Krystal Biotech Announces Initiation of Pivotal Phase 3 Study of Beremagene Geperpavec in Patients with Dystrophic Epidermolysis Bullosa

July 28, 2020

- **The randomized, double-blind GEM-3 trial will compare repeat dosing of either B-VEC or placebo in approximately 30 dystrophic epidermolysis bullosa (DEB) patients**
- **Top line data and BLA filing are anticipated in 2021; EMA aligned on pivotal study design and an MAA is anticipated shortly after BLA**

PITTSBURGH, July 28, 2020 (GLOBE NEWSWIRE) -- Krystal Biotech, Inc. (Nasdaq:KRYS), a fully integrated gene therapy company driven by its proprietary, engineered herpes simplex virus type 1 vector (HSV-1) platform, today announced the initiation of GEM-3 study, a multi-center, placebo-controlled, double-blinded, Phase 3 clinical study of beremagene geperpavec ("B-VEC", previously "KB103") for the treatment of dystrophic epidermolysis bullosa (DEB) patients.

"Despite the logistical challenges associated with COVID-19, Stanford and I are excited to begin this pivotal study," said Dr. Peter Marinkovich, M.D., associate professor of dermatology and director of the Blistering Disease Clinic at Stanford University, and primary investigator for the trial. "We and the other study sites have worked closely with the Krystal team to ensure safe trial practices in the context of the ongoing pandemic, enabled by the out-patient nature of B-VEC dosing."

Suma Krishnan, founder and chief operating officer of Krystal Biotech added, "The initiation of the pivotal study marks an important milestone toward our goal of a potential painless, convenient, and corrective approach to treat patients suffering from this debilitating disease. We look forward to having a home dosing protocol in place in the upcoming months that, we believe, would further improve the quality of life of our patients and their caregivers."

This clinical progress follows announcement of positive results from the GEM-1 and GEM-2 studies. B-VEC is a topical, re-dosable gene therapy in development for the treatment of both the dominant and recessive forms of DEB, a rare and severe monogenic skin disease for which there is currently no approved treatment. The U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) have each granted B-VEC orphan drug designation for the treatment of DEB, and the FDA has granted B-VEC fast track designation and rare pediatric designation for the treatment of DEB. In addition, in 2019, the FDA granted Regenerative Medicine Advanced Therapy (RMAT) to B-VEC for the treatment of DEB and the EMA granted PRIority MEdicines (PRIME) eligibility for B-VEC to treat DEB.

B-VEC is manufactured in-house using the commercial process and at scale in Krystal's fully functional GMP ANCORIS facility, located near corporate headquarters in Pittsburgh.

"Our existing facility has the capacity to support our commercial launch in the U.S.," said Krish Krishnan, chairman and chief executive officer of Krystal Biotech. "We look forward to getting ASTRA, our second GMP facility operational in 1H 2022 to supplement ANCORIS, as we expand beyond the U.S. markets into EU and the rest of the world."

About the GEM-3 Pivotal Study
The GEM-3 trial is a randomized, double-blind, intra patient placebo-controlled multicenter study designed to evaluate the efficacy and safety of B-VEC for patients suffering from both recessive and dominant forms of dystrophic epidermolysis bullosa. The trial aims to enroll approximately thirty (30) participants with DEB, aged 6 months or older at time of consent. Investigator identified wound pairs, up to three in each patient, will be treated once weekly for six months with either B-VEC or placebo.

Dosing
The dose administered to each wound is dependent on the size of the wound and ranges from $4x10^8$ to $1.2x10^9$ PFU per wound. The maximum weekly dose, administered once weekly per patient, is defined by patient age as outlined in the table below.

Maximum Weekly Dose Per Subject:

Age	Maximum Weekly Dose
≥ 6 months to < 3 years	1.6x10^9 PFU/week
≥ 3 years to < 6 years	2.4x10^9 PFU/week
≥ 6 years	3.2x10^9 PFU/week

Weekly dosing will be continued until the wound is completely closed, and re-dosing may occur at any point throughout the study should a wound re-open. In addition to the primary target wound pair(s), additional wounds (secondary wounds) may be selected to be treated with B-VEC which will give the treating physicians flexibility to treat a larger number of wounds.

Endpoints
The Primary Outcome Measure is complete wound healing determined by the Investigator, as compared to baseline in B-VEC treated wounds versus placebo treated at Weeks 20, 22 and 24.

Secondary endpoints to be evaluated in the study include complete wound healing at Weeks 8, 10 and 12; the mean change in pain severity (using either a VAS or FLACC-R Scale) per primary wound site associated with wound dressing; the proportion of primary wound sites with ≥75% healing assessed via Canfield photography. Additional exploratory measures include relative time to wound closure from baseline, duration of wound closure, mean reduction in wound surface area in B-VEC treated versus placebo treated wounds, mean change in Quality of Life in addition to Skindex score

as compared to baseline at Week 24. Throughout the study, participants will complete questionnaires, have images captured of their study wounds, undergo physical exams, have vital signs and safety labs monitored.

About Krystal Biotech

Krystal Biotech, Inc. (NASDAQ:KRYS) is a gene therapy company dedicated to developing and commercializing novel treatments for patients suffering from dermatological 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 and KB407; the clinical utility of B-VEC, KB105 and KB407, and Krystal's plans for filing of regulatory approvals and efforts to bring B-VEC, KB105 and KB407 to market; the market opportunity for and the potential market acceptance of B-VEC, KB105 and KB407; 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 and 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 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.

CONTACTS:

Investors:
Ashley R. Robinson
LifeSci Advisors
arr@lifesciadvisors.com

Media:
Darren Opland, Ph.D.
LifeSci Communications
darren@lifescicomms.com

Source: Krystal Biotech, Inc.