uniQure Announces Positive 52-Week Clinical Data from HOPE-B Pivotal Trial of Etranacogene Dezaparvovec Gene Therapy in Patients with Hemophilia B and Provides Regulatory Update

June 22, 2021

~ Sustained increases in Factor IX (FIX) levels with mean FIX activity of 41.5 percent of normal in full study population one year following a single administration of etranacogene dezaparvovec ~

~ Held pre-BLA submission meeting with FDA and aligned on primary endpoint analysis ~

LEXINGTON, Mass. and AMSTERDAM, June 22, 2021 (GLOBE NEWSWIRE) -- uniQure N.V. (NASDAQ: QURE), a leading gene therapy company advancing transformative therapies for patients with severe medical needs, today announced positive 52-week clinical data on all patients from its pivotal, Phase III HOPE-B gene therapy trial of etranacogene dezaparvovec, an investigational adeno-associated virus five (AAV5)-based gene therapy for the treatment of patients with severe and moderately severe hemophilia B. These are the first clinical data to be reported from a Phase III gene therapy study in hemophilia B and, with 54 patients, the largest set of hemophilia B patients receiving a single gene therapy investigational product to date.

Data from the HOPE-B pivotal study showed that participants continued to demonstrate durable, sustained increases in Factor IX (FIX) activity at 52-weeks post-infusion with a mean FIX activity of 41.5 percent of normal, as measured by a one-stage APTT-based clotting assay, compared to a mean FIX activity of 39.0 percent of normal at 26-weeks of follow-up. There continued to be no clinically significant correlation between pre-existing neutralizing antibodies to AAV5 (NAbs) and FIX activity in patients with NAb titers up to 678.2, a range expected to include more than 93 percent of the general population.

During the 52-week period, a single dose of etranacogene dezaparvovec significantly reduced the annualized rate of bleeding requiring treatment by 80 percent from a prospectively collected 3.39 at baseline to 0.68 bleeding episodes per year (p-value <0.0001). The annualized rate of spontaneous bleeding requiring treatment was also significantly reduced by 85 percent from a prospectively collected 1.16 at baseline to 0.18 bleeds per year during the 52-week period (p-value <0.0001).

Usage of FIX replacement therapy (IU/year and infusions/year) in all patients declined 96 percent during the 52-week period, with 52 of 54 patients (96 percent) successfully discontinuing their prophylactic infusions. As previously announced, of the two non-responders, one patient only received a partial dose (less than 10 percent of the dosage) due to an infusion reaction and a second patient had an unusually high pre-existing NAb titer of 3,212, which is expected in less than 1 percent of the general population.

Etranacogene dezaparvovec continues to be generally well-tolerated with no treatment-related serious adverse events. No inhibitors to FIX have been reported and no consistent relationship between safety and pre-existing NAb titers has been observed.

“We continue to be very encouraged by the data generated from the HOPE-B pivotal study of etranacogene dezaparvovec, which have been accepted for presentation at the annual International Society on Thrombosis and Haemostasis congress taking place next month,” stated Ricardo Dolmetch, Ph.D., president of research and development at uniQure. “The 52-week data show mean FIX activity in the normal range and increase our confidence in the potential durability and long-term benefits of etranacogene dezaparvovec, bringing us one step closer to our goal of delivering this groundbreaking therapy to fulfill an unmet medical need for patients living with hemophilia B.”

Regulatory Update

The Company and its partner, CSL Behring, have had recent communications with U.S. Food and Drug Administration (FDA), including a pre-biologics licensing application (BLA) submission meeting held on June 4, 2021. The FDA confirmed that the primary evidence of durability of effect to inform regulatory decision-making will come from patients followed for at least a 52-week period beginning when etranacogene dezaparvovec-derived FIX levels have achieved steady state, rather than when etranacogene dezaparvovec is administered. This feedback was based upon review of statistical analysis plans, as no clinical data was provided or discussed. All patients in the HOPE-B pivotal study achieved steady-state FIX activity levels by 26-weeks after administration of etranacogene dezaparvovec. As a result, uniQure will now conduct as the sole primary endpoint a non-inferiority analysis of annualized bleeding rates (ABR) at 78 weeks after the administration (approximately 52-weeks after steady-state is achieved). The Company expects all patients to complete their 78-week follow-up visits by the end of the third quarter of 2021, and the Company and CSL Behring expect to submit the BLA in first quarter of 2022.

About the HOPE-B Pivotal Clinical 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 classified as severe or moderately severe (defined as less than or equal to 2% of normal FIX activity) 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 ABR. After the six-month lead-in period, patients received a single intravenous administration of etranacogene dezaparvovec at the 2x1013 gc/kg dose. Patients were not excluded from the trial based on their pre-existing NAbs to AAV5. Forty-three percent of patients in the study had pre-existing NAbs to AAV5 up to a maximum observed pre-dosing titer of over 3,200.

About Etranacogene Dezaparvovec

Etranacogene dezaparvovec consists of an AAV5 viral vector carrying a gene cassette with the patent-protected Padua variant of Factor IX (FIX-Padua). Etranacogene dezaparvovec has been granted Breakthrough Therapy Designation by the United States Food and Drug Administration and access to Priority Medicine (PRIME) regulatory initiative by the European Medicines Agency. uniQure and CSL Behring entered into a commercialization and license agreement providing CSL Behring exclusive global commercialization rights to etranacogene dezaparvovec. The collaboration combines uniQure’s differentiated gene therapy candidate in hemophilia B and CSL Behring’s strong global reach and commercial infrastructure in hematology in an effort to accelerate access of etranacogene dezaparvovec to hemophilia B patients around the world.

AAV5-based gene therapies have been demonstrated to be safe and well tolerated in a multitude of clinical trials, including being well-tolerated to date in six uniQure trials conducted in nearly 90 patients in hemophilia B and other indications. No patient treated in clinical trials with the uniQure’s AAV5 gene therapies

has experienced any confirmed cytotoxic T-cell-mediated immune response to the capsid. Additionally, pre-clinical and clinical data show that AAV5-based gene therapies may be viable treatments in patients with pre-existing antibodies to AAV5, thereby potentially increasing patient eligibility for treatment compared to other gene therapy product candidates.

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, Fabry disease, spinocerebellar ataxia Type 3 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, whether patients in the Hope-B pivotal trial will complete their 78-week follow-up visits by the end of the third quarter of 2021, whether CSL Behring will submit a BLA for etranacogene dezaparvovec in the first quarter of 2022, whether the clinical data proves to be meaningful for the long-term outlook for hemophilia gene therapy or etranacogene dezaparvovec, whether etranacogene dezaparvovec has the potential to provide well-tolerated, long-term clinical benefits, and whether AAV5-based gene therapies can provide clinical benefit to patients with pre-existing neutralizing antibodies. Our 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 and our collaborators' clinical development activities, clinical results, collaboration arrangements, corporate reorganizations and strategic shifts, regulatory oversight, product commercialization and intellectual property claims, as well as the risks, uncertainties and other factors described under the heading "Risk Factors" in uniQure's periodic securities filings, including is Annual Report on Form 10-K filed March 2, 2020 and Quarterly Report on Form 10-Q filed on May 10, 2021. Given these risks, uncertainties and other factors, you should not place undue reliance on these forward-looking statements, and we assume no obligation to update these forward-looking statements, even if new information becomes available in the future.

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