased functionality of the AAT protein. The predominant disease manifestation of severe AAT deficiency is emphysema, as lower levels of functional AAT are insufficient to fully protect the lungs from the enzymatic activity of neutrophil elastase and progressive destruction of the lung tissue. There are an estimated 90,000 to 100,000 people in the US with severe AAT deficiency.

Building on the positive preclinical experience with repeat-dose gene delivery to the lungs with KB407, KB408 leverages the same formulation and route of administration. Initial preclinical data show:

- KB408 successfully transduces primary airway epithelial cells in vitro, leading to production and secretion of full length, normal human AAT protein;
- In healthy immunocompetent mice administered a single dose of KB408 or vehicle control to the airways, analyses of lung tissue samples 24 hours post-dose show efficient vector transduction and human AAT transgene expression;
- Analysis of bronchoalveolar lavage fluid harvested at the same 24-hour timepoint shows secretion of full-length AAT protein in dosed animals; and
- Quantitative analysis of lung fluid harvests at necropsy reveals no evidence of local immune activation/toxicity.

Next steps:
More detailed preclinical data will be presented at a future scientific conference. In addition, the Company has submitted a pre-IND (Investigational New Drug) briefing package and is scheduled to meet with the U.S. Food and Drug Administration (FDA) regarding the preclinical IND enabling study requirements in 2Q21, which will determine next steps and timelines for the program.

About Krystal Biotech
Krystal Biotech, Inc. (NASDAQ:KRYS) is a pivotal-stage gene therapy company leveraging its novel, redosable gene therapy platform and in-house

manufacturing capabilities to develop therapies to treat serious rare diseases. For more information, please visit http://www.krystalbio.com.

Forward-Looking Statements

Any statements in this press release about future expectations, plans and prospects for Krystal Biotech, Inc., including but not limited to statements about the development of Krystal's product candidates, such as plans for the design, conduct and timelines of ongoing clinical trials of beremagene geperpavec ("B-VEC"), KB105, KB104, KB301, KB407, and KB408; the clinical utility of B-VEC, KB105, KB104, KB301, KB407 and KB408, and Krystal's plans for filing of regulatory approvals and efforts to bring B-VEC, KB105, KB104, KB301, KB407 and KB408 to market; the market opportunity for and the potential market acceptance of B-VEC, KB105, KB104, KB301, KB407 and KB408; plans to pursue research and development of other product candidates; the sufficiency of Krystal's existing cash resources; the unanticipated impact of COVID-19 on Krystal's business operations, pre-clinical activities and clinical trials; 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: the uncertainties inherent in the initiation and conduct of clinical trials, availability and timing of data from clinical trials, whether results of early clinical trials or trials will be indicative of the results of ongoing or future trials, uncertainties associated with regulatory review of clinical trials and applications for marketing approvals, the availability or commercial potential of product candidates including B-VEC, KB105, KB104, KB301, KB407 and KB408, 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 Krystal'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 Krystal's views as of the date of this release. Krystal anticipates that subsequent events and developments will cause its views to change. However, while Krystal 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 Krystal's views as of any date subsequent to the date of this release.

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