uniQure Announces Initial AMT-191 Phase I/IIa Data Showing Sustained Increases in α-Gal A Enzyme Activity in Patients with Fabry Disease

September 5, 2025

~ All patients in the first cohort achieved between 27- to 208-fold increases in α-Gal A activity relative to mean normal level ~

~ All patients in first cohort discontinued enzyme replacement therapy ~

~ Preliminary data show AMT-191 has a manageable safety profile at the highest dose ~

~ Updated clinical results expected in the first half of 2026 ~

LEXINGTON, Mass. and AMSTERDAM, Sept. 05, 2025 (GLOBE NEWSWIRE) -- uniQure N.V. (NASDAQ: QURE), a leading gene therapy company advancing transformative therapies for patients with severe medical needs, today announced initial safety and exploratory efficacy data from the first cohort of its Phase I/IIa trial of AMT-191, an investigational gene therapy for the treatment of Fabry disease. The preliminary data were presented at the International Congress of Inborn Errors of Metabolism (ICIEM) in Kyoto, Japan.

Fabry disease is a genetic lysosomal storage disorder caused by a deficiency of the α-galactosidase A (α-Gal A) enzyme, leading to toxic accumulation of globotriaosylsphingosine (lyso-Gb3) that can damage the kidneys, heart, nervous system, eyes, gut and skin. AMT-191 is designed as a one-time, intravenously administered, investigational AAV5-based gene therapy that incorporates a proprietary, highly potent promoter designed to achieve supraphysiological α-Gal A expression.

As of the July 24, 2025 study cutoff date, all four patients in the first cohort, Cohort A ($6x10^{13}$ genome copies/kilogram (gc/kg)), showed substantial increases in α-Gal A activity, ranging from 27- to 208-fold above the mean normal level[1]. Sustained elevated levels were observed in all four patients in the first cohort as of the study cutoff date, which was as long as 45 weeks post-treatment for the first treated patient and 12 weeks post-treatment for the most recently treated patient. All four patients were withdrawn from enzyme replacement therapy (ERT) and maintained stable plasma lyso-Gb3 levels through the cutoff date.

“These initial findings from the first cohort are encouraging, with all patients showing robust increases in α-Gal A activity and an ability to withdraw from ERT,” stated Walid Abi-Saab, M.D., chief medical officer of uniQure. “The early data highlight the potential of AMT-191 as a transformative one-time treatment option for people living with Fabry disease. I look forward to sharing additional data from our dose-finding study expected in the first half of 2026.”

Based on data observed to date, AMT-191 showed a manageable safety profile. At the $6x10^{13}$ gc/kg dose, two Serious Adverse Events (SAEs) unrelated to AMT-191 (stroke, diplopia), two related SAEs (chest pain, increased troponin), and one possibly related SAE (leptomeningeal enhancement) were observed in two patients. Additionally, one patient experienced an asymptomatic Grade 3 liver enzyme elevation that resolved with corticosteroid therapy. This event, classified as a dose-limiting toxicity per protocol, was not considered serious and did not require hospitalization. No loss of α-Gal A expression was observed in this patient.

Enrollment was completed in a second, lower dose cohort, Cohort B ($2x10^{13}$ gc/kg), consisting of three patients. As of the study cutoff date, all patients had less than three months of follow-up. To date, no SAEs were reported in the second cohort. uniQure expects to present updated results from the Phase I/IIa clinical trial in the first half of 2026.

About the Phase I/IIa Clinical Program of AMT-191

The Phase I/IIa clinical trial of AMT-191 is a multi-center, open-label trial being conducted in the United States consisting of three dosing cohorts of three or more adult male patients each receiving an intravenous infusion of AMT-191. Patients were not excluded from the trial based on pre-existing neutralizing anti-bodies to AAV5. Patients continue to receive their regular enzyme replacement therapy until meeting withdrawal criteria and will be followed for a period of 24 months. The trial will explore the safety, tolerability, and early signs of efficacy by measuring the expression of lysosomal enzyme α-Gal A. Additional details are available on www.clinicaltrials.gov (NCT06270316).

AMT-191 has been granted both Orphan Drug and Fast Track designation by the U.S. Food and Drug Administration.

About Fabry Disease

Fabry disease is an X-linked genetic disorder resulting from a deficiency of GLA. Based on a 2020 study published in the Journal of Therapeutics and Clinical Risk Management, the prevalence is estimated to be between one in 40,000 and one in 117,000 individuals. The current standard of care for Fabry disease is bi-weekly infusions of enzyme replacement therapy, a treatment with limited effectiveness in many patients due to poor cross-correction, with inefficient clearance of substrates in the target organs, in particular the kidney and the heart.

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. 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. 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. Examples of these forward-looking statements include, but are not limited to, statements regarding the potential of AMT-191 as a transformative one-time intravenously administered option for treating Fabry disease and the Company's plans to present updated Phase I/IIa clinical trial data for AMT-191 in the first half of 2026. The Company's actual results could differ materially from those anticipated in these forward-looking statements for many reasons. These risks and uncertainties include, without limitation, risks associated with the clinical results and the development and timing of the Company's programs; the Company's interactions with regulatory authorities, which may affect the initiation, timing and progress of clinical trials and pathways and timing for regulatory approval; the Company's ability to continue to build and maintain the company infrastructure and personnel needed to achieve its goals; the Company's effectiveness in managing current and future clinical trials and regulatory processes; the continued development and acceptance of gene therapies; the Company's ability to demonstrate the therapeutic benefits of its gene therapy candidates in clinical trials; the Company's ability to obtain, maintain and protect intellectual property; and the Company's ability to fund its operations and to raise additional capital as needed. 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 with the SEC on May 9, 2025 and July 29, 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 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] Normal range (1.38 – 8.66 nmol); mean normal of 3.57 nmol