



uniQure announces positive CHMP opinion for etranacogene dezaparvovec – gene therapy for adults with hemophilia B

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

LEXINGTON, Mass. and AMSTERDAM, Dec. 16, 2022 (GLOBE NEWSWIRE) -- [uniQure](#) N.V. (NASDAQ: QURE), a leading gene therapy company advancing transformative therapies for patients with severe medical needs, announced that its partner, global biotechnology leader [CSL](#) (ASX: CSL), has received a positive opinion recommending conditional marketing authorization (CMA) for etranacogene dezaparvovec from the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA). Etranacogene dezaparvovec is a one-time gene therapy for the treatment of appropriate adults with hemophilia B that reduces the rate of annual bleeds after a single infusion.^{1,2} uniQure conducted the multi-year clinical development program for etranacogene dezaparvovec and will leverage its leading gene therapy manufacturing capabilities to supply CSL for commercialization.

"We are very pleased with this positive opinion recommending conditional marketing authorization for etranacogene dezaparvovec," said [Matt Kapusta](#), chief executive officer of uniQure. "The program's multi-year clinical journey began in Europe with our first-in-human Phase I/II study, and the favorable CHMP opinion moves etranacogene dezaparvovec one step closer to the European hemophilia B community. We look forward to continuing our partnership with CSL to help bring this potentially life-changing treatment option to people with hemophilia B."

Etranacogene dezaparvovec was recently approved by the U.S. Food and Drug Administration. CSL licensed the exclusive global rights to etranacogene dezaparvovec from uniQure in May 2021, and is now solely responsible for the further development, registration, and commercialization of the therapy. uniQure is responsible for the global commercial supply of etranacogene dezaparvovec.

The positive CHMP opinion is based on findings from the pivotal HOPE-B trial, the largest gene therapy trial in hemophilia B to date.^{3,4} These findings showed that hemophilia B patients treated with etranacogene dezaparvovec demonstrated stable and durable increases in mean Factor IX (FIX) activity levels (with a mean FIX activity of 36.9%) which led to an adjusted annualized bleed rate (ABR) reduction of 64%.¹ Following infusion of etranacogene dezaparvovec, 96% of patients discontinued routine FIX prophylaxis.¹

The HOPE-B study 24 months analysis showed a sustained and durable effect of etranacogene dezaparvovec.^{5,6} In a clinical setting, etranacogene dezaparvovec continued to be generally well-tolerated with no serious treatment-related adverse events.^{5,6}

The positive opinion from the CHMP will now be reviewed by the European Commission, which has the authority to approve medicines for the European Union member states.

About Hemophilia B

Hemophilia B is a life-threatening rare 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 treatments for moderate to severe hemophilia B include life-long prophylactic infusions of factor IX to temporarily replace or supplement low levels of the blood-clotting factor.

About Etranacogene Dezaparvovec

Etranacogene dezaparvovec is an adeno-associated virus five (AAV5)-based gene therapy given as a one-time treatment for moderately severe to severe hemophilia B patients. 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 Factor IX (FIX-Padua), which generates FIX proteins that are 5x-8x more active than normal.

About the Pivotal HOPE-B Trial

The pivotal Phase III HOPE-B trial is an ongoing, multinational, open-label, single-arm study to evaluate the safety and efficacy of etranacogene dezaparvovec. Fifty-four adult hemophilia B patients classified as having a diagnosis of moderately severe or severe hemophilia B and 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.

Results from the pivotal HOPE-B study demonstrated that etranacogene dezaparvovec produced mean FIX activity of 36.9 IU/dL at 18 months post infusion. At 24 months follow-up, FIX activity remained stable at 36.7 IU/dL. After the six-month lead-in period post-infusion, the adjusted annualized bleeding rate (ABR) (1.51) for all bleeds was reduced by 64 percent ($p=0.0002$) and all FIX-treated bleeds was reduced by 77 percent (3.65 to 0.83; $p<0.0001$) over months seven to 18. 96 percent of subjects treated with a full dose of etranacogene dezaparvovec discontinued use of routine 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).

Further analyses showed that there was no clinically meaningful correlation between patient AAV5 NAb levels at baseline and FIX activity.

No serious adverse reactions were reported. 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," "establish," "estimate," "expect," "goal," "intend," "look forward to," "may," "plan," "potential," "predict," "project," "seek," "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, statements about whether etranacogene dezaparvovec will be approved in Europe, whether we are able to bring etranacogene dezaparvovec to people living with hemophilia B, and whether the treatment will be life-changing. 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 postponement in our clinical trial for Huntington's disease, the impact of financial and geopolitical events 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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¹ Miesbach W et al. Oral presentation at 15th EAHAD meeting, February 2022

² Summary of Product Characteristics: etranacogene dezaparvovec. Data on file.

³ ASH Clinical News. New HOPE for Hemophilia B: One-Time Gene Therapy Abolishes Bleeding in Most Patients. Available at: <https://ashpublications.org/ashclinicalnews/news/5441/New-HOPE-for-Hemophilia-B-One-Time-Gene-Therapy>. [Accessed December 2022]

⁴ [ClinicalTrials.gov](https://clinicaltrials.gov). HOPE-B: Trial of AMT-061 in Severe or Moderately Severe Hemophilia B Patients. Available at: <https://clinicaltrials.gov/ct2/show/NCT03569891>. [Accessed December 2022]

⁵ Miesbach W et al. Poster presentation at ASH meeting, December 2022

⁶ Pipe S et al. Poster presentation at ASH meeting, December 2022

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