



uniQure Announces 36 Weeks of Follow-Up Data from Phase IIb Study of AMT-061 and Long-Term Follow-Up Data for AMT-060 in Patients with Hemophilia B

July 6, 2019

~ FIX Activity Up to 54% of Normal, with Mean of 45% of Normal, at 36 Weeks
After Administration of AMT-061 in Phase IIb Study ~

~ Clinical Benefit and Tolerability of AMT-060 Maintained in All Patients
Through up to 3.5 Years of Follow-up ~

LEXINGTON, Mass. and AMSTERDAM, the Netherlands, July 06, 2019 (GLOBE NEWSWIRE) -- [uniQure N.V.](#) (NASDAQ: QURE), a leading gene therapy company advancing transformative therapies for patients with severe medical needs, today announced updated clinical data on the three patients treated in the Company's ongoing Phase IIb study of [AMT-061](#), an investigational [AAV5](#)-based gene therapy containing a patent-protected FIX-Padua variant for the treatment of patients with severe and moderately severe hemophilia B. In addition, the Company presented up to 3.5 years of follow-up data on the 10 patients in the Phase I/II trial of AMT-060, its first-generation gene therapy for the treatment of hemophilia B. These clinical data were presented on Saturday, July 6 in oral presentations at the 27th Congress of the International Society on Thrombosis and Haemostasis (ISTH), taking place in Melbourne, Australia.

AMT-061 (AAV5-Padua hFIX variant) an Enhanced Vector for Gene Transfer in Adults with Severe or Moderate-Severe Hemophilia B: Follow-Up Out to 36 Weeks

The Phase IIb study of [AMT-061](#) is an open-label, single-dose, single-arm, multi-center trial being conducted in the United States. Three patients with severe hemophilia (endogenous Factor IX (FIX) activity less than or equal to one percent) were enrolled in the study and received a single intravenous infusion of 2×10^{13} vc/kg. Prior to the administration of AMT-061, all three patients showed low levels of pre-existing neutralizing antibodies to AAV5 but were not excluded from the trial on that basis. Patients in the Phase IIb study will be followed for 52 weeks to assess FIX activity, bleeding rates and usage of FIX replacement therapy, and will be monitored for five years to evaluate the safety of AMT-061.

Featured in an oral presentation at ISTH, the 36 weeks of follow-up data show that all three patients have sustained increases in FIX levels after the one-time administration of AMT-061, with two of the three patients maintaining FIX activity in the normal range. Mean FIX activity for the three patients at 36 weeks after administration was 45% of normal, with the first patient achieving FIX activity of 54% of normal, the second patient achieving FIX activity of 30% of normal and the third patient achieving FIX activity of 51% of normal. The second and third patients had previously screen-failed and were excluded from another gene therapy study due to pre-existing neutralizing antibodies to a different AAV vector. Reported FIX activity was measured using an activated partial thromboplastin time (aPTT) assay performed at a central laboratory.

No patient in the study has experienced a material loss of FIX activity, reported any bleeding events or required any infusions of FIX replacement therapy for bleeds. One patient underwent hip surgery due to a pre-existing condition and was treated perioperatively with short-acting factor replacement. This was reported by the investigator as a serious adverse event unrelated to AMT-061.

"These updated data continue to show that a single administration of AMT-061 is well-tolerated and has the potential to increase FIX activity into the normal range for people living with hemophilia B," stated [Matt Kapusta](#), chief executive officer of uniQure. "We continue to be very pleased with these results, which as of this data report show durable increases in FIX activity with no bleeds and no requirement for infusions of FIX replacement therapy or immunosuppression. We believe AMT-061 has the potential to be a first- and best-in-class gene therapy for patients with hemophilia B, and we remain focused on our goal of completing enrollment in our ongoing [HOPE-B pivotal trial](#) by the end of this year."

Stable Expression of FIX and Maintained Reductions in Bleeding and FIX Consumption Following AMT-060 Gene Therapy with up to 3.5 Years of Follow-Up

In the ongoing Phase I/II study of AMT-060, all 10 patients continue to show long-term meaningful clinical impact, including sustained increases in FIX activity and improvements in their disease state as measured by reduced usage of FIX replacement therapy and decreased bleeding frequency. At up to 3.5 years of follow-up, AMT-060 continues to be safe and well-tolerated, with no new serious adverse events and no development of inhibitors since the last reported data.

