



uniQure Announces FDA Acceptance of Biologics License Application for Etranacogene Dezaparvovec under Priority Review

May 24, 2022

If approved, etranacogene dezaparvovec would be the first gene therapy option for people living with hemophilia B

LEXINGTON, Mass. and AMSTERDAM, May 24, 2022 (GLOBE NEWSWIRE) -- [uniQure N.V.](#) (NASDAQ: QURE), a leading gene therapy company advancing transformative therapies for patients with severe medical needs, today announced that the U.S. Food and Drug Administration (FDA) has accepted for priority review the Biologics License Application (BLA) submitted by CSL Behring for etranacogene dezaparvovec, an investigational gene therapy for the treatment of adults with hemophilia B.

CSL Behring is uniQure's global commercialization partner for etranacogene dezaparvovec and is solely responsible for all regulatory activities, including filings and agency interactions, associated with etranacogene dezaparvovec.

uniQure led the multi-year clinical development of etranacogene dezaparvovec, including the pivotal Phase III HOPE-B clinical trial, and the company will be responsible for the global commercial supply of etranacogene dezaparvovec.

"Etranacogene dezaparvovec has the potential to be the first gene therapy approved in hemophilia B and the acceptance of the BLA marks an important milestone in uniQure's mission of delivering the promise of gene therapy to people living with rare diseases," stated Matt Kapusta, chief executive officer of uniQure. "uniQure has been a leader in gene therapy for nearly 25 years and, if approved, etranacogene dezaparvovec would represent our second gene therapy to complete its journey to patients. We are proud of this accomplishment, which is a culmination of significant contributions from all our employees, clinical investigators and the hemophilia community. We are pleased with the promising results generated from our HOPE-B pivotal study, the largest gene therapy trial in hemophilia B to date and, assuming FDA approval, we look forward to partnering with our colleagues at CSL Behring to bring this life-changing treatment option to people with hemophilia B."

Etranacogene dezaparvovec was specifically designed to make near-normal blood-clotting ability possible by addressing the underlying cause of hemophilia B: a faulty gene that causes a deficiency in clotting Factor IX (FIX). Etranacogene dezaparvovec has been shown in clinical trials to significantly reduce the rate of annual bleeds in trial participants after a single one-time infusion and, if approved, would be the first ever gene therapy treatment option for the hemophilia B community.

The BLA is supported by results from the pivotal HOPE-B trial, which demonstrated in trial participants a reduction in adjusted annualized bleeding rate (ABR) of 64% and superiority to prophylaxis treatment at 18 months post-treatment compared to a 6-month run in period ($p=0.0002$).

Priority review of a BLA is reserved for medicines that, if approved, would be potentially significant improvements in the safety or effectiveness of the treatment, diagnosis, or prevention of serious conditions when compared to standard applications. Upon acceptance for priority review, the FDA goal is to take action on the BLA in 6 months as compared to 10 months for standard review. Previously, the [European Medicines Agency \(EMA\) accepted the Marketing Authorization Application \(MAA\) for etranacogene dezaparvovec](#) under its accelerated assessment procedure.

About Hemophilia B

Hemophilia B is a life-threatening degenerative disease. People with the condition are particularly vulnerable to bleeds in their joints, muscles, and internal organs, leading to pain, swelling, and joint damage. Current treatment includes life-long prophylactic infusions of FIX to temporarily replace or supplement low levels of the blood-clotting factor.

About Gene Therapy in Hemophilia B

Gene therapy has the potential to enable more normal clotting in patients with hemophilia B. Gene therapy achieves this with modified non-infectious viruses that serve as "vectors" that can enter certain cells. Vectors carry genetic instructions to specific cells. Once delivered, the new genetic instructions allow the cellular machinery to produce their own stable levels of FIX. A certain type of vector, called an adeno-associated virus, or AAV, dissolves after delivering its genetic instructions. These genetic instructions remain in the target cells, but never actually become a part of a person's own DNA.

About Etranacogene Dezaparvovec

Etranacogene dezaparvovec (also known as CSL222, previously known as AMT-061) uses a specific type of AAV, called AAV5, as its vector. The AAV5 vector carries the Padua gene variant of FIX (FIX-Padua), which generates FIX proteins that are 5x-8x more active than normal. Preclinical and clinical data show that AAV5-based gene therapies may be clinically effective in a large percentage of hemophilia B patients with pre-existing antibodies to AAV vectors, thereby potentially increasing patient eligibility for treatment.

