uniQure Announces Positive Interim Data Update Demonstrating Slowing of Disease Progression in Phase I/II Trials of AMT-130 for Huntington's Disease

July 9, 2024

~ Achieved statistically significant, dose-dependent, and durable evidence of potential therapeutic benefit; Patients receiving high-dose AMT-130 showed 80% slowing of disease progression in the composite Unified Huntington's Disease Rating Scale (cUHDRS) at 24 months compared to a propensity score-weighted external control ~

~ Achieved statistically significant lowering of CSF neurofilament light protein (NfL) compared to baseline at 24 months in patients treated with AMT-130; Mean CSF NfL levels for both doses were below baseline at 24 months ~

~ Granted first-ever Regenerative Medicine Advanced Therapy (RMAT) designation in Huntington's disease; uniQure expects to meet with the FDA in the second half of 2024 to discuss potential for expedited clinical development ~

~ Investor conference call and webcast today at 8:30 a.m. ET ~

LEXINGTON, Mass. and AMSTERDAM, July 09, 2024 (GLOBE NEWSWIRE) -- uniQure N.V. (NASDAQ: QURE), a leading gene therapy company advancing transformative therapies for patients with severe medical needs, today announced updated interim data including up to 24 months of follow-up data from 29 treated patients enrolled in the ongoing U.S. and European Phase I/II clinical trials of AMT-130 for the treatment of Huntington's disease.

"We are very pleased with these new data demonstrating a statistically significant, dose-dependent slowing of the progression of Huntington's disease and lowering of NfL in the CSF at 24 months," stated Walid Abi-Saab, M.D., chief medical officer of uniQure. "We believe this is the first clinical trial of any investigational medicine for Huntington's disease to show evidence of a potential long-term clinical benefit and reduction of a key marker of neurodegeneration. Moreover, given the one-time administration of AMT-130, we are in a unique position to continue accumulating longer-term patient outcomes from the Phase I/II studies to support the emerging therapeutic benefit. We look forward to holding an initial, multi-disciplinary RMAT meeting with the FDA later this year to discuss the potential for expedited clinical development of AMT-130."

"These updated results are exciting and provide compelling evidence of potential therapeutic benefit," stated Victor Sung, M.D., professor of neurology at the University of Alabama at Birmingham (UAB), director of the UAB Huntington's Disease Clinic, co-director of the UAB School of Medicine Neuroscience Module, and trustee on the National Board of the Huntington's Disease Society of America. "The preservation of motor and cognitive function observed through two years, combined with reduced NfL levels below baseline, defy expectations about the natural progression of Huntington's disease. cUHDRS, in particular, has been shown to be a robust and sensitive measure of disease progression, and offers an opportunity for enhanced clinical trial efficiency relative to individual measurements. These long-term data provide encouraging support of durable disease-modification and offer much needed hope for a community that is in desperate need of therapeutic options."

Exploratory Efficacy and Safety Data[1]

uniQure is conducting two multi-center Phase I/II clinical trials of AMT-130 in the U.S. (n=26) and Europe/UK (n=13). A total of 29 patients received one of two doses of AMT-130 (n=12 low dose; n=17 high dose) and 10 control patients received imitation surgery. Across both studies, 24-month follow-up data from a total of 21 patients (n=12 low dose; n=9 high dose) were available for analysis as of a March 31, 2024 cut-off date.

For the first time, uniQure conducted a statistical analysis of clinical outcomes for the 21 treated patients at 24 months compared to an expanded, propensity-weighted external control (n=154) developed in collaboration with the Cure Huntington's Disease Initiative (CHDI) using data from the TRACK-HD, TRACK-ON and PREDICT-HD natural history studies. The external control includes patients that met the Phase I/II clinical trial eligibility criteria, and whose data contributions were statistically weighted using propensity scoring to closely match the baseline characteristics of patients treated with AMT-130. Disease-related outcomes for these well-balanced cohorts were then compared after 24 months follow-up.

