Krystal Biotech Announces Positive Interim Results from Placebo-Controlled Phase 1/2 Clinical Trial of KB103

October 15, 2018

KB103 is Krystal's first "off-the-shelf", topical, gene therapy candidate to treat patients suffering from Dystrophic Epidermolysis Bullosa.

Results on 2 patients met all primary efficacy (presence of functional COL7 expression, observation of NC1 and NC2 reactive anchoring fibrils and continued expression following repeat administration) and safety endpoints (no adverse events, inflammation or irritation) in topically administered KB103 wounds.

With respect to secondary endpoints – topically administered KB103 wounds closed in 2 weeks and continue to stay closed to date. Topically administered placebo administered wounds took 10 weeks to close in patient 1 and did not completely close throughout the study in patient 2.

KB103 when administered intradermally to intact skin shows presence functional COL7 expression and anchoring fibrils in both patients.

The Phase 1/2 study is anticipated to be complete in 1H 2019 and a pivotal Phase 3 study is anticipated to commence in 2H 2019.

Management and the Principal Investigator to host a webcast at 8:45 a.m. EST – webcast/conference call details below.

PITTSBURGH, Oct. 15, 2018 (GLOBE NEWSWIRE) -- Krystal Biotech, Inc. (Nasdaq:KRYS), a gene therapy company dedicated to developing and commercializing novel treatments for patients suffering from dermatological diseases, today announced positive interim results from its ongoing placebo-controlled Phase 1/2 clinical trial of KB103.

GEM Study Status update

Two adult Recessive Dystrophic Epidermolysis Bullosa ("RDEB"), NC1[+] patients aged 35 and 28 years old have completed treatment with topical KB103 to date. The patients were re-dosed during the study. In each patient, two wounds with an approximate surface area of 10 cm^2 were randomized to receive either topical KB103 or placebo (for a total of 4 wounds evaluated). KB103 was also injected intradermally in both patients to intact skin to evaluate the mechanism of action of KB103 and validate molecular correction. Both KB103-treated wounds and intradermally injected intact skin were biopsied to assess functional COL7 expression and anchoring fibril formation. KB103-treated wounds were also evaluated for clinically relevant healing compared to placebo-treated wounds and to baseline. They were also monitored for general and recombinant viral infection and autoimmune response at each evaluation.

"Results on 2 patients demonstrate a meaningful clinical benefit and suggest that KB103 can afford a simple, convenient, painless way to administer treatment for patients suffering with this debilitating disease," said Dr. Peter Marinkovich, MD, Associate Professor of Dermatology, Stanford University and Principal Investigator in the GEM study. "These early data are encouraging and we look forward to continuing the study in pediatric populations."

Interim Data Update

Results on 2 patients met all primary efficacy (presence of functional COL7 expression, observation of NC1 and NC2 reactive anchoring fibrils and continued expression following repeat administration) and safety endpoints (no adverse events, inflammation or irritation) in topically administered KB103 wounds.

1. Analysis of KB103-treated wounds demonstrates clearly detectable robust functional COL7 expression by immunofluorescence (IF) in the biopsy samples from the two treated patients as early as Day 2 of treatment. Functional COL7 was determined by staining the tissue samples with NP185 and LH24 antibodies that bind to NC1 and NC2 domains of the COL7 protein respectively. Both of the patients were NC1 positive at baseline. The tissues from the skin biopsies show the presence of both the NC1 and NC2 domains demonstrating production of functional COL7 that has linearly deposited along the Basement Membrane Zone (BMZ).
2. NC1 and NC2 reactive anchoring fibrils were observed by immunoelectron microscopy (IEM) as early as Day 14 and up to the last biopsy for both patients.
3. *Safety data from both patients show that KB103 was well tolerated. No serious adverse events, and no product-related adverse events* were reported. No inflammation or irritation was observed at KB103-treated wounds. In addition, no antibody response was noted for type VII collagen (COL7).
4. Repeat administration of KB103 in both patients demonstrated continued expression of COL7 expression with no immune or safety concerns.

With respect to secondary endpoints – topically administered KB103 wounds closed in 2 weeks and continue to stay closed to date. Topically administered placebo wounds took 10 weeks to close in patient 1 and did not completely close throughout the study in patient 2.

5. In Patient 1, the wounds administered with KB103 closed in 2 weeks while wounds administered with placebo closed in 10 weeks. In Patient 2, the wounds administered with KB103 closed in 2 weeks also - demonstrating a faster rate of wound closure on KB103- administered wounds to date compared to placebo. Patient 2's placebo-administered wound did not fully close throughout the study.
6. To date, both of the patient's KB103-treated wounds remain closed, representing 4.5 months of total closure for Patient 1 and 3.5 months of total closure for Patient 2. Patient 1 has chosen to discontinue bandaging on the KB103-treated wound that previously required regular bandaging.

