Krystal Biotech Announces Positive Results from Phase 2 Clinical Trial (“GEM-2 study”) of KB103 and Receives Regenerative Medicine Advanced Therapy (“RMAT”) Designation from FDA for KB103

June 24, 2019

- *Safety data from all patients show that KB103 was well tolerated with no adverse events reported*
- *Five out of six wounds treated with KB103 in the Phase 2 trial closed 100% during the trial*
- *The average time to complete 100% wound closure on KB103 treated wounds in Phase 2 trial was 23 days*
- *With the exception of one chronic wound, the remaining KB103 treated wounds in Phase 2 trial remained 100% closed at 90 day timepoint.*
- *The duration of wound closure on two patients in Phase 1 trial as of the last follow up was 184 days (6.6 months) and 174 days (6.2 months).*
- *RMAT designation granted to KB103 based on positive interim data from GEM-1 and GEM-2 study*

PITTSBURGH, June 24, 2019 (GLOBE NEWSWIRE) -- Krystal Biotech, Inc. (Nasdaq: KRYS), a gene therapy company dedicated to developing and commercializing novel treatments for patients suffering from rare dermatological diseases, today announced positive results from its Phase 2 placebo-controlled clinical trial of KB103 (GEM-2) study and an update on results from Phase 1 (GEM-1) study.

GEM-2 Study of KB103

In the Phase 2 trial, four additional patients (two adults (ages 22 and 19) and two pediatric (ages 14 and 15)) with severe generalized recessive dystrophic epidermolysis bullosa (“RDEB”) were enrolled in December 2018. Prior to dosing, three wounds of size up to 20cm^2 were selected on each patient for the trial and subsequently randomized to receive either KB103 or placebo in a 2:1 (KB103: placebo) ratio. A total of four KB103-treated recurring wounds and two KB103-treated chronic wounds were included in the trial results. Having established the presence of type VII collagen (COL7) and anchoring fibrils in the Phase 1 portion of the trial and acknowledged by the FDA, the endpoints of the Phase 2 portion were revised toward a focus on clinical improvement.

One of the four patients (aged 19) voluntarily dropped out of the trial after 30 days due to an inability to travel to the clinical trial site. The dropout was unrelated to any safety or efficacy issues with KB103. Data from this patient was excluded from the overall analysis. The Phase 2 analysis was conducted on remaining three patients (six KB103 treated wounds and three placebo treated wounds) in the Phase 2 trial. With respect to the six KB103 treated wounds on patients enrolled for the duration of the Phase 2 trial, two were categorized as chronic and four as recurring based on patient reporting. Chronic wounds remain open for greater than 12 weeks while recurring wounds open and close spontaneously.

Earlier in the Phase 1 trial, two adult patients with severe generalized RDEB were evaluated. In each patient, two wounds with an approximate surface area of 10 cm^2 were randomized to receive either topical KB103 or placebo.

Clinical Data Update

Safety data from all patients in Phase 2 trial at 90 day timepoint show that KB103 was well tolerated. No serious adverse events, and no drug-related adverse events were reported. No inflammation or irritation was observed in KB103-treated wounds. In addition, no antibody response was noted for COL7.

Clinical Endpoint: Percent of Wound Closure

1. Five out of six wounds (four recurring and two chronic) treated with KB103 in the Phase 2 trial closed 100% during the trial.
2. The wound that did not close completely has been reported by the patient to be a chronic deep wound that has remained open for more than four years. It was closed 35% at the 30 day measurement and 42% at the 90 day measurement timepoint. The other chronic wound treated with KB103 in the trial took 41 days to close completely.
3. In the combined Phase 1 and Phase 2 trials, seven out of eight wounds treated with KB103 closed 100%.
4. None of the placebo treated wounds closed fully during the duration of the study to determine time to 100% wound closure. At 90 day timepoint, all three placebo wounds remained fully open.

Clinical Endpoint: Time to 100% wound closure

5. The average time to 100% wound closure on all KB103 treated wounds (five out of six) in the Phase 2 trial was 23.4 days (median 22 days). On the four recurring wounds, the average time to 100% wound closure was 19 days (median 21 days).
6. The average time to 100% wound closure on all KB103 treated wounds (two out of two) in the Phase 1 trial was 12 days (median 12 days).
7. The average time to 100% wound closure on all KB103 treated wounds in the combined Phase 1 and Phase 2 trials (seven out of eight) was 20.14 days (median 20 days).

