



## uniQure Presents New Preclinical Data on AMT-130 in Huntington's Disease at CHDI's 12th Annual Huntington's Disease Therapeutics Conference

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- One-time Administration of AMT-130 Demonstrates for the First Time Efficacy in Large Animal Model
- Strong Dose-Dependent Reduction of Mutant Huntingtin Protein and Widespread Vector Distribution in Brain
- IND-enabling Toxicology Study to Commence in 2H 2017 --

LEXINGTON, Mass. and AMSTERDAM, the Netherlands, April 26, 2017 (GLOBE NEWSWIRE) -- [uniQure N.V.](#) (NASDAQ:QURE), a leading gene therapy company advancing transformative therapies for patients with severe medical needs, today presented new preclinical data on AMT-130, a gene therapy candidate for the treatment of [Huntington's disease](#) (HD), at the 12th Annual CHDI HD Therapeutics Conference in Malta.

Data from the study demonstrate widespread and effective AAV5 vector distribution and extensive silencing of the human mutant huntingtin gene (HTT) in minipigs, among the largest HD animal models available for testing. AMT-130 consists of an AAV5 vector carrying a DNA cassette encoding artificial micro-RNA (miHTT) that silences the huntingtin gene. The proof-of-concept study was performed by uniQure in collaboration with Prof. Jan Motlik, Director of the Institute of Animal Physiology and Genetics in the Czech Republic and Ralf Reilmann, Founding Director of the George Huntington Institute in Germany.

"Using AAV vectors to deliver micro-RNAs directly to the brain represents a highly innovative approach to treating Huntington's disease," stated Prof. Motlik. "This study demonstrated that a single administration of AAV5-miHTT resulted in significant reductions in HTT mRNA in all regions of the brain transduced by AMT-130, as well as in the cortex. Consistent with the reduction in HTT mRNA, we also observed a clear dose-dependent reduction in mutant huntingtin protein levels in the brain, with similar trends in the cerebral spinal fluid. Taking into account the similarities of CHDI's proprietary transgenic pig model to the human brain, these results provide additional data to support moving forward with clinical trials of uniQure's promising gene therapy for Huntington's disease."

### Preclinical Data Findings

Researchers in the study investigated the feasibility, efficacy and safety of AMT-130 in diseased animals with a larger brain size using a transgenic HD minipig model developed by Prof. Motlik and supported by the CHDI Foundation. AMT-130 was administered bilaterally into the striatum and thalamus of the minipigs using convection-enhanced, real-time MRI-guided delivery.

Three months after treatment, widespread, dose-dependent distribution of the vector was observed throughout the minipig brain that corresponded strongly with the miHTT expression. Expression of mutant HTT mRNA was significantly reduced in all regions of the brain transduced by AMT-130 by 50% to 80%, as well in the cortex by up to 40%, compared with control. Researchers also observed a dose-dependent reduction in mutant huntingtin protein levels of more than 50% in the brain, as well as similar trends in cerebral spinal fluid. Both the surgical procedure and AAV5-miHTT treatment were well tolerated with no adverse events.

"This study is an important step in our Huntington's disease gene therapy program, demonstrating for the first time in a large animal model that AAV5 can be used safely and effectively to deliver micro-RNAs to silence mutant huntingtin," stated Pavlina Konstantinova, Ph.D., director of new therapeutic target discovery at uniQure. "We are very encouraged by the significant reductions in mutant huntingtin protein, and believe that knock-down of this magnitude has the potential to significantly alter the course of the disease. The positive data from this study, together with data from our previous studies in rodent models showing strong reductions in huntingtin and prevention of neuronal dysfunction, provide strong proof of concept for AMT-130 as a potential groundbreaking treatment for patients suffering from Huntington's disease. We look forward to commencing the toxicology study in non-human primates later this year, which we expect to support an Investigational New Drug (IND) application for AMT-130 in 2018."

### **About Huntington's Disease**

Huntington's disease is a rare, inherited neurodegenerative disorder that leads to loss of muscle coordination, behavioral abnormalities and cognitive decline, resulting in complete physical and mental deterioration over a 12- to 15-year period of time. The disease is caused by an autosomal dominant mutation, a cytosine-adenine-guanine (CAG) expansion, in the first exon of the huntingtin gene leading to a non-functional, aggregation prone mutated protein. Despite the clear etiology, there are no therapies available to treat the disease, delay onset or slow progression of a patient's decline.

### **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, Huntington's disease and cardiovascular diseases. [www.uniQure.com](http://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, statements regarding the winding down of our Glybera program, the development of our other gene therapy product candidates, the success of our collaborations and the risk of cessation, delay or lack of success of any of our ongoing or planned clinical studies and/or development 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 corporate reorganizations and strategic shifts, collaboration arrangements, our and our collaborators' clinical development activities, 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 2016 Annual Report on Form 10-K filed on March 15, 2017. 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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