Krystal Biotech Provides Update on the Clinical Trial Evaluating Topical KB105 for the Treatment of TGM-1 Associated Ichthyosis

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- *New data include update from the fourth patient treated in the Phase 1/2 trial*

- *Repeat topical KB105 dosing continues to be well tolerated with no adverse events or evidence of immune response*

PITTSBURGH, July 01, 2021 (GLOBE NEWSWIRE) -- Krystal Biotech Inc., ("Krystal") (NASDAQ: KRYS), the leader in redosable gene therapies for rare diseases, today announced updated results from the Phase 1/2 clinical trial evaluating topical administration of KB105 in patients with autosomal recessive congenital ichthyosis (ARCI) associated with mutations in the *TGM1* gene. These data show that repeat doses of KB105 continue to be well tolerated with no adverse events and with no evidence of immune response, systemically or at the sites of application. Phenotypic improvement, based on the IGA scale, was observed at each KB105 dosing site at varying time points throughout the 30-day dosing period, with the maximum effect observed in the treatment areas that received the highest KB105 dose.

These results build on previous data showing a dramatic increase in KB105-mediated TGM-1 expression and activity in 3 patients, which correlated with an improvement on the IGA scale after KB105 topical treatment, with or without pretreatment of the area through micro-needling. No drug-related adverse effects were reported.

"The totality of the data from our Phase 1/2 trial is encouraging, showing that topical application of KB105 to exfoliated skin results in detectable and correctly localized and functionally active TGM-1 enzyme," said Suma Krishnan, Chief Operating Officer of Krystal Biotech. "With this data in hand, we look forward to having continued discussions with patients and physicians to determine the optimal dosing regimen and endpoints to take forward into the next Phase 2 cohort, which we expect will include pediatric patients, in 2022."

Initial Phase 2 Data

An adult subject, aged 63, was enrolled and four 100cm^2 treatment areas were identified. Each treatment area was assigned to receive repeat doses of 4.0x10^9 PFU (n=2 treatment areas) or 1.0x10^{10} PFU (n=2 treatment areas). Each area was dosed on Day 1 and 3, after which dosing continued either every 3 days (n=2 treatment areas) or every 6 days (n=2 treatment areas) up to day 30. Treatment areas were clinically evaluated at pre- and post-KB105 application timepoints, using a 5-point IGA scale (0 = clear; 1 = almost clear; 2 = mild; 3 = moderate; 4 = very severe).

Repeated topical doses of KB105 were well tolerated, and no drug-related adverse effects were reported. No vector shedding or systemic viral exposure was detected at any time point. Improvement on the IGA scale was observed in each treatment area, with the maximum effect observed in TA3 and TA4 that received the highest dose; at day 27, the investigator assigned an IGA score of 2, which was improved as compared to baseline score of 4 in each area. Variable 1-point improvements were observed at other time points and in the treatment areas that received the lowest dose. As in the Phase 1 portion of the trial, TGM1 turnover was observed to be variable but relatively rapid, and the observed IGA improvements were not sustained through day 60.

More detailed data is available in the Company's corporate presentation, which is available at https://ir.krystalbio.com/.

Phase 1 Review

The Phase 1 portion of the study enrolled 3 adult subjects, on whom four 20cm^2 treatment areas were identified. One site received placebo, and three sites each received topical doses of 2.0x10^9 PFU at varying frequencies, up to 5 or 6 repeat doses throughout the 90-day study period. All 3 subjects showed a dramatic increase in KB105-mediated TGM-1 expression and activity, which correlated with an improvement in scaling with KB105 topical treatment, with or without pretreatment of the area through micro-needling. No drug-related adverse effects were reported. Pre-existing immunity to HSV-1 had no impact on KB105 efficacy, and repeat dosing with KB105 did not exacerbate immune response to HSV-1. KB105-mediated TGM-1 was correctly localized and functionally active based on an in situ activity assay. KB105 treated areas showed reduced reversion to ichthyotic scaling phenotype which correlated with molecular correction. These data were previously presented at the Society for Investigative Dermatology (SID) 2020 annual meeting. The presentation is available here.

In these subjects, TGM1 turnover was observed to be variable and rapid, and pharmacokinetic data suggested that the optimal dosing frequency may be more frequent. Further, phenotypic evaluation was limited by small treatment areas. Based on these Phase 1 results, the dose, dosing frequency, and size of the treatment areas were adjusted for Phase 2.

Next Steps

Krystal intends to discuss these data with patients and key opinion leaders to help inform next steps. In particular, the company will assess the optimal dosing frequency as well as additional clinical endpoints, including a novel scale designed for ichthyosis. The Company intends to complete these discussions by the end of the year, and continue dosing in the Phase 2 trial, in 2022.

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 KB105 and the clinical utility of KB105 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 will be indicative of the results of ongoing or future trials, uncertainties associated with regulatory review of clinical trials and applications for marketing approvals 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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