uniQure Announces HOPE-B Clinical Trial Data Published in the New England Journal of Medicine, Demonstrating Durability and Other Benefits of HEMGENIX® (etranacogene dezaparvovec-drlb)

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~ Data follow the historic approval of the first gene therapy for hemophilia B, which has been shown in clinical trials to reduce the rate of annual bleeds, reduce or eliminate the need for prophylactic therapy and generate elevated and sustained factor IX levels for years after a one-time infusion ~

~ 18-month data support the ongoing benefit of HEMGENIX® ~

~ HEMGENIX® is approved for adults with hemophilia B in the United States, European Union and European Economic Area ~

LEXINGTON, Mass. and AMSTERDAM, Feb. 23, 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) today announced the publication in the New England Journal of Medicine (NEJM) (Vol. 388 No. 8) of results from the pivotal HOPE-B clinical study evaluating the efficacy, durability and safety of HEMGENIX® (etranacogene dezaparvovec-drlb). HEMGENIX® is the first and only gene therapy approved for the treatment of adults with hemophilia B who currently use factor IX prophylaxis therapy, or have current or historical life-threatening bleeding, or have repeated, serious spontaneous bleeding episodes.

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. HEMGENIX® was approved in November 2022 by the U.S. Food and Drug Administration (FDA), and in February 2023 by the European Commission (EC) for the European Union.

Results from the HOPE-B trial, the largest gene therapy study in hemophilia B to date, were considered by the authors to demonstrate that HEMGENIX® is superior to routine factor IX prophylaxis in Annualized Bleeding Rate (ABR), factor IX activity, factor IX therapy consumption, factor IX infusion rate, and spontaneous and joint bleeding ABR. Increased factor IX activity was also apparent from week 3 and maintained over 18 months. There were no reported serious adverse events related to treatment with HEMGENIX®.

Notably, the results published in NEJM show the ABR of spontaneous bleeding episodes and all joint bleeding episodes decreased by 71% (95% CI: 0.12, 0.71) and 78% (95% CI: 0.10, 0.46), respectively, from lead-in period to post-treatment. Further, 96.3% of patients discontinued factor IX prophylaxis from day 21 through month 18 post-treatment. Annualized factor IX infusions also significantly decreased from 72.5 infusions per participant during lead-in period (95% CI: 63.6, 82.7) to 2.5 infusions (95% CI: 0.92, 6.96) post-treatment.

The most common adverse reactions (incidence ≥5%) were elevated ALT, headache, blood creatine kinase elevations, flu-like symptoms, infusion-related reactions, fatigue, malaise and elevated AST.

“The results published in NEJM add to the established body of evidence demonstrating the long-term efficacy and safety of HEMGENIX® and confirm that this innovative new medicine not only restores blood clotting factor to near normal levels and significantly reduces factor use, but also that gene therapy may reduce the burden of care and improve quality of life for people living with this life-long condition,” said Dr. Steven Pipe, Professor and the Laurence A. Boxer Research Professor of Pediatrics and Professor of Pathology at the University of Michigan and lead investigator of the HOPE-B study. “HOPE-B was also the first and only phase 3 study to demonstrate efficacy of a gene therapy for hemophilia B in individuals with circulating neutralizing antibodies that have the potential to interfere with the effects of treatment. Results from HOPE-B suggest that HEMGENIX® may be effective in a broad range of hemophilia B patients, regardless of prior exposure to common adeno-associated viruses.”

“We at uniQure are incredibly pleased to have the clinical results from the global HOPE-B pivotal trial featured in such a prominent peer-reviewed journal,” said Ricardo Dolmetsch, Ph.D., president of research and development at uniQure. “These results highlight the potential benefits of this novel gene therapy approach and further reinforce that those treated with HEMGENIX® in clinical trials have achieved durable factor IX activity levels and remained free of prophylactic factor IX replacement for years following a single administration. uniQure is immensely proud to have led the multi-year clinical development program for HEMGENIX® that included the HOPE-B pivotal trial.”

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.

HEMGENIX® is a registered trademark of CSL Behring.

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 moderately severe to severe hemophilia B and requiring prophylactic factor IX replacement therapy were enrolled in a prospective, six-month or longer 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 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 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 ABR 52 weeks after achievement of stable factor IX expression (months 7 to 18) 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. Secondary endpoints included assessment of factor IX activity.

No serious treatment-related 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 HEMGENIX® by independent molecular tumor characterization and vector integration analysis. No inhibitors to factor IX were reported.

Long-term 24-month data presented at the 54th American Society of Hematology (ASH) 2022 Annual Meeting and Exposition and at The European Association for Haemophilia and Allied Disorders (EAHAD) 2023 Annual Meeting continue to reinforce the potential long-lasting efficacy and safety of HEMGENIX® and the ongoing benefit of this treatment for people living with hemophilia B.

Important Safety Information (ISI)

What is HEMGENIX®?
HEMGENIX®, etranacogene dezaparvovec-drlb, is a one-time gene therapy for the treatment of adults with hemophilia B who:

- Currently use Factor IX prophylaxis therapy, or
- Have current or historical life-threatening bleeding, or
- Have repeated, serious spontaneous bleeding episodes.

HEMGENIX® is administered as a single intravenous infusion and can be administered only once.

What medical testing can I expect to be given before and after administration of HEMGENIX®?
To determine your eligibility to receive HEMGENIX®, you will be tested for Factor IX inhibitors. If this test result is positive, a retest will be performed 2 weeks later. If both tests are positive for Factor IX inhibitors, your doctor will not administer HEMGENIX® to you. If, after administration of HEMGENIX®, increased Factor IX activity is not achieved, or bleeding is not controlled, a post-dose test for Factor IX inhibitors will be performed.

HEMGENIX® may lead to elevations of liver enzymes in the blood; therefore, ultrasound and other testing will be performed to check on liver health before HEMGENIX® can be administered. Following administration of HEMGENIX®, your doctor will monitor your liver enzyme levels weekly for at least 3 months. If you have preexisting risk factors for liver cancer, regular liver health testing will continue for 5 years post-administration. Treatment for elevated liver enzymes could include corticosteroids.

What were the most common side effects of HEMGENIX® in clinical trials?
In clinical trials for HEMGENIX®, the most common side effects reported in more than 5% of patients were liver enzyme elevations, headache, elevated levels of a certain blood enzyme, flu-like symptoms, infusion-related reactions, fatigue, nausea, and feeling unwell. These are not the only side effects possible. Tell your healthcare provider about any side effect you may experience.

What should I watch for during infusion with HEMGENIX®?
Your doctor will monitor you for infusion-related reactions during administration of HEMGENIX®, as well as for at least 3 hours after the infusion is complete. Symptoms may include chest tightness, headaches, abdominal pain, lightheadedness, flu-like symptoms, shivering, flushing, rash, and elevated blood pressure. If an infusion-related reaction occurs, the doctor may slow or stop the HEMGENIX® infusion, resuming at a lower infusion rate once symptoms resolve.

What should I avoid after receiving HEMGENIX®?
Small amounts of HEMGENIX® may be present in your blood, semen, and other excreted/secreted materials, and it is not known how long this continues. You should not donate blood, organs, tissues, or cells for transplantation after receiving HEMGENIX®.

Please see full prescribing information for HEMGENIX®.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

You can also report side effects to CSL Behring's Pharmacovigilance Department at 1-866-915-6958.

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 HEMGENIX® may be effective for people living with hemophilia B. 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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