- A statistically significant, dose-dependent, slowing in disease progression measured by cUHDRS was observed through 24 months in patients receiving the high dose of AMT-130.
    - At 24 months, the mean change in cUHDRS for patients receiving the high-dose of AMT-130 was -0.2 compared to -1.0 for patients in the propensity score-weighted external control, representing an 80% slowing of disease progression (p=0.007).
    - At 24 months, the mean change in cUDHRS for patients receiving the low-dose of AMT-130 was -0.7 compared to -1.0 for patients in the propensity score-weighted external control, representing a 30% slowing of disease progression (p=0.21).
    - cUHDRS has been demonstrated to be the most sensitive measurement of clinical progression in Huntington's disease patients[2].

- Trends in measurements of motor and cognitive function showed near-baseline stability throughout the 24 months of follow-up in patients receiving the high dose of AMT-130.

- A statistically significant reduction of NfL in cerebrospinal fluid (CSF) was observed in patients treated with AMT-130.

    - Patients treated with AMT-130 had a mean reduction in CSF NfL of 11% compared to baseline (p=0.02) at 24 months.

    - Mean CSF NfL levels for both high and low doses were below baseline at 24 months.

    - CSF NfL is a well-characterized biomarker of neurodegeneration that has been shown to be strongly associated with the clinical severity of Huntington's disease. An independent natural history study demonstrated a 26% increase in CSF NfL at 24 months in patients with early manifest Huntington's disease (n=19).

- Based on data observed to date, AMT-130 remains generally well-tolerated, with a manageable safety profile at both doses. There were no new AMT-130-related serious adverse events reported.

Next Steps

Based on the encouraging data from this interim analysis, uniQure anticipates the following next steps:

- In the second half of 2024, uniQure expects to hold a Type B, multi-disciplinary RMAT meeting with U.S. Food and Drug Administration (FDA) to present these updated data and discuss potential expedited clinical development pathways and accelerated approval.

- In the second half of 2024, uniQure expects to complete enrollment of the third cohort of the U.S. Phase I/II study exploring AMT-130 in combination with immunosuppression. In the first half of 2025, uniQure anticipates presenting safety data from this cohort.

- In mid-2025, uniQure expects to present another interim analysis from the ongoing Phase I/II studies of AMT-130. The data will include a 36-month comparison of treated patients to the propensity score-weighted external control.

Investor Conference Call and Webcast Information

uniQure management will host an investor conference call and webcast today, Tuesday, July 9 at 8:30 a.m. ET. The event will be webcast under the Events & Presentations section of uniQure's website at https://www.uniqure.com/investors-media/events-presentations, and following the event a replay will be archived for 90 days. Interested parties participating by phone will need to register using this online form. After registering for dial-in details, all phone participants will receive an auto-generated e-mail containing a link to the dial-in number along with a personal PIN number to use to access the event by phone. If you are joining the conference call, please dial in 15 minutes before the start time.

About the Phase I/II Clinical Program of AMT-130

uniQure is conducting two multi-center, dose-escalating, Phase I/II clinical trials to explore the safety, tolerability, and exploratory efficacy signals of AMT-130 for the treatment of Huntington's disease. In the U.S. study, a total of 26 patients with early manifest Huntington's disease were randomized to treatment (n=6 low-dose; n=10 high dose) or an imitation (sham) surgical procedure (n=10). Treated patients received a single administration of AMT-130 through MRI-guided, convection-enhanced stereotactic neurosurgical delivery directly into the striatum (caudate and putamen). The study consists of a blinded 12-month core study period followed by unblinded long-term follow-up of treated patients for five years. An additional four control patients crossed over to treatment.

The European open-label Phase Ib/II study of AMT-130 enrolled 13 patients with early manifest Huntington's disease (n=6 low dose; n=7 high dose). 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.

A third cohort of up to 12 patients is currently being enrolled between both U.S. and EU sites to explore both doses of AMT-130 in combination with immunosuppression and using the current, established stereotactic administration procedure.

Additional details are available on www.clinicaltrials.gov (NCT0543017, NCT04120493)

AMT-130 was granted the FDA's Regenerative Medicine Advanced Therapy (RMAT) designation, the first for Huntington's disease.

