# uniQure Delivers Oral Presentation on Broad Set of Preclinical Data on AMT-130 in Huntington's Disease at the 2018 American Academy of Neurology Annual Meeting

April 25, 2018

**Mutant Huntingtin Protein Reduced by a Median of 68% in the Deep Structures of the Brain and a Median of 47% in the Frontal Cortex at 6 Months in a Large Diseased Animal Model**

LEXINGTON, Mass. and AMSTERDAM, the Netherlands, April 25, 2018 (GLOBE NEWSWIRE) -- uniQure N.V. (NASDAQ:QURE), a leading gene therapy company advancing transformative therapies for patients with severe medical needs, today presented an overview of its preclinical data establishing proof-of-concept for AMT-130, its proprietary gene therapy candidate for the treatment of Huntington's disease, at the 2018 American Academy of Neurology (AAN) Annual Meeting in Los Angeles, California. AMT-130 comprises a recombinant AAV5 vector carrying a DNA cassette encoding an engineered microRNA that non-selectively lowers or knocks-down human huntingtin protein.

Data from multiple studies in Huntington's disease animal models across three different species show that a single intraparenchymal administration of AMT-130 into the striatum, resulted in a dose-dependent and sustained reduction of mutant huntingtin protein (mHTT) in both the deep structures of the brain and the cortex. This therapeutic approach is directed to the primary targets of the caudate and putamen, which are most affected in Huntington's disease patients. Once administered in the studies, AMT-130 spread to the cerebral cortex and lowered mHTT in the frontal areas of the brain that show neuropathological changes later in the course of the disease, providing evidence that AMT-130 spread from the injection sites to the cerebral cortex.

"Data from these preclinical studies show the potential of AMT-130 to alter the course of this devastating disease after a one-time administration," stated Sander van Deventer, M.D., Ph.D., chief scientific officer at uniQure. "We are particularly encouraged by the strong knockdown observed in the deep structures of the brain known to be impacted at the onset of disease, as well as the cerebral cortex. We believe that the sustained reduction of huntingtin protein, followed by the prevention of neuronal dysfunction and improved motor-coordination in animal models, provide strong proof-of-concept for AMT-130 as a potential groundbreaking treatment for patients suffering from Huntington's disease."

Preclinical Data Findings Across Several Animal Models

Proof-of-concept for AMT-130 was established through preclinical studies in three different Huntington's disease mouse models, a Huntington's disease rat model and a Huntington's disease minipig model. The oral presentation at AAN included the following data:

- Transgenic minipigs, one of the largest Huntington's disease animal models available, were used to study the feasibility, efficacy and tolerability of AMT-130. A dose-dependent distribution of the AAV5 vector was detected throughout the brain and was correlated with microRNA expression, reduction of human mHTT and lowering of messenger RNA. Human mHTT was significantly reduced by a median of 68% in the striatum and a median of 47% in the frontal cortex at 6 months after administration of AMT-130.

- All proof-of-concept studies demonstrated a long-term suppression of mHTT after the administration of AMT-130, with up to an 88% reduction of mHTT after 7 months and reduced aggregation up to 12 months in two Huntington's disease mouse models. This sustained reduction in mHTT resulted in significant improvement of striatal neuronal function without any serious adverse effects related to the treatment.

- The mechanistic proof-of-concept of AMT-130 was demonstrated in the rapidly-progressing R6/2 Huntington's disease mouse model. This mouse model is characterized by an early onset of motor symptoms and a reduced life-span. After the striatal delivery of AMT-130, these transgenic mice demonstrated an improvement in motor-coordination, reduced body weight loss, and an increase in median survival by 24%, as compared to the control group.

The administration procedure and AMT-130 treatment were well tolerated with no serious adverse events across all animal models.

"We are in the process of completing our non-human primate toxicology studies, which we plan to use to support an Investigational New Drug (IND) application for AMT-130 later this year. We continue to work toward our goal of being the first AAV gene therapy to enter clinical development for Huntington's disease," said Joseph J. Higgins, M.D., F.A.A.N., Vice President of Clinical Development at uniQure.

An overview of the preclinical data presented at AAN can be found in the Investor section of uniQure's corporate website.

**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) repeat expansion in the first exon of the huntingtin gene, that leads to the production of a non-functional, mutated protein that aggregates in the brain. Despite the clear etiology of HD, 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

**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, our upcoming anticipated milestones, the development of our gene therapy product candidates, the filing of any Investigational New Drug (IND) application or other regulatory filings, the timing of and the ability to engage in clinical development of AMT-130, including relative to other potential AAV gene therapies for Huntington's disease, 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 our and our collaborators' clinical development activities, 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 Annual Report on Form 10-K filed on March 14, 2018. 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:** | | **FOR MEDIA:** |
|---|---|---|
| **Maria E. Cantor** | **Eva M. Mulder** | **Tom Malone** |
| Direct: 339-970-7536 | Direct: +31 20 240 6103 | Direct: 339-970-7558 |
| Mobile: 617-680-9452 | Mobile: +31 6 52 33 15 79 | Mobile:339-223-8541 |
| m.cantor@uniQure.com | e.mulder@uniQure.com | t.malone@uniQure.com |

t.malone@uniQure.com