Clinical Endpoint: Duration of wound closure

8. In Phase 1 trial, the duration of wound closure on two patients following 100% wound closure as of the last follow up was 184 days (6.6 months) and 174 days (6.2 months).
9. The average duration of wound closure at 90 day timepoint in Phase 2 trial on all recurring wounds was 71 days (median 68 days) which is the most up to date measurement available. We will continue to monitor the ongoing duration of wound closure in the Phase 2 trial.
10. The duration of wound closure on the chronic wound that closed 100% on Day 41 was 49 days.

11. We will provide a further update on final duration of wound closure prior to commencing Phase 3 pivotal trial but preliminary results indicate that duration of wound closure at 120 day timepoint was 101 days.

Mechanistic Endpoints:

1. Patients were biopsied on KB103 treated wounds on Day 30. To not interfere with wound healing, a second biopsy is anticipated to be done at end of trial, based on patient schedules.
2. Analysis of KB103-treated wounds demonstrates detectable functional COL7 expression by immunofluorescence (IF) in the biopsy samples from treated samples.
3. Functional COL7 was determined by staining the tissue samples with antibodies that bind to NC1 and NC2 domains of the COL7 protein respectively. The tissues from the skin biopsies show the presence of both NC1 and NC2 domains demonstrating production of functional COL7 that is linearly deposited along the Basement Membrane Zone (BMZ).
4. Similar staining was observed using immuno electron-microscopy. End of trial biopsy will be evaluated for mature anchoring fibrils.

“New treatments for patients suffering from EB are desperately needed, especially one that provides a convenient, painless way to administer treatment for patients suffering with this debilitating disease and to reduce their travel burden,” said Dr. Peter Marinkovich, M.D., associate professor of dermatology, Stanford University and principal investigator in the GEM study. “These exciting data in the Phase 1/2 trials are supportive of this very promising new approach for treating this debilitating disease.”

Ongoing and next steps

We recently enrolled and increased frequency of dosing on two additional patients to study chronic wounds in more detail and in preparation of designing a robust pivotal trial. We anticipate commencing the Phase 3 pivotal trial before year end 2019 and will provide a clinical update on these additional patients prior to commencing a pivotal trial.

KB103’s RMAT designation follows our recent announcement of the Priority Medicines, or PRIME designation received from the EMA, and we look forward to collaborating closely with the EMA and initiating a clinical trial in the EU in the upcoming months. The RMAT pathway is analogous to the Breakthrough Therapy designation designed for traditional drug candidates and medical devices and was specifically created by the U.S. Congress in 2016 to get important new cell therapy and gene therapy products to the patient earlier. Just like the Breakthrough designation, it allows companies developing regenerative medicine therapies to interact with the FDA more frequently in the clinical testing process, and RMAT-designated products may be eligible for priority review and accelerated approval.

Conference Call

Management, along with the principal investigator on the study – Dr. Peter Marinkovich, M.D., Stanford University, will elaborate on the clinical data during a webcasted conference call today at 8:45 a.m. EST. To join online please click: https://www.netroadshow.com/nrs/home/#!/?show=ef9bf999 or www.netroadshow.com and enter the entry code: KRYS2019 or visit www.netroadshow.com and enter the entry code: KRYS2019
*Dial in details will appear after you’ve launched the presentation and agreed to the disclaimer.

If you require assistance or do not have access to a computer or mobile device, please join by phone: U.S. Toll Free: 1.877.820.2105 or International: +1.470.279.7412 and enter the entry code: KRYS2019

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 Regenerative Medicine Advanced Therapy (“RMAT”)

Established under the 21st Century Cures Act, RMAT designation is a program designed to expedite the development and approval of regenerative medicine products, including gene therapy products. An investigational therapy is eligible for the RMAT designation if it is intended to treat, modify, reverse or cure a serious or life-threatening disease or condition, and preliminary clinical evidence indicates a potential to address unmet medical needs for that disease or condition. The designation includes all the benefits of the FDA's Fast Track and Breakthrough Therapy designations and enables the ability to work more closely and frequently with the FDA to discuss surrogate or intermediate endpoints to support the potential acceleration of approval and satisfy post-approval requirements.

About the Priority Medicines (PRIME) Initiative

PRIME is a program launched by the European Medicines Agency (EMA) to enhance support for the development of medicines that target an unmet medical need. This voluntary program is based on enhanced interaction and early dialogue with developers of promising medicines, to optimize development plans and speed up evaluation so these medicines can reach patients earlier. Through PRIME, the EMA offers early and proactive support to medicine developers to optimize the generation of robust data on a medicine’s benefits and risks and enable accelerated assessment of medicines applications. The goal of the initiative is to help patients benefit as early as possible from therapies that may significantly improve their quality of life.

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 trial 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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