uniQure Announces Publications on AAV Gene Therapy Approach to Treating Amyotrophic Lateral Sclerosis (ALS) and Frontotemporal Dementia (FTD) in the Journal *Molecular Therapy Nucleic Acids*

~ Data Highlighted in Two Publications Demonstrate Early Preclinical Proof of Concept of AAV-based Gene Therapy to Silence Mutated *C9orf72* Gene, A Frequent Cause of Familial ALS and FTD ~

Lexington, MA and Amsterdam, the Netherlands, February 15, 2019 — uniQure N.V. (NASDAQ: QURE), a leading gene therapy company advancing transformative therapies for patients with severe medical needs, today announced two recent online publications of preclinical studies showing significant silencing, or knockdown, of the mutated gene most commonly known to lead to onset of amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD), two devastating neurodegenerative diseases. The proof-of-concept studies were conducted by uniQure scientists and utilized the Company's miQURE™ technology, a proprietary, next-generation gene-silencing platform.

Both studies are published in the scientific journal, *Molecular Therapy Nucleic Acids.* The first manuscript entitled, "Artificial microRNAs targeting *C9orf72* can reduce accumulation of the intra-nuclear transcripts in ALS and FTD patients" describes the design and *in vitro* characterization of artificial micro-RNA (miC) that silence the mutated *C9orf72* gene. The second manuscript entitled, "Targeting RNA-mediated toxicity in *C9orf72* ALS/FTD by RNAi based gene therapy" reports that an AAV vector carrying a DNA cassette encoding miC silences the mutated *C9orf72* gene in iPSC-neurons derived from an FTD patient and in an ALS mouse model that carries the human gene with the *C9orf72* mutation. The studies show significant silencing of *C9orf72* in human-derived iPSC neurons, and the mutated C9orf72 was also reduced in the cell nucleus. AAV5-miC injected into the striatum of ALS mice reduced mutated *C9orf72* in the transduced areas.

"These findings are potentially significant for the treatment of ALS and FTD patients, and the ability to silence *C9orf72* transcripts in the nucleus may prove to be critical for therapeutic efficacy of gene therapies for these diseases," stated Sander van Deventer, M.D., Ph.D., chief scientific officer of uniQure. "In ALS, mutated *C9orf72* transcipts are confined to the cell nucleus causing so-called RNA foci, which are toxic clumps of mutated *C9orf72* RNA that sequester critical proteins, resulting in cellular dysfunction and death. Whereas most miRNA constructs exclusively target cytoplasmic mRNA, AAV5-miC significantly reduced formation of RNA foci in the nuclei of neurons from *C9orf72* mice."

"Taken together, these preclinical findings further support the feasibility of advancing this program through research and potentially into development of a promising gene therapy with the potential to alleviate the toxicity caused by the mutated *C9orf72* in ALS and FTD," he added. "These data illustrate the potential of our miQURE platform to degrade disease-causing genes, without off-target toxicity. We are very pleased to have these data published in a highly relevant journal for the field and look forward to further exploring this opportunity."

About miQURE™

miQURE is uniQure's novel technology platform designed to degrade disease-causing genes, without off-target toxicity, and induce silencing of the entire target organ through secondary exosome-mediated

delivery. Gene therapy candidates designed with miQURE incorporate proprietary, therapeutic miRNA constructs that can be delivered using AAVs to potentially provide long-lasting activity.

Preclinical studies of miQURE-based gene therapies have demonstrated several important advantages, including enhanced tissue-specificity, improved nuclear and cytoplasmic gene lowering and no off-target effects associated with impact to the cellular miRNA or mRNA transcriptome. miQURE technology has been incorporated in AMT-130, an investigational gene therapy for Huntington's disease, and is expected to be applied to AMT-150 for SCA3.

About ALS and FTD

ALS (amyotrophic lateral sclerosis) is a devastating neurodegenerative disease characterized by progressive degeneration of the upper and lower motor neurons leading to muscle atrophy and paralysis. There is no disease-modifying therapy for ALS and most patients die with respiratory failure within 3-5 years after the onset of symptoms.

A significant number of ALS patients also develop FTD (frontotemporal dementia), a presenile form of dementia characterize by degeneration of neurons in the frontal and temporal lobes of the brain leading to behavioral changes. The most common genetic cause of familial and sporadic ALS and FTD is an expanded GGGGCC (G_4C_2) repeat in the first intron of the chromosome 9 open reading frame 72 (*C9orf72*) gene. Both ALS and FTD often occur at a relatively young age and have a major impact on the patients and their families. A mutation in the *C9orf72* gene is considered the most frequent cause of familial ALS and FTD, with some patients developing both diseases.

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 other severe genetic 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 development of our gene therapy product candidates, whether the results of pre-clinical studies are potentially significant or prove to be safe or effective in the treatment of ALS and FTD patients, whether the ability to silence C9orf72 transcripts in the nucleus proves to be critical for therapeutic efficacy of gene therapies for these diseases, whether programs involving our miQURE™ technology are advanced through research or into development or become promising as gene therapies or can alleviate the toxicity caused by the mutated C9orf72 in ALS and FTD or in other genes or in other diseases, delay or lack of success of any of our ongoing or planned clinical studies and/or development of our product candidates, and the scope of protection of our proprietary technologies. 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, the success of our pre-clinical and other research and development efforts, 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 November 6, 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.

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