



uniQure announces the European Commission approval of the first gene therapy for adults with hemophilia B

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~ Historic approval represents the first gene therapy in Europe to treat hemophilia B and provides a new treatment option for patients that reduces the rate of annual bleeds, reduces or eliminates the need for prophylactic therapy, and generates elevated and sustained factor IX levels ~

~ Approval marks uniQure's second internally-developed and manufactured gene therapy to achieve licensure in the European Union ~

LEXINGTON, Mass. and AMSTERDAM, Feb. 21, 2023 (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 conditional marketing authorization (CMA) from the European Commission for HEMGENIX® (etranacogene dezaparvovec), the first and only one-time gene therapy for the treatment of severe and moderately severe hemophilia B.

HEMGENIX is approved for the treatment of adults with severe and moderately severe hemophilia B (congenital Factor IX deficiency) in adult patients without a history of Factor IX inhibitors. It is the first approved gene therapy for hemophilia B in the European Union (EU) and European Economic Area (EEA).

"The European approval of HEMGENIX represents another major milestone in the field of genomic medicine and innovation in the treatment of people living with hemophilia B," said [Matt Kapusta](#), chief executive officer of uniQure. "This achievement is based on more than a decade of research and clinical development led by uniQure, and we are grateful for the tireless dedication of our employees, clinicians, patients and their families who made this possible."

[Hemophilia B](#) is a rare, lifelong bleeding disorder caused by a single gene defect, resulting in insufficient production of factor IX, a protein primarily produced by the liver that helps blood clots form. Treatments for moderate to severe hemophilia B include prophylactic infusions of factor IX replacement therapy to temporarily replace or supplement low levels of blood-clotting factor and, while these therapies are effective, those with hemophilia B must adhere to strict, lifelong infusion schedules. They may also still experience spontaneous bleeding episodes as well as limited mobility, joint damage or severe pain as a result of the disease. For appropriate patients, HEMGENIX has been shown in clinical trials to allow people living with hemophilia B to produce their own factor IX, which can lower the risk of bleeding.

"The approval of HEMGENIX in Europe is the essence of great science delivering a medicine that we believe can transform the treatment paradigm for both people living with hemophilia B and the healthcare professionals who treat them," said Dr. Bill Mezzanotte, head of research & development and chief medical officer, CSL. "HEMGENIX, and our partnership with uniQure, underscore CSL's promise to pursue, develop and deliver disruptive innovations when patients can benefit, particularly in disease states we know well like hemophilia B."

The European Commission's decision follows the CHMP's positive opinion in December 2022, based on findings from the pivotal HOPE-B trial, the largest gene therapy trial in hemophilia B to date. These findings showed that hemophilia B patients treated with HEMGENIX demonstrated stable and durable increases in mean Factor IX activity levels (with a mean Factor IX activity of 36.9%) which led to an adjusted annualized bleed rate (ABR) reduction of 64%. Following infusion, 96% of patients discontinued routine Factor IX prophylaxis and mean Factor IX consumption was reduced by 97% at 18 months post-treatment, compared to the lead-in period.

The HOPE-B study 24-month analysis continued to show a sustained and durable effect of HEMGENIX. In a clinical setting, the treatment is generally well-tolerated with no serious treatment-related adverse events.

uniQure conducted the research and clinical development for the product, which included three clinical trials across 34 global sites and involving 67 adults with hemophilia B. In May 2021, uniQure and CSL completed a licensing transaction providing CSL Behring with exclusive rights to commercialize and continue clinical development of HEMGENIX globally. uniQure is responsible for the global [manufacturing](#) of the product at its licensed Lexington, Massachusetts facility. Under the terms of the agreement, uniQure has received payments from CSL totaling approximately \$500 million and is eligible to receive up to an additional \$1.5 billion in commercial milestone payments and tiered, double-digit royalties in a range up to a low-twenties percentage of net product sales arising from the collaboration.

"This approval marks an important step forward in the treatment of hemophilia B, which could be transformative for people who are debilitated by bleeds into their muscles, joints and internal organs, alleviating the burden of lifelong intravenous infusions of Factor IX products," said Professor Wolfgang Miesbach, head of coagulation disorders at the Comprehensive Care Center, University Hospital of Frankfurt. "Data from the HOPE-B study demonstrate the potential of HEMGENIX to remove the need for routine prophylaxis, by providing durable Factor IX activity, as well as improved bleeding outcomes and quality of life for people with hemophilia B."

The multi-year clinical development of HEMGENIX was led by uniQure and sponsorship of the clinical trials transitioned to CSL after it licensed global rights to commercialize the treatment. In the United Kingdom, The Medicines and Healthcare products Regulatory Agency is currently reviewing CSL's submission for HEMGENIX. HEMGENIX was approved by the U.S. Food and Drug Administration in November 2022. Product information on HEMGENIX, including its prescribing information, will be provided by CSL Behring.

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 HEMGENIX

HEMGENIX is a gene therapy that reduces the rate of abnormal bleeding in eligible people with hemophilia B by enabling the body to continuously produce factor IX, the deficient protein in hemophilia B. It uses AAV5, a non-infectious viral vector, called an adeno-associated virus (AAV). The AAV5 vector carries the Padua gene variant of Factor IX (FIX-Padua) to the target cells in the liver, generating factor IX proteins that are 5x-8x more active than normal. These genetic instructions remain in the target cells, but generally do not become a part of a person's own DNA. Once delivered, the new genetic instructions allow the cellular machinery to produce stable levels of factor IX.

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 HEMGENIX. Fifty-four adult hemophilia B patients classified as having a diagnosis of moderately severe or severe hemophilia B and requiring prophylactic Factor IX 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 HEMGENIX® at the 2×10^{13} gc/kg dose. Patients with pre-existing neutralizing antibodies (NAbs) to AAV5 were not excluded from the trial. A total of 54 patients received a single dose of HEMGENIX 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 Factor IX 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 Factor IX transgene expression.

Results from the pivotal HOPE-B study demonstrated that HEMGENIX produced mean Factor IX activity of 36.9 IU/dL at 18 months post infusion. At 24 months follow-up, Factor IX 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 Factor IX-treated bleeds was reduced by 77 percent (3.65 to 0.83; $p<0.0001$) over months seven to 18. From day 21 through to months 7 to 24, 52 of 54 (96.3%) treated patients remained free of continuous routine Factor IX prophylaxis. The mean consumption of Factor IX replacement therapy significantly decreased by 248,392.6 IU/year/patient (96.52%; 1-sided $p<0.0001$) between month 7 to 24 following treatment with HEMGENIX® compared to standard of care routine Factor IX prophylaxis during the lead-in period.

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

No serious adverse reactions were identified. One death resulting from urosepsis and cardiogenic shock in a 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 HEMGENIX® by independent molecular tumor characterization and vector integration analysis. No inhibitors to Factor IX were reported.

About uniQure

uniQure is delivering on the promise of gene therapy – single treatments with potentially curative results. The recent approval of our gene therapy for hemophilia B – an historic achievement based on more than a decade of research and clinical development – represents a major milestone in the field of genomic medicine and ushers in a new treatment approach for patients living with hemophilia. We are now leveraging our modular and validated technology platform to advance a [pipeline](#) of proprietary gene therapies for the treatment of patients with Huntington's disease, refractory temporal lobe epilepsy, ALS, Fabry disease, and other severe 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 we are able to bring AMT-061 to people living with hemophilia B and whether the treatment will be transformational. 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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