uniQure Announces Publications of Preclinical Data for AMT-130 in Huntington's Disease Showing Safety of Administration in NHPs and Widespread Long-Term HTT-Lowering in the Brain

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Publication in Science Translational Medicine shows local striatal delivery of microRNA-gene therapy results in widespread brain huntingtin protein lowering in Huntington's disease minipigs

LEXINGTON, Mass. and AMSTERDAM, April 08, 2021 (GLOBE NEWSWIRE) -- uniQure N.V. (NASDAQ: QURE), a leading gene therapy company advancing transformative therapies for patients with severe medical needs, today announced that three manuscripts on preclinical data from its gene therapy candidate AMT-130 in Huntington's disease have been accepted for publication, in the journals *Science Translational Medicine, Brain Science*, and *Brain Communications.* The publications show the safety and efficacy of AMT-130 in the deep brain structures of a large animal model and outline a promising novel efficacy biomarker for AMT-130.

"Taken together, these publications demonstrate widespread biodistribution and strong, durable efficiency of AMT-130 in disease-relevant regions in a large brain," stated Ricardo Dolmetsch, Ph.D., president of research and development at uniQure. "The data provide further support for the potential therapeutic value of AMT-130, and we remain enthusiastic about our Phase I/II clinical trial of AMT-130 in patients with Huntington's disease."

Widespread and Sustained Target Engagement in Huntington Disease Minipigs

The paper published this week in *Science Translational Medicine* examines the translatability and long-term durability of AMT-130 in transgenic Huntington's disease minipigs, which were used to assess the biodistribution and target engagement in a larger brain. The minipig model is the largest diseased animal model available, generally weighing up to 300 pounds.

AMT-130 was administered by MRI-guided convention-enhanced delivery (CED) at a single dose, bilaterally in the caudate and putamen. Vector DNA distribution and transgene expression in minipig brains demonstrated extensive brain coverage comparable at the interim sacrifice timepoints of 6- and 12-months post administration, leading to significant lowering of mutant huntingtin (mHTT) protein in the brain.

At 12 months, the most pronounced mHTT protein lowering was observed in the putamen (85%), caudate (80%) and amygdala (78%), followed by thalamus (56%) and cerebral cortex (44%).

The publication, "Widespread and Sustained Target Engagement in Huntington Disease Minipigs upon Intrastriatal MicroRNA-based Gene Therapy," is available online in the journal *Science Translational Medicine* (DOI: 10.1126/scitranslmed.abb8920).

Well-tolerated in non-human primates and rats

In addition, a GLP toxicity study of AMT-130 in non-human primates and rats was published in January 2021 in the journal *Brain Science*. The study demonstrated an excellent safety profile and biodistribution after MRI-guided CED of AMT-130 in the treated animals. One-time bilateral administration in the caudate and putamen resulted in widespread vector DNA and miHTT transgene distribution in the brain, particularly in areas associated with HD pathology. Intrastriatal administration of AAV5-miHTT was well tolerated, with no clinically relevant changes in either species.

The publication, "Intrastriatal Administration of AAV5-miHTT in Non-Human Primates and Rats Is Well Tolerated and Results in miHTT Transgene Expression in Key Areas of Huntington Disease Pathology," is available online in the journal *Brain Science* (DOI: 10.3390/brainsci11020129).

Monitoring Durability of MicroRNA-based Therapies

A third manuscript was published last week in the journal *Brain Communications*, examining the potential use of measuring therapeutic HTT microRNA (miHTT) in extracellular vesicles in CSF as sources to monitor the expression and durability of gene therapies in the brain. After AAV treatment in non-human primates, the secretion of mature engineered microRNA molecules was confirmed, with extracellular microRNA levels correlating with viral dose and cellular microRNA expression in neurons. In investigating the detection of engineered microRNAs over time in the CSF of non-human primates after a single intrastriatal injection of AAV5-miHTT, quantifiable engineered microRNA levels enriched in extracellular vesicles were detected in the CSF up to two years after brain infusion.

The results confirm the long-term expression (up to two years) of AAV5-delivered microRNAs in non-human primates and provide further support for the potential use of extracellular vesicle-associated microRNAs as novel biomarkers in ongoing clinical trials of gene therapies for neurodegenerative diseases, including AMT-130.

The publication, "Secreted therapeutics: Monitoring durability of microRNA-based gene therapies in the central nervous system," is available online in the journal *Brain Communications* (DOI: 10.1093/braincomms/fcab054).

About AMT-130

AMT-130 comprises a recombinant AAV5 vector carrying a DNA cassette encoding a microRNA that lowers Huntingtin protein in Huntington's disease patients. AMT-130 is uniQure's first clinical program incorporating its proprietary miQURE™ platform. miQURE is designed to degrade disease-causing genes without off-target toxicity and induce silencing of the entire target organ through secondary exosome-mediated delivery.

About Huntington's Disease

Huntington's disease is a rare, inherited neurodegenerative disorder that leads to motor symptoms including chorea, and behavioral abnormalities and cognitive decline resulting in progressive 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 currently approved 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, 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 we will advance our Phase I/II gene therapy clinical trial of AMT-130 in Huntington's disease. uniQure's actual results could differ materially from those anticipated in these forward-looking statements for many reasons, including, without limitation, risks associated with the impact of the ongoing COVID-19 pandemic on our Company and the wider economy and health care system, our Commercialization and License Agreement with CSL Behring, the regulatory approval of that transaction, our clinical development activities, clinical results, collaboration arrangements, 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 periodic securities filings, including its Annual Report on Form 10-K filed March 1, 2021. Given these risks, uncertainties and other factors, you should not place undue reliance on these forward-looking statements, and uniQure assumes no obligation to update these forward-looking statements, even if new information becomes available in the future.

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