



Krystal Biotech Announces Positive Topline Results from GEM-3 Pivotal Trial of VYJUVEK™ in Patients with Dystrophic Epidermolysis Bullosa

November 29, 2021

- Pivotal GEM-3 trial met its primary endpoint of complete wound healing at six-month timepoints, and its secondary endpoint of complete wound healing at three-month timepoints
- VYJUVEK™ was well tolerated, with no drug-related serious adverse events or discontinuations
- Biologics License Application (BLA) on track to be submitted to U.S. Food and Drug Administration (FDA) in 1H22
- Conference call to discuss results scheduled for today, Monday, November 29, 2021 at 8:00 a.m. EST

PITTSBURGH, Nov. 29, 2021 (GLOBE NEWSWIRE) -- [Krystal Biotech, Inc.](#), ("Krystal") (NASDAQ: KRY5), the leader in redosable gene therapies for rare diseases, today announced positive topline results from the pivotal GEM-3 trial of investigational beremagene geperpavec (B-VEC), now known as VYJUVEK™, for the treatment of dystrophic Epidermolysis Bullosa (dystrophic EB).

The primary endpoint of the trial evaluated complete wound healing of topical VYJUVEK™ compared to placebo at six-month timepoints and met statistical significance. VYJUVEK™ is the first non-invasive, topical and redosable gene therapy in development, and the only genetically corrective approach to treat dystrophic EB that has successfully completed a double blinded Phase 3 trial.

Highlights of Topline Results from the GEM-3 Trial

- 31 patients (31 primary matched-wound pairs) were enrolled and evaluable for safety and efficacy per the primary intent-to-treat (ITT) analysis
- 67% of wounds treated with VYJUVEK™ achieved the primary endpoint of investigator assessed complete wound healing at the six-month timepoints as compared to 22% of wounds treated with placebo (absolute difference (95% CI): 45.8% (23.6%-68.0%); $p < 0.005$)
- 71% of wounds treated with VYJUVEK™ achieved the secondary endpoint of investigator assessed complete wound healing at the three-month timepoints as compared to 20% of wounds treated with placebo (absolute difference (95% CI): 51.0% (29.3%-72.6%); $p < 0.005$)
- In an ad-hoc analysis, the trial also demonstrated a statistical difference between the active and placebo groups for wounds that demonstrated complete wound healing at both the three- and six-month timepoints ($p < 0.005$)
- VYJUVEK™ was well tolerated. No drug-related serious adverse events or discontinuations due to treatment were reported. One mild drug-related adverse event was reported during the trial.
- The immunogenicity profile of VYJUVEK™ (as measured by anti-HSV-1 and anti-COL7 antibodies) was consistent with the prior GEM-1/2 study where we observed no meaningful change in anti-HSV-1 or anti-COL7 antibodies

"Dystrophic Epidermolysis Bullosa is referred to as 'the worst disease you've never heard of' because of the incredibly devastating reality that patients with this genetic condition face, and we are thrilled to announce positive results from our pivotal GEM-3 trial of VYJUVEK™ which showed that this topical gene therapy led to durable wound healing in dystrophic EB wounds," said Suma Krishnan, Founder and Chief Operating Officer of Krystal. "With these results in hand, we look forward to advancing discussions with regulatory authorities and will work quickly to bring this potential first-ever treatment to patients with dystrophic EB and their families who are in desperate need."

"Today's positive B-VEC results represent the culmination of years of study on the molecular basis and genetic correction of this disease. Finally, dystrophic EB patients may have an easily administered genetically targeted therapy which has been shown to promote durable wound healing in this clinical trial. This is a long overdue milestone for patients living with this disease, and one that has potential to drastically change the treatment paradigm," said Dr. Peter Marinkovich, M.D., Bullous Disease Clinic Director and Associate Professor of Dermatology at Stanford University.

Next Steps

Based on these results, Krystal intends to file a Biologics License Application (BLA) with the U.S. Food and Drug Administration (FDA) in the first half of 2022 as the first step in executing its global regulatory and commercialization strategy to bring this investigational therapy to patients in need. The Company expects to submit a Marketing Authorization Application (MAA) in Europe shortly after the BLA. Exploration of the potential regulatory path forward in other geographies, including Japan, is underway. Krystal will continue to manufacture VYJUVEK™ using the commercial scale process at its in-house cGMP manufacturing facility, ANCORIS, which was designed to support potential launch. The Company is currently constructing its second, larger, facility ASTRA, which is expected to come on-line in 2022 to help support a potential global launch and the pipeline.

