uniQure Announces Publication of Preclinical Data for AMT-130 in Huntington's Disease Supporting Non-Selective HTT-Lowering Approach

Lexington, MA and Amsterdam, the Netherlands, December 19, 2019 — uniQure N.V. (NASDAQ: QURE), a leading gene therapy company advancing transformative therapies for patients with severe unmet medical needs, today announced two publications of preclinical data from its gene therapy candidate AMT-130 in Huntington's disease, in the journals *Nucleic Acids Research* and *Molecular Therapy – Methods & Clinical Development*.

The first publication in *Nucleic Acids Research* examines the tolerability and efficacy of non-selective huntingtin protein (HTT) lowering using an AAV5 encoded micro-RNA targeting human HTT (AAV5-miHTT) in the humanized Hu128/21 mouse model of Huntington's disease. The Hu128/21 model represents a genetically accurate model of Huntington's disease, as it expresses both the mutant and wild type full-length human HTT transgene. The animals received bilateral intrastriatal infusions by convection-enhanced delivery of either the control dose, or three ascending doses at the onset of the disease and were evaluated for 7 months, when sacrifice occurred.

A dose-dependent suppression of full length HTT (both wild-type and mutant) was observed 7 months after a single injection of AAV5-miHTT, with reductions of 92% in the striatum and 64% in the frontal cortex. AAV5 also showed broad distribution at all time points evaluated and was clearly observed in the striatum, the hippocampus and the cortex. These data are consistent with prior studies and further demonstrate that AAV5 undergoes anterograde and retrograde axonal transport following infusion, resulting in broad transduction of the structures affected by Huntington's disease. AAV5-miHTT resulted in both cognitive and psychiatric improvements, as well as the prevention of neuronal degeneration, indicating the potential therapeutic benefit of non-selective HTT lowering. The authors concluded that the Hu128/21 model is not ideal for evaluating therapeutic changes in motor performance as a result of inherently increasing obesity in the mice that likely contributed to progressive motor deficits. The authors did cite improved motor coordination in an R6/2 mouse model that better demonstrates the characteristic weight loss associated with Huntington's disease.

Tolerability was evaluated using measures of gliosis, brain morphology, body weight and survival. Results demonstrated that non-selective knock down of HTT was safe and well tolerated in the humanized mouse model, even in the absence of background mouse wild-type HTT. Additionally, there were no lateral ventricle size changes observed at any dose tested.

"The impact on many features of Huntington's disease with the AMT-130 gene therapy approach are encouraging and support its continued assessment in patients with this debilitating disease." stated Michael R. Hayden, Killiam Professor of Medical Genetics at the CMMT and the University of British Columbia, and co-author of the study.

These findings were further supported by a recently published study in *Molecular Therapy - Methods & Clinical Development*, on neuronal and astrocytic cell cultures derived from induced pluripotent stem cells (iPSCs) from two Huntington's disease patients with different CAG-repeat lengths.

Results from this study demonstrated significant non-selective reduction of up to 68% of human HTT in Huntington's disease patient-derived iPSC neurons and astrocytes, with no observed toxicity or off-target effects in gene expression and regulation.

"These results are very encouraging in the context of AMT-130 as a potential gene therapy for Huntington's disease, where durable and potent suppression of huntingtin protein is needed in the striatum and cortex," stated Sander van Deventer, M.D., Ph.D., EVP research and product development. "Moreover, these studies examine for the first time the tolerability and efficacy of non-selective human HTT lowering and demonstrate the approach is well-tolerated, even in the absence of background wild-type huntingtin protein. The data provide further support for the potential safety and efficacy of AMT-130 and we remain excited to advance our recently initiated Phase I/II clinical trial of AMT-130 in patients with Huntington's disease."

The publication, "Potent and sustained huntingtin lowering via AAV5 encoding miRNA preserves striatal volume and cognitive function in a humanized mouse model of Huntington disease", is available online in the journal Nucleic Acids Research.

The publication, "AAV5-miHTT Lowers Huntingtin mRNA and Protein without Off-Target Effects in Patient-Derived Neuronal Cultures and Astrocytes", is available online in journal Molecular Therapy - *Methods & Clinical Development.*

About AMT-130
AMT-130 is a gene therapy product candidate consisting of an AAV5 vector carrying an artificial micro-RNA specifically tailored to silence the huntingtin gene, leveraging our proprietary miQURE™ silencing technology. The therapeutic goal is to inhibit the production of the mutant protein (mHTT). Using AAV vectors to deliver micro-RNAs directly to the brain for non-selective knockdown of the huntingtin gene represents a highly innovative and promising approach to treating Huntington's disease.

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. The disease is an autosomal dominant condition with a disease-causing CAG repeat expansion in the first exon of the huntingtin gene, that leads to the production and aggregation of abnormal protein in the brain. Despite the clear etiology of Huntington's disease, there are no therapies to delay the onset or to slow the disease's progression.

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, hemophilia A, 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 AMT-130 may prove to be clinically safe or efficacious or become a successful treatment for patients suffering from Huntington's disease. 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 28, 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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