All five patients in the second dose cohort of 2×10^{13} gc/kg continue to be free of routine FIX replacement therapy at up to 3 years after treatment. During the last 12 months of observation, the mean annualized bleeding rate was 0.7 bleeds, representing an 83% reduction to the year prior to treatment. During this same period, the usage of FIX replacement therapy declined 96% compared to the year prior to treatment. Steady-state mean yearly FIX activity at 3 years was 7.9%, as compared to 7.1% in the first year and 8.4% in the second year.

AMT-060 is uniQure's first-generation gene therapy, consisting of an AAV5 vector carrying a gene cassette with the wild-type FIX gene. Data from this Phase I/II trial of AMT-060 will be part of the regulatory submission for marketing approval of AMT-061.

"The Phase I/II study of AMT-060 continues to demonstrate the impressive long-term safety and tolerability of uniQure's gene therapy platform in hemophilia B," stated Professor Frank W.G. Leebeek, M.D., Ph.D. of the Erasmus University Medical Center in Rotterdam, the Netherlands. "We have now demonstrated evidence of durable clinical benefits, including sustained FIX activity, improved disease phenotype and substantial reductions in spontaneous bleeds for up to 3.5 years after administration. These data are very encouraging for uniQure's hemophilia B program."

About AMT-061

AMT-061 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. Additional patents are pending in the European Union.

AAV5-based gene therapies have been demonstrated to be safe and well tolerated in a multitude of clinical trials, including four uniQure trials conducted in 25 patients in hemophilia B and other indications. No patient treated in clinical trials with the Company's AAV5 gene therapies has experienced any cytotoxic T-cell-mediated immune response to the capsid. Additionally, preclinical and clinical data show that AAV5-based gene therapies may be clinically effective in patients with pre-existing antibodies to AAV5, thereby potentially increasing patient eligibility for treatment compared to other gene therapy product candidates.

About the Pivotal Phase III HOPE-B Study

The pivotal Phase III HOPE-B trial is a multinational, multi-center, open-label, single-arm study to evaluate the safety and efficacy of AMT-061. Approximately 55 adult hemophilia B patients classified as severe or moderately severe will be enrolled in a six-month observational period during which time they will continue to use their current standard of care to establish a baseline control. After the six-month lead-in period, patients will receive a single intravenous administration of AMT-061 at the 2×10^{13} gc/kg dose confirmed in the Phase IIb trial. Dosing of patients in the HOPE-B pivotal trial is now underway.

The primary endpoint of the study will be based on the FIX activity level achieved following the administration of AMT-061, and the secondary endpoints will measure annualized FIX replacement therapy usage, annualized bleed rates and safety.

Patients enrolled in the HOPE-B pivotal trial will be tested for the presence of pre-existing neutralizing antibodies to AAV5 but will not be excluded from the trial based on their titers. Previous studies performed by uniQure suggest that AAV5 gene therapies may be viable treatments for at least 97% of patients.

About the Phase I/II study of AMT-060

The Phase I/II study is an open-label, multi-center study including 10 patients each receiving a one-time, 30-minute, intravenous administration of AMT-060, without the prophylactic use of corticosteroids. The study includes two dose cohorts of five patients each, with the first cohort receiving 5×10^{12} gc/kg and the second cohort receiving 2×10^{13} gc/kg. Nine patients in the trial were classified as having severe (<1% FIX activity) hemophilia. One patient in the low-dose cohort had a moderate/severe (1.5% FIX activity) phenotype.

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 and partnered gene therapies to treat patients with hemophilia B, hemophilia A, Huntington's disease, Fabry disease, spinocerebellar ataxia Type 3 and cardiovascular 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, the completion of our Phase IIb study, the ability of AMT-061 to provide all people living with hemophilia B access to a one-time treatment capable of normalizing FIX activity or eliminating the need for replacement therapy or reducing or eliminating the risk of immune responses that require immunosuppression or that may lead to a loss of efficacy, the ability of AMT-061 to be a first-in-class or best-in-class gene therapy for patients with hemophilia B, the ability of AMT-061 to provide durable clinical benefits, including sustained FIX activity, improved disease phenotype or substantial reductions in spontaneous bleeds, our ability to complete enrollment in our ongoing HOPE-B pivotal trial by the end of this year, our ability to achieve any of our other planned near term or other milestones, the risk of cessation, delay or lack of success of any of our ongoing or planned clinical studies, and/or the development and regulatory approval of our product candidates. 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 April 29, 2019. 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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