uniQure Provides Regulatory Update on AMT-130 for Huntington's Disease

June 2, 2025

~ Alignment with FDA continues to support Accelerated Approval pathway ~

~ BLA submission planned for first quarter of 2026 ~

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

LEXINGTON, Mass. and AMSTERDAM, June 02, 2025 (GLOBE NEWSWIRE) -- uniQure N.V. (NASDAQ: QURE), a leading gene therapy company advancing transformative therapies for patients with severe medical needs, today provided a regulatory update on AMT-130, its investigational gene therapy for the treatment of Huntington's disease. Following recent Type B meetings and further guidance from the U.S. Food and Drug Administration (FDA), the Company has reached alignment with the FDA on several key components of the statistical analysis plan and Chemistry, Manufacturing and Controls (CMC) information that will support a Biologics License Application (BLA) submission expected in the first quarter of 2026.

"We are very pleased with our continued, productive engagement with the FDA and the progress we've made toward a planned BLA submission for AMT-130 in the first quarter of 2026," said Walid Abi-Saab, M.D., chief medical officer of uniQure. "We are pursuing an accelerated approval pathway supported by multiple years of clinical data – a rigorous and differentiated approach that reflects the urgent need in Huntington's disease and our commitment to delivering the first disease-modifying treatment for people affected by this devastating disease. We are grateful to the FDA for their continued engagement and look forward to sharing three-year top-line data in the third quarter of 2025."

Statistical Analysis Plan

In the second quarter of 2025, the Company held a Type B meeting with the FDA to discuss the proposed use of external control data and the prospectively defined statistical analysis plan (SAP) in support of the planned BLA submission for AMT-130. The FDA continued to support its prior agreement that the composite Unified Huntington's Disease Rating Scale (cUHDRS) may serve as an acceptable registrational, intermediate clinical endpoint for accelerated approval. The FDA agreed that the primary efficacy analysis for the BLA will evaluate the 3-year change in cUHDRS in high-dose AMT-130 patients compared to a propensity score-adjusted external control arm. The Company plans to use propensity score-weighted external control derived from the ENROLL-HD dataset for the primary analysis and to submit certain sensitivity analyses, including one using a propensity score-matched external control, as additional support.

The FDA also agreed that ENROLL-HD – a large, prospective, longitudinal, natural history study of patients with Huntington's disease – may be acceptable as the external control dataset for the primary analysis of the trial data along with additional sensitivity analyses using the TRACK-HD/TRACK-ON and PREDICT-HD datasets. To date, approximately 33,000 patients have enrolled in ENROLL-HD. Compared to previously used natural history studies like TRACK-HD and PREDICT-HD, ENROLL-HD offers a substantially larger sample size, lower attrition rates, and longer average patient follow-up. The Company expects the larger sample size to reduce variability in the external control data and enhance the robustness of the SAP.

The Company plans to submit an updated SAP consistent with discussions from the recently held Type B meeting to the FDA in the second quarter of 2025.

Chemistry, Manufacturing and Controls (CMC)

In the first quarter of 2025, the Company held a Type B meeting with the FDA to discuss CMC requirements in support of the planned BLA submission for AMT-130. The FDA agreed that validation of the AMT-130 manufacturing process should be possible using experience and prior knowledge from the etranacogene dezaparvovec-drlb (HEMGENIX®) process, complemented with additional full-scale AMT-130 GMP batches and a single Process Performance Qualification (PPQ) batch.

The FDA also agreed with the Company's proposed drug product release testing plan, including the proposed potency assay, pending completion of qualification and specification setting activities.

Next Steps for the Planned BLA Submission

Based on these recent Type B meetings with the FDA, the Company continues to prepare for a BLA submission for AMT-130 in the treatment of Huntington's disease. Certain key next steps and expected timing include:

- Q2 2025: submit updated SAP to the FDA
- Q3 2025: initiate PPQ run and present topline Phase I/II data per the SAP
- Q4 2025: hold pre-BLA meeting with the FDA
- Q1 2026: submit BLA with a request for priority review designation

Investor Conference Call and Webcast Information

uniQure management will host an investor conference call and webcast today, Monday, June 2, 2025 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 studies 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).

A third cohort enrolled an additional 12 patients across sites in the U.S. and EU. This cohort was randomized to explore both doses of AMT-130 in combination with immunosuppression, using the current, established stereotactic administration procedure.

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

AMT-130 has been granted the FDA's Regenerative Medicine Advance Therapy (RMAT) designation and Breakthrough Therapy designation, the first therapy for Huntington's disease to receive an RMAT designation.

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 availability of accelerated approval pathways and the need for additional pre-approval studies for AMT-130; the Company's anticipated timing of the BLA submission; the Company's plans to submit a revised SAP and CMC information to the FDA; the Company's ability to deliver a potentially life-changing therapy to people living with Huntington's disease and related timeline for doing so; the potential clinical and functional effects of AMT-130; the Company's plans to continue clinical development of AMT-130; the Company's plans to share clinical data of AMT-130 in the third quarter of 2025; and the utility of the ENROLL-HD patient dataset with respect to Phase I/II study. The Company may not actually achieve the plans, intentions or expectations disclosed in these forward-looking statements. Furthermore, the Company's actual results could differ materially from the plans, intentions and expectations 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 interim data from the trials may not be predictive of later data readouts that will serve as a basis for further regulatory interactions, may not support BLA submissions or accelerated approvals, may not be satisfactory to the FDA and other regulators, and new analyses of existing data and results may produce different conclusions than established as of the date hereof; risks related to the Company's current and future interactions with regulatory authorities, which may affect the initiation, timing and progress of clinical trials, its BLA submission plans and pathways to regulatory approval; risks related to the Company's ability to pursue business development efforts with respect to AMT-130; risks related to the Company's use of propensity-weighted external controls in connection with its statistical analysis of clinical outcomes to date; uncertainties as to the FDA's and other regulatory authorities' interpretation of the data from the Company's Phase I/II clinical trials of AMT-130 and acceptance of the Company's clinical programs and the regulatory approval process; later developments with the FDA and other regulators that could be inconsistent with the feedback received 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, will lead to regulatory approval; 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 27, 2025, its Quarterly Reports on Form 10-Q filed May 9, 2025, 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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