uniQure Announces Positive Top-Line Data from the HOPE-B Pivotal Trial of Etranacogene Dezaparvovec Gene Therapy in Patients with Hemophilia B

November 19, 2020

~ Phase III study in 54 patients met primary endpoint with mean Factor IX activity of 37% of normal at 26 weeks ~

~ Patients achieved significant increases in Factor IX activity irrespective of pre-existing neutralizing antibodies, potentially supporting broad patient access ~

~ Increases in Factor IX activity were sustained for up to 18 months with near elimination of bleeding ~

~ Mean annualized usage of FIX replacement therapy declined by 96 percent after dosing compared to the observational lead-in period ~

~ Etranacogene dezaparvovec was well-tolerated with no treatment-related serious adverse events ~

~ Data selected for late-breaker oral presentation on December 8, 2020 at the Annual Meeting of the American Society of Hematology (ASH) ~

LEXINGTON, Mass. and AMSTERDAM, Nov. 19, 2020 (GLOBE NEWSWIRE) -- uniQure N.V. (NASDAQ: QURE), a leading gene therapy company advancing transformative therapies for patients with severe medical needs, today announced positive top-line data 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. This is the first data set to be reported from a Phase III gene therapy study in hemophilia B and, with 54 patients, the largest set of patients receiving a single gene therapy investigational product to be reported to date. These clinical data were published today as a late-breaking abstract, one of only six accepted for presentation at the 62nd Annual Meeting of the American Society of Hematology (ASH) and will be featured as an oral presentation in the conference on December 8, 2020. The abstract is available here.

"We are extremely pleased that these top-line pivotal data show that a single administration of etranacogene dezaparvovec gene therapy led to sustained increases of Factor IX (FIX) to functionally-curative levels capable of eliminating the need for regular infusions to control and prevent bleeding episodes," stated Ricardo Dolmetsch, Ph.D., president of research and development at uniQure. "Most impressively, these data also demonstrate the potential to achieve clinical benefit in patients with a range of pre-existing neutralizing antibodies representative of the general population. The ability to dose a gene therapy in patients with pre-existing neutralizing antibodies has not been demonstrated for any other gene therapy and illustrates the potentially unique ability of our AAV5 platform to address the needs of a broad set of patients living with hemophilia B and other disorders."

The pivotal, Phase III HOPE-B clinical trial of etranacogene dezaparvovec is an open-label, single-dose, single-arm, multi-national trial in adult males with severe or moderately severe hemophilia. All patients required prophylactic routine FIX replacement prior to entering the clinical trial, and patients were not excluded from the trial based on pre-existing neutralizing antibodies (NAbs) to AAV5.

Patients in the HOPE-B clinical study were initially enrolled into a prospective, observational lead-in period of at least six months during which bleeding events and FIX replacement therapy usage were monitored. Fifty-four patients received a single intravenous infusion of etranacogene dezaparvovec gene therapy at $2x10^{13}$ gc/kg, including 23 patients who had pre-existing NAbs to AAV5. Patients are then evaluated to assess FIX activity determined by a one-stage assay performed at a central laboratory, annualized bleeding rates and usage of Factor IX replacement therapy. Patients will be monitored for five years to evaluate the safety of etranacogene dezaparvovec.

HOPE-B Primary Endpoint of FIX Activity at 26 Weeks Achieved, Irrespective of Pre-Existing NAbs

FIX activity in the 54 patients increased rapidly after dosing from ≤2% to a mean of 37.2 percent at 26 weeks, meeting the first primary endpoint. No correlation between pre-existing NAbs and FIX activity was found in patients with NAb titers up to 678.2, a range expected to include more than 95% of the general population; one patient with a NAb titer of 3,212.3 did not show an increase in FIX activity.

During the 26-week period after dosing, 72 percent of patients (39/54) reported no bleeding events. Fifteen patients reported a total of 21 bleeds[1]. Mean annualized usage of FIX replacement therapy, a secondary endpoint in the clinical trial, declined by 96 percent.

Etranacogene dezaparvovec was generally well-tolerated with no treatment-related serious adverse events. Most adverse events were classified as mild (81.5 percent). Most common events included transaminase elevation treated with steroids per protocol (9 pts; 17%), infusion-related reactions (7 pts; 13%), headache (7 pts; 13%) and influenza-like symptoms (7 pts; 13%). Liver enzyme elevations resolved with a tapering course of corticosteroids and FIX activity remained in the mild range in the steroid treated patients. No relationship between safety and NAbs titers was observed.

"We believe that etranacogene dezaparvovec has the potential to be a first- and best-in-class gene therapy for patients with hemophilia B," stated Matt Kapusta, chief executive officer of uniQure. "We are very pleased to have met the 26-week FIX primary endpoint and to feature these promising data at the upcoming ASH conference. Based on interactions with the FDA and EMA, we plan to incorporate FIX activity and bleeding rates at 52 weeks as additional co-primary endpoints in the study. We look forward to holding our pre-BLA meeting with the FDA and completing the last patient's 52-week follow-up visit in the first quarter of 2021."

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). uniQure holds multiple issued patents in the United States and Canada broadly covering methods of treating bleeding disorders, including hemophilia B, using AAV gene therapy with the FIX-Padua variant. 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. In June 2020, the Company and CSL Behring entered into a licensing agreement providing CSL Behring with exclusive global rights to etranacogene dezaparvovec. This licensing agreement is subject to antitrust regulatory review in the United States, Australia and the United Kingdom that is currently ongoing.

AAV5-based gene therapies have been demonstrated to be safe and well tolerated in a multitude of clinical trials, including five uniQure trials conducted in nearly 80 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.

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[1] Total bleeds include any bleeding event reported after the treatment of etranacogene dezaparvovec, including spontaneous, traumatic, and those associated with unrelated medical procedures, whether or not FIX treatment was required.

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 etranacogene dezaparvovec will be the first-in-class or best-in-class gene therapy for patients with hemophilia B, whether AAV5-based gene therapies can provide clinical benefit to patients with pre-existing neutralizing antibodies, and whether uniQure will conduct the 52-week follow-up visit of the last patient and its pre-BLA meeting with the FDA in the first quarter of 2021 or ever. Our actual results could differ materially from those anticipated in these forward-looking statements for many reasons, including, without limitation, risks associated with 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 Quarterly Report on Form 10-Q filed on October 27, 2020. 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.

uniQure Contacts

FOR INVESTORS:

Maria E. Cantor
Direct: 339-970-7536
Mobile: 617-680-9452
m.cantor@uniQure.com

Chiara Russo
Direct: 617-306-9137
Mobile: 617-306-9137
c.russo@uniQure.com

FOR MEDIA:

Tom Malone
Direct: 339-970-7558
Mobile:339-223-8541
t.malone@uniQure.com