uniQure Announces Clinical Update on First Patients in Phase I/II Clinical Trial of AMT-130 Gene Therapy for the Treatment of Huntington's Disease

~ Treatment was well tolerated with no significant safety issues related to AMT-130 in first two treated patients through one year of follow-up ~

~ Neurofilament Light Chain (NfL) rose as expected immediately following surgery and returned to baseline in treated patients ~

~ A total of 19 patient procedures have been performed in the U.S. Phase I/II clinical trial, with higher-dose cohort enrollment expected to be completed by mid-2022 ~

~ Screening initiated in European open-label Phase I/II study ~

~ Conference call today at 8:30 a.m. ET ~

Lexington, MA and Amsterdam, the Netherlands, December 16, 2021 — uniQure N.V. (NASDAQ: QURE), a leading gene therapy company advancing transformative therapies for patients with severe medical needs, today announced initial observations on the first four patients enrolled in the lower-dose cohort of its ongoing Phase I/II clinical trial of AMT-130 for the treatment of Huntington's disease. Two of the four enrolled patients received AMT-130, and two patients experienced an imitation (sham) surgery in this randomized, blinded clinical trial being conducted in the United States.

"We are pleased with these data that support the tolerability of AMT-130, a potential one-time gene-therapy approach for Huntington's disease," stated Ricardo Dolmetsch, Ph.D., president of research and development at uniQure. "Neurofilament light chain, a key biomarker of injury in the brain, trended downward and returned to baseline levels in the treated patients, and structural MRI data are consistent with the safety profile of AMT-130. Based on recommendations of the DSMB and steering committee, we will disclose efficacy data including volumetric MRI changes once all patients in the first two cohorts are unblinded. We look forward to evaluating safety, biomarker and functional data on a larger number of patients and over a longer period during the ongoing study."

"AMT-130 appears to be generally well tolerated both immediately after surgical administration and at one year of follow up in these four patients," stated Jody Corey-Bloom, M.D., PhD, professor of neurosciences at University of California, San Diego and chairperson of the Data Safety Monitoring Board (DSMB) for AMT-130. "We are encouraged by the early data in two treated patients and will continue to provide comprehensive safety oversight of the program as additional patients are enrolled and the trial expands into Europe. The DSMB will continue to oversee the conduct of this important program, and will evaluate safety, biomarker, imaging, and functional data as the program advances."

One-Year Observations on AMT-130

The first four patients were a heterogeneous group representing a spectrum of Stage I-II early manifest disease with 41-44 CAG repeats, baseline Total Functional Capacity scores of 10-13 and Total Motor Scores of 7-23.

- AMT-130 was generally well tolerated in the treated patients at the lower dose of $6x10^{12}$ vector genomes (vg).
- There have been no serious adverse events (SAEs) to date related to AMT-130 in these patients.
- NfL increased as expected immediately following the AMT-130 surgical procedure and returned to baseline in the two treated patients. NfL remained relatively constant in the two untreated control patients.
- Structural magnetic resonance imaging did not reveal any clinically meaningful safety findings in either treated or control patients at one year of follow-up.
- Measurements of total and mutant HTT protein in the cerebral spinal fluid of the four patients were highly variable and inconclusive.
- The safety profile of AMT-130 in the low-dose cohort to date supports continued enrollment of patients in the higher-dose cohort of $6x10^{13}$ vg. Nineteen patients have been enrolled in the clinical trial to date, including 9 of 16 in the higher-dose cohort.

A clinical update on the low-dose cohort of ten patients, largely focused on safety, is expected in the second quarter of 2022 after patient unblinding. Full safety and efficacy data from the first two cohorts in the Phase I/II clinical trial are expected in the first half of 2023 after all patients in the higher-dose cohort have achieved one year of follow-up.

Planned Expansion of Phase I/II Studies of AMT-130

The U.S. Phase I/II clinical trial of AMT-130 for the treatment of Huntington's disease is exploring the safety, tolerability, and efficacy signals in a planned 26 total patients with early manifest Huntington's disease split into a 10 patient, low-dose cohort followed by a 16 patient, higher-dose cohort; patients will be randomized to treatment with AMT-130 or an imitation (sham) surgery. The multi-center trial consists of a blinded 12-month core study period followed by unblinded long-term follow-up for five years. A total of 16 patients in the clinical trial will receive a single administration of AMT-130 through MRI-guided, convection-enhanced stereotactic neurosurgical delivery directly into the striatum (caudate and putamen).

uniQure also plans to initiate a third cohort in the ongoing U.S. Phase I/II clinical trial in the second half of 2022 that will explore the use of alternative stereotactic navigation systems to simplify placement of catheters for infusions of AMT-130. This will be explored in two steps and include up to 18 additional randomized patients who will receive the higher dose of $6x10^{13}$ vg.

The European, open-label Phase Ib/II study of AMT-130 will enroll 15 patients with early manifest Huntington's disease across two dose cohorts. Screening has been initiated, and the first procedures in the lower-dose cohort are expected to be complete in early 2022. Together with the U.S. study, the European study is intended to establish safety, proof of concept, and the optimal dose of AMT-130 to take forward into Phase III development or into a confirmatory study should an accelerated registration pathway be feasible.

AMT-130 is uniQure's first clinical program focusing on the central nervous system (CNS) incorporating its proprietary miQURE® platform.

Investor Conference Call and Webcast Information

uniQure management will host an investor conference call and webcast today, Thursday, December 16, 2021, at 8:30 a.m. ET. The conference call may be accessed by dialing (833) 962–1471 for domestic callers and +44 0800 0288 438 for international callers. The conference call ID: 2866185. Please specify

to the operator that you would like to join the "uniQure Conference Call." If you are joining the conference call, please dial-in 15 minutes before the start time. The webcast of the conference call may also be accessed through the Investors & Newsroom section of the uniQure website. Following the live webcast, a replay of the call will be archived for several weeks.

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 temporal lobe epilepsy, Alzheimer's, Parkinson's and ALS. 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 be able to evaluate data on a larger number of patients or over a longer period during the ongoing study; whether safety data on the first cohort of ten patients will be available in the second quarter of 2022 or ever; whether full safety and efficacy data from the Phase I/II clinical trial will be available for cohorts 1 and 2 in the first half of 2023 or ever; whether 16 patients or any patients in the clinical trial will receive a higher dose administration of AMT-130; whether we will initiate a third cohort in the ongoing U.S. Phase I/II clinical trial in the second half of 2022 or ever; whether we will enroll 15 patients or any patients in a European, open-label Phase Ib/II study of AMT-130; whether we will complete the first procedures in the low-dose cohort of the European study in early 2022 or ever; whether the European study will establish safety, proof of concept, or the optimal dose of AMT-130 to take forward into Phase III development or into a confirmatory study or for any purpose; and whether an accelerated registration pathway will be feasible or available at all. Our 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, 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 periodic securities filings, including its Annual Report on Form 10-K filed March 1, 2021 and Quarterly Report on Form 10-Q filed on October 25, 2021. 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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