"We founded Krystal less than six years ago with the goal of developing a non-invasive, genetically corrective therapy for dystrophic EB. We offer our deepest gratitude to the patients, caregivers, investigators, and of course to the broader Krystal team who worked tirelessly to help us reach this exciting moment in the progression of the VYJUVEK™ program," said Krish Krishnan, Chairman and CEO of Krystal. "These pivotal data provide important validation of our redosable gene delivery technology, emboldening us to expand our pipeline to address other genetic skin diseases, continue to explore the potential in genetic lung diseases, and invest in growing the platform capability to address new organ systems as well."

Investor Conference Call, Webcast and Presentation Information

Krystal will host an investor conference call and webcast today, Monday, November 29, at 8:00 a.m. ET, to discuss topline results from the pivotal GEM-3 trial and the VYJUVEK™ program. To participate in the conference call, please dial 1-877-407-4018 (domestic) or 1-201-689-8471 (international) and refer to conference ID 13725260. The webcast, which will include presentation slides, will be available live and for replay on Krystal's website at www.krystalbio.com in the Investors section.

About the GEM-3 Trial

The GEM-3 trial (NCT04491604) was a randomized, double-blind, intra-patient placebo-controlled study designed to evaluate the efficacy and safety of VYJUVEK™ for the treatment of dystrophic EB. Thirty-one (31) patients were enrolled across three sites and ranged in ages from one (1) year to forty-four (44) years old.

In each patient, a primary wound pair was identified by the investigator; one wound was randomized to receive a weekly topical application of VYJUVEK™ and the other to receive placebo. Wounds were dosed once-weekly with either VYJUVEK™ or placebo until closure. Weekly application was resumed if wounds re-opened at any point in the study.

The primary outcome measure was complete wound healing determined by the Investigator in VYJUVEK™ treated wounds versus placebo treated at the six-month timepoints, meaning week 22 and Week 24 *or* Week 24 and Week 26. Secondary endpoints included investigator assessed complete wound healing at the three-month timepoints, meaning weeks 8 and 10 *or* 10 and 12 and mean change in pain severity using either a VAS or FLACC-R Scale at weeks 22, 24 and 26.

In addition to the primary target wound pair(s), additional wounds (secondary wounds) were selected and treated with VYJUVEK™ giving the treating physicians and patients flexibility to treat multiple wounds during the weekly application. For more information about the pivotal GEM-3 study, visit www.clinicaltrials.gov (NCT04491604).

Subjects returned to the clinical site 30 days following the last dosing visit (Week 26) for safety evaluation by the investigator and subsequently had the option to roll into the Open Label Extension (OLE) Study (NCT04917874). In addition, new participants who were unable to participate in the Phase 3 study but met all enrollment criteria are eligible to enroll in the OLE.

About Dystrophic EB (DEB)

DEB is a rare and severe monogenic disease that affects the skin and mucosal tissues. It is caused by one or more mutations in a gene called *COL7A1*, which is responsible for the formation of the protein type VII collagen protein (COL7) that forms anchoring fibrils that bind the dermis (inner layer of the skin) to the epidermis (outer layer of the skin). The lack of functional anchoring fibrils leads to extremely fragile skin that blisters and tears from minor friction or trauma. DEB patients suffer from open wounds, which leads to skin infections, fibrosis which can cause fusion of fingers and toes, and ultimately an increased risk of developing squamous cell carcinoma, which in severe cases can be fatal.

About VYJUVEK™

VYJUVEK™ is an investigational non-invasive, topical gene therapy designed to deliver two copies of the *COL7A1* gene when applied directly to DEB wounds. Unlike the current standard of care, VYJUVEK™ was designed to treat DEB at the molecular level by providing the patient's skin cells the template to make normal COL7 protein, thereby addressing the fundamental disease-causing mechanism.

The FDA and the EMA have each granted VYJUVEK™ orphan drug designation for the treatment of DEB, and the FDA has granted VYJUVEK™ 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 VYJUVEK™ for the treatment of DEB and the EMA granted PRiority MEDicines ("PRIME"), eligibility for VYJUVEK™ to treat DEB.

About Krystal Biotech

Krystal Biotech, Inc. (NASDAQ:KRY5) 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>, and follow @KrystalBiotech on [LinkedIn](https://www.linkedin.com/company/krystalbiotech) and [Twitter](https://twitter.com/KrystalBiotech).

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 clinical trials of VYJUVEK™; the clinical utility of VYJUVEK™, and Krystal's plans for filing of regulatory approvals and efforts to bring VYJUVEK™ to market; plans to pursue research and development of other product candidates; 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 VYJUVEK™, 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:

Investor Contact

Whitney Ijem
Krystal Biotech
wijem@krystalbio.com

Media Contact

Julie Normart
Real Chemistry
jnormart@realchemistry.com



Source: Krystal Biotech, Inc.