NEWS RELEASE

# First Gene Therapy for Hemophilia B, CSL's HEMGENIX®, Approved by the European Commission

*HEMGENIX® underscores CSL's promise to deliver life-changing innovations that have the potential to help patients lead full lives*

**MARBURG, GERMANY – February 20, 2023** – Global biotechnology leader CSL (ASX: CSL) today announced that the European Commission has granted conditional marketing authorization (CMA) for HEMGENIX® (etranacogene dezaparvovec), the first and only one-time gene therapy for the treatment of severe and moderately severe hemophilia B (congenital Factor IX deficiency) in adults without a history of Factor IX inhibitors. In the ongoing clinical trial, HEMGENIX® reduced the rate of annual bleeds with a single infusion by delivering a functional gene that acts as a blueprint for coagulation Factor IX, a protein important for blood clotting.[1] It is the first approved gene therapy for hemophilia B in the European Union (EU) and European Economic Area (EEA).

"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."

People living with hemophilia B currently require lifelong treatment of intravenous infusions of Factor IX to maintain sufficient levels, which can have a significant impact on their quality of life and wellbeing.[2] According to the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP), there is 'an unmet medical need for new therapeutic approaches that might free patients from the burden of frequent infusions, or episodically at the time of a bleeding event'.[3]

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.[4,5] 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%.[1] Following infusion of

HEMGENIX®, 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.[1]

The HOPE-B study 24-month analysis continued to show a sustained and durable effect of HEMGENIX®.[6] In a clinical setting, the treatment is generally well-tolerated with no serious treatment-related adverse events.[5]

“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.”

“At CSL Behring, our promise is simple – to save and improve lives – and we achieve this by living our core values of patient focus, innovation, integrity, collaboration, and superior performance,” commented Lutz Bonacker, Senior Vice President and General Manager of Commercial Operations Europe, CSL Behring. “The approval of HEMGENIX® in Europe is a result of that focus and a milestone for the hemophilia B community, and we now need to work to ensure that as many eligible patients across Europe can access this innovative treatment as possible. We are fully committed to working together with payers and other stakeholders to achieve this.”

The European Commission has the authority to approve medicines for EU Member States, as well as well as in the EEA countries of Iceland, Norway and Liechtenstein.

The multi-year clinical development of HEMGENIX® was led by uniQure (Nasdaq: QURE) 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 (MHRA) is currently reviewing CSL’s submission for HEMGENIX®. HEMGENIX® was approved by the U.S. Food and Drug Administration in November 2022.

## 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 an adeno-associated virus five (AAV5)-based gene therapy given as a one-time treatment for moderately severe to severe hemophilia B patients. HEMGENIX® (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 naturally occurring Padua gene variant of Factor IX (Factor IX-Padua), which generates Factor IX 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 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 2x10^13 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 CSL**

CSL Limited (ASX: CSL; USOTC: CSLLY) is a leading global biotechnology company with a dynamic portfolio of lifesaving medicines, including those that treat hemophilia and immune deficiencies, as well as vaccines to prevent influenza. Since our start in 1916, we have been driven by our promise to save lives using the latest technologies. Today, CSL – including our three businesses, CSL Behring, CSL Seqirus, and CSL Vifor – provides lifesaving products to patients in more than 100 countries and employs 30,000 people. Our unique combination of commercial strength, R&D focus, and operational excellence enables us to identify, develop and deliver innovations so our patients can live life to the fullest. For inspiring stories about the promise of biotechnology, visit CSLBehring.com/Vita and follow us on Twitter.com/CSL.
For more information visit www.csl.com.

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**References**

1. Miesbach W *et al.* Oral presentation at 15th EAHAD meeting, February 2022.
2. Srivastava A *et al*. WFH Guidelines for the Management of Hemophilia, 3rd edition. Haemophilia 2020; 26(Suppl 6):1-158.
3. European Medicines Agency. First Gene therapy to treat haemophilia B. Available at: https://www.ema.europa.eu/en/news/first-gene-therapy-treat-haemophilia-b. [Accessed February 2023].
4. European Medicines Agency. HEMGENIX Summary of Positive Opinion. Available at https://www.ema.europa.eu/en/medicines/human/summaries-opinion/hemgenix [Accessed February 2023].
5. 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 February 2023].
6. Coppens *et al.*, EAHAD 2023 16th Annual Congress, Latest Clinical Trial Results Session 5, February 2023.