About Huntington's Disease

Huntington's disease is a rare, inherited neurodegenerative disorder that leads to motor symptoms including chorea, 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. According to 2021 study in Neuroepidemiology, approximately 70,000 people have been diagnosed with Huntington's disease in the U.S. and Europe, with hundreds of thousands of others at risk of inheriting the disease. Despite the clear etiology of Huntington's disease, there are currently no 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. The approvals of uniQure's gene therapy for hemophilia B – an historic achievement based on more than a decade of research and clinical development – represent a major milestone in the field of genomic medicine and ushers in a new treatment approach for patients living with hemophilia. uniQure is now advancing a pipeline of proprietary gene therapies for the treatment of patients with Huntington's disease, refractory temporal lobe epilepsy, ALS, Fabry disease, and other severe diseases. www.uniQure.com

uniQure Forward-Looking Statements

This press release contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. All statements other than statements of historical fact are forward-looking statements, which are often indicated by terms such as "anticipate," "believe," "could," "establish," "estimate," "expect," "goal," "intend," "look forward to", "may," "plan," "potential," "predict," "project," "seek," "should," "will," "would" and similar expressions and the negatives of those terms. Forward-looking statements are based on management's beliefs and assumptions and on information available to management as of the date of this press release. Examples of these forward-looking statements include, but are not limited to, statements concerning: the Company's plans to meet with regulatory authorities to discuss the potential for expedited clinical development; the timing of the Company's planned meeting and discussions with regulatory authorities; the Company's ability to continue accumulating long-term patient data; the potential clinical and functional effects of AMT-130; the Company's plans to continue clinical development of AMT-130; the potential for accelerated regulatory pathways; the Company's use of a natural history cohort as a basis for comparison with respect to the efficacy of AMT-130; the Company's enrollment plans with respect to the third cohort studying AMT-130 in combination with immunosuppression and plans to present safety data from this cohort; the utility of NfL in CSF as an effective biomarker and indicator of clinical severity; and the Company's plans to present further interim analyses. The Company's actual results could differ materially from those anticipated in these forward-looking statements for many reasons. These risks and uncertainties include, among others: risks related to the Company's Phase I/II clinical trials of AMT-130, including the risk that such trials will be unable to demonstrate data sufficient to support further clinical development and the risk that interim data from the trials may not be predictive of later data readouts; risks related to the Company's ability to pursue business development efforts with respect to AMT-130; risks related to the Company's interactions with regulatory authorities, which may affect the initiation, timing and progress of clinical trials and pathways to regulatory approval; risks related to the Company's use of propensity-weighted external controls in connection with its statistical analysis of clinical outcomes to date, and whether regulatory authorities will accept the Company's approach as a basis for accelerated approval; risks related to the Company's use of nominal p values as a basis for its statistical analyses; whether the measurements that the Company is evaluating continue to be viewed as robust and sensitive measurements of disease progression; whether RMAT designation or any accelerated pathway, if granted, will lead to regulatory approval; the Company's ability to conduct and fund a Phase III or confirmatory study for AMT-130; the Company's ability to continue to build and maintain the infrastructure and personnel needed to achieve its goals; the Company's effectiveness in managing current and future clinical trials and regulatory processes; the Company's ability to demonstrate the therapeutic benefits of its gene therapy candidates in clinical trials; the continued development and acceptance of gene therapies; the Company's ability to obtain, maintain and protect its intellectual property; and the Company's ability to fund its operations and to raise additional capital as needed and on acceptable terms. These risks and uncertainties are more fully described under the heading "Risk Factors" in the Company's periodic filings with the U.S. Securities & Exchange Commission (SEC), including its Annual Report on Form 10-K filed with the SEC on February 28, 2024 and in other filings that the Company makes with the SEC from time to time. Given these risks, uncertainties and other factors, you should not place undue reliance on these forward-looking statements and, except as required by law, the Company assumes no obligation to update these forward-looking statements, even if new information becomes available in the future.

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[1] All p-values are nominal and unadjusted. Statistical comparisons of patients treated with AMT-130 to the propensity score-weighted external control were conducted on a post-hoc basis.

[2] Tabrizi SJ, et al. Neurology. 2019; 92(15).