KB103 when administered intradermally to intact skin on both patients shows presence functional COL7 expression and anchoring fibrils.

7. Analysis of KB103-treated intact skin revealed clearly detectable functional COL7 expression by immunofluorescence in biopsy samples collected from the intradermal injection sites.
8. Clinical data from two patients were submitted to the FDA. FDA acknowledges molecular correction as evidenced by expression of COL7 and anchoring fibrils. Consequently, the protocol has been amended to remove the intradermal arm for patients in the Phase 1/2 trial going forward.
9. Per discussion with the FDA, the amended protocol will now enroll pediatric patients and will focus on evaluating durability of wound closure in preparation for selecting endpoints for Phase 3 clinical trial. With safety and molecular correction established, the revised Phase 1/2 protocol allows for increased dosing and KB103 administration to larger wound areas.

Conference Call

Management, along with the Principal Investigator on the Study – Dr. Peter Marinkovich, MD, Stanford University, will elaborate on the clinical data during a webcasted conference call today at 8:45 a.m. EST. The dial-in details of the call are +1-877-524-6431 or +1-786-815-8673, conference ID: 4487935. The live webcast can be accessed at https://edge.media-server.com/m6/p/5d7wxq73

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.

About KB103

KB103 is Krystal's lead product candidate that seeks to use gene therapy to treat dystrophic epidermolysis bullosa, or DEB, an incurable skin blistering condition caused by a lack of collagen in the skin. KB103 is a replication-defective, non-integrating viral vector that has been engineered employing Krystal's STAR-D platform to deliver functional human COL7A1 genes directly to the patients' dividing and non-dividing skin cells. HSV-1 is Krystal's proprietary vector that can penetrate skin cells more efficiently than other viral vectors. Its high payload capacity allows it to accommodate large or multiple genes and its low immunogenicity makes it a suitable choice for direct and repeat delivery to the skin.

About Dystrophic Epidermolysis Bullosa

Dystrophic epidermolysis bullosa, or DEB, is an incurable, often fatal skin blistering condition caused by a lack of collagen protein in the skin. It is caused by mutations in the gene coding for type VII collagen, or COL7, a major component of anchoring fibrils, which connect the epidermis to the underlying dermis, and provide structural adhesion between these skin layers in a normal individual. The lack of COL7 in DEB patients causes blisters to occur in the dermis as a result of separation from the epidermis. This makes the skin incredibly fragile, leading to blistering or skin loss at the slightest friction or knock. It is progressive and incredibly painful.

The most severe form of DEB is recessive DEB, or RDEB, which is caused by null mutations in the COL7A1 gene. DEB also occurs in the form of dominant DEB, or DDEB, which is considered to be a milder form of DEB. There are no known treatments affecting the underlying cause of either form of the disease, and the current standard of care for DEB patients is limited to palliative treatments. Krystal is developing KB103 for the treatment of the broad DEB population, including both recessive and dominant forms of the disease.

Forward-Looking Statements

This press release on announcing positive interim data from Krystal's phase 1/2 trial evaluating KB103 in patients suffering from Dystrophic epidermolysis bullosa, or DEB, contains "forward-looking statements" regarding matters that are not historical facts, including statements relating to the Company's clinical trials, including plans to commence a pivotal Phase 3 study in 2H 2019. There can be no assurance that the data contained in these results will be replicated in additional current and future patients enrolled in this or any future trial or that these results will prove clinically meaningful in the development of KB103 as a potential drug. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. Words such as "anticipates," "plans," "expects," "intends," "will," "potential," "hope" and similar expressions are intended to identify forward-looking statements. These forward-looking statements are based upon current expectations of the Company and involve assumptions that may never materialize or may prove to be incorrect. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of various risks and uncertainties. Detailed information regarding factors that may cause actual results to differ materially from the results expressed or implied by statements in this press release relating to the Company may be found in the Company's periodic filings with the Securities and Exchange Commission, including the factors described in the section entitled "Risk Factors" in its annual report on Form 10-K for the fiscal year ended December 31, 2017, and supplemented from time to time and the Company's Quarter Reports on Form 10-Q and other filings submitted by the Company to the SEC, copies of which may be obtained from the SEC's website at www.sec.gov. The parties do not undertake any obligation to update forward-looking statements contained in this press release.

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