Krystal Biotech Announces Early Evidence of Monotherapy Activity in Heavily Pre-Treated Patients with Advanced Non-Small Cell Lung Cancer

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Preliminary clinical data in post-anti-PD-1 NSCLC patients demonstrated a 27% ORR and 73% DCR in monotherapy trial

Monotherapy activity with inhaled KB707 provides further evidence of successful repeat administration of HSV-1 based inhaled lung gene delivery and builds on recent clinical data update for CF and AAT deficiency respiratory disease programs

PITTSBURGH, Dec. 18, 2024 (GLOBE NEWSWIRE) -- Krystal Biotech, Inc. (the “Company”) (NASDAQ: KRYS), a commercial-stage biotechnology company, announced today initial clinical results from its ongoing KYANITE-1 study evaluating inhaled KB707 in patients with solid tumors of the lung. KB707 administered via inhalation demonstrated early evidence of monotherapy activity that was most pronounced in patients with advanced non-small cell lung cancer (NSCLC), where an objective response rate (ORR) of 27% and disease control rate (DCR) of 73% were observed as of data cut-off on December 6, 2024.

“The inhaled local delivery of cytokine that maximizes efficacy and limits systemic toxicity is truly innovative,” said Wen Wee Ma, MBBS, Vice Chair of Research and Director of the Novel Cancer Therapeutics Center at Cleveland Clinic. “To see potential benefit as a monotherapy in NSCLC patients who have progressed after standard of care treatments is very encouraging and provides much needed hope.”

KYANITE-1 is an ongoing, open-label, multicenter, dose escalation and expansion study evaluating inhaled KB707 for the treatment of solid tumors of the lung. Treatments of either 10^8 PFU or 10^9 PFU of KB707 were evaluated in dose escalation, following which 10^9 PFU was selected for dose expansion. Frequency of KB707 administration has been consistent throughout dose escalation and expansion, with patients receiving KB707 via inhalation once weekly for the first three weeks, then once every three weeks. Trial objectives include evaluation of safety, tolerability, and tumor response measured using RECIST v1.1 criteria. Additional details of the KYANITE-1 study can be found at www.clinicaltrials.gov under NCT identifier NCT06228326.

The first patient in KYANITE-1 was dosed on April 17, 2024. A total of 37 patients were enrolled and received at least one dose of inhaled KB707, including 17 patients with a diagnosis of advanced NSCLC. All patients had malignant lesions in the lung at baseline.

Inhaled KB707 has been safe and generally well tolerated to date in this diverse, heavily pre-treated patient population with advanced disease, and amenable to administration in an outpatient setting. Treatment-emergent adverse events have been predictable and consistent with both the underlying disease and known adverse event profiles of interleukin-2 and interleukin-12. The majority of treatment-related adverse events have been mild to moderate in severity and transient, with no Grade 4 or 5 adverse events observed.

Clinical activity observed to date in the KYANITE-1 study has shown the most therapeutic benefit in patients with advanced NSCLC. As of the data cut-off, 11 NSCLC patients were evaluable for response with at least one radiographic scan and RECIST v1.1 evaluation. Patients included in the analysis were heavily pre-treated with 4 median lines of prior therapy and all had received at least one line of prior immunotherapy. In this NSCLC patient analysis cohort, an ORR of 27%, with three partial responses, has been achieved. DCR to date has been 73% with 7 out of 11 patients still remaining on treatment. Duration of treatment for patients included in the analysis ranged from 10.3 to 33.3 weeks as of data cut-off.

In addition to preliminary evidence of abscopal effect and treatment benefit outside of the lung, treatment responses in lesions of the lung were especially notable. Among the same 11 evaluable NSCLC patients, the ORR in target lung lesions specifically was 36%, with three partial responses and one complete response, and DCR was 82%.

“Signals of monotherapy activity with inhaled KB707, although early, are an exciting milestone for our program and highlight the significant potential of our vectorized cytokine approach in the treatment of difficult cancers,” said Suma Krishnan, President of Research and Development of Krystal Biotech. “These data add to a rapidly growing clinical dataset, generated across multiple programs and patient populations, demonstrating that our HSV-1 platform can safely and repeatedly deliver functional genetic material to the lung and impact the course of disease. We are excited about the implications for our platform and the prospect of delivering meaningful clinical benefit to patients suffering from rare and serious lung diseases.”

Based on positive initial results in monotherapy, the Company has amended the KYANITE-1 protocol to add two cohorts evaluating inhaled KB707 for the treatment of advanced NSCLC in combination with either anti-programmed cell death protein 1 (PD-1) therapy or anti-PD-1 therapy and chemotherapy. No patients have been enrolled in the combination expansion cohorts to date.

The Company expects to disclose detailed and updated results of KYANITE-1 at future scientific conference(s).

About IL-2, IL-12, and KB707

IL-2 and IL-12 are secreted cytokines with complementary functions promoting cell-mediated immunity in humans. Both IL-2 and IL-12 have been shown to elicit anti-tumor immune responses in preclinical or clinical models and have been extensively studied for their potential in cancer immunotherapy. Despite promising signs of efficacy, it has proven difficult to effectively harness IL-2 and IL-12 for therapeutic benefit, as systemic administration is often poorly tolerated, and their inherently short half-lives necessitate high dose levels and extremely frequent dose intervals. KB707 is a modified HSV-1 vector designed to deliver genes encoding both human IL-12 and IL-2 directly to a patient’s tumor(s) and promote systemic immune-mediated tumor clearance. KB707 targets solid tumors that are accessible via intratumoral injection or inhalation.

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 first 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 X (formerly Twitter).

Forward-Looking Statements

Any statements in this press release about future expectations, plans, and prospects for Krystal Biotech, Inc., including statements about the significant potential of the Company's vectorized cytokine approach in the treatment of difficult cancers; the Company's HSV-1 platform and its ability to safely and repeatedly deliver functional genetic material to the lung and impact the course of disease; the Company's expectation that it will disclose detailed and updated results of KYANITE-1 at future scientific conference(s); 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 inherent in the initiation and conduct of clinical trials 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 press 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 press release.

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