About the Pivotal HOPE-B Trial

The pivotal Phase III HOPE-B trial is a multinational, open-label, single-arm study to evaluate the safety and efficacy of etranacogene dezaparvovec. Fifty-four adult hemophilia B patients requiring prophylactic FIX replacement therapy were enrolled in a prospective, six-month observational period during which time they continued to use their current standard of care therapy to establish a baseline Annual Bleeding Rate (ABR). After the six-month lead-in period, patients received a single intravenous administration of etranacogene dezaparvovec at the 2×10^{13} gc/kg dose. Patients were not excluded from the trial based on pre-existing neutralizing antibodies (NAbs) to AAV5. A total of 54 patients received a single dose of etranacogene dezaparvovec in the pivotal trial, with 53 patients completing at least 18 months of follow-up. The primary endpoint in the pivotal HOPE-B study was 52-week ABR after achievement of stable FIX expression compared with the six-month lead-in period. For this endpoint, ABR was measured from month seven to month 18 after infusion, ensuring the observation period represented a steady-state FIX transgene expression. Secondary endpoints included assessment of FIX activity and statistical superiority of ABR after dosing.

Results from the pivotal HOPE-B study demonstrated that etranacogene dezaparvovec produced mean FIX activity of 39.0 IU/dL at six months and 36.9 IU/dL at 18 months post infusion. After the six-month lead-in period post-infusion, the adjusted annualized bleeding rate (ABR) for all bleeds was reduced by 64 percent (4.19 to 1.51 p=0.0002) and all FIX-treated bleeds was reduced by 77 percent (3.65 to 0.83; p<0.0001) over months seven to 18. In addition, 98 percent of subjects treated with a full dose of etranacogene dezaparvovec discontinued use of prophylaxis, with an overall 97 percent reduction in mean unadjusted annualized FIX consumption of 257338.8 IU/yr/participant to 8486.6 IU/yr/participant (from lead-in period to months 13-18).

Etranacogene dezaparvovec was generally well-tolerated with the majority of adverse events (80.4 percent) considered mild. One death resulting from urosepsis and cardiogenic shock in a 77-year-old patient at 65 weeks following dosing was considered unrelated to treatment by investigators and the company sponsor. A serious adverse event of hepatocellular carcinoma was determined to be unrelated to treatment with etranacogene dezaparvovec by independent molecular tumor characterization and vector integration analysis. No inhibitors to FIX were reported.

About uniQure

uniQure is delivering on the promise of gene therapy – single treatments with potentially curative results. We are leveraging our modular and validated technology platform to rapidly advance a [pipeline](#) of proprietary gene therapies to treat patients with hemophilia B, Huntington's disease, refractory temporal lobe epilepsy, Fabry disease, and other diseases. www.uniQure.com

uniQure Forward-Looking Statements

This press release contains forward-looking statements. All statements other than statements of historical fact are forward-looking statements, which are often indicated by terms such as "anticipate," "believe," "could," "estimate," "expect," "goal," "intend," "look forward to," "may," "plan," "potential," "predict," "project," "should," "will," "would" and similar expressions. Forward-looking statements are based on management's beliefs and assumptions and on information available to management only as of the date of this press release. These forward-looking statements include, but are not limited to, the potential timelines for and outcome of BLA review. The Company's actual results could differ materially from those anticipated in these forward-looking statements for many reasons, including, without limitation, risks associated with the impact of the ongoing COVID-19 pandemic on our Company and the wider economy and health care system, our Commercialization and License Agreement with CSL Behring, our clinical development activities, clinical results, collaboration arrangements, regulatory oversight, product commercialization and intellectual property claims, as well as the risks, uncertainties and other factors described under the heading "Risk Factors" in the Company's periodic securities filings, including its Annual Report on Form 10-K filed February 25, 2022. Given these risks, uncertainties and other factors, you should not place undue reliance on these forward-looking statements, and the Company assumes no obligation to update these forward-looking statements, even if new information becomes available in the future.

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The logo for uniQure, featuring the word "uniQure" in a bold, orange, sans-serif font. The "Q" is stylized with a dot.