uniQure Announces New Preclinical Data in Hemophilia A and Fabry Disease in Oral Presentations at the 22nd ASGCT Annual Meeting

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LEXINGTON, Mass. and AMSTERDAM, the Netherlands, May 02, 2019 (GLOBE NEWSWIRE) -- uniQure N.V. (NASDAQ: QURE), a leading gene therapy company advancing transformative therapies for patients with severe medical needs, will present today new preclinical data on its gene therapy candidates AMT-180 for the treatment of hemophilia A and AMT-190 for the treatment of Fabry disease. These data will be featured today in back-to-back oral presentations at the 22nd American Society for Gene and Cell Therapy (ASGCT) Annual Meeting in Washington D.C.

AMT-180 for Hemophilia A

Hemophilia A is an X-linked bleeding disorder resulting from a deficiency in coagulation Factor VIII that serves as a cofactor for Factor IX in the activation of the coagulation cascade. About 30 percent of the hemophilia A patient population develops inhibitors to Factor VIII over the course of the disease.

AMT-180 comprises a recombinant AAV5 vector incorporating a proprietary modified Factor IX hat, when activated through normal mechanisms, induces thrombin generation independently of Factor VIII.

Data from multiple *in vitro* and *in vivo* studies show that a single intravenous administration of AMT-180 results in dose-dependent, therapeutically meaningful Factor VIII-independent activity as measured by thrombin generation and one-stage clotting assay. AMT-180 is a differentiated approach that is suggested to be hepatocyte-friendly and non-thrombogenic based on the studies conducted to date and is expected to reduce and potentially prevent bleedings in hemophilia A patients with and without inhibitors.

AMT-180 Preclinical Data Findings

Proof-of-concept for AMT-180 was established through studies across two different animal models. The oral presentation at ASGCT features the following data:

- Preclinical studies in FVIII-depleted human plasma show that AMT-180 induced clinically relevant thrombin activation, and up to 29% of Factor VIII-independent activity, in plasma with and without inhibitors.
- The mechanistic proof-of-concept of AMT-180 was demonstrated in a hemophilia A mouse model, where a single intravenous administration of AMT-180 resulted in sustained, dose-dependent hemostatic effect as measured by one-stage clotting assay.
- The studies further demonstrate that AMT-180 shows activation kinetics similar to native FIX and is not hyperactive.
- A pilot study in non-human primates demonstrated that a single administration of AMT-180 resulted in sufficient FIX protein expression that translates to clinically relevant Factor VIII-independent activity in humans. No elevation of coagulation activation markers or signs of thrombi formation were observed.

“Data from these preclinical studies show the exciting potential of AMT-180 to provide clinically meaningful Factor VIII-independent activity after a one-time administration.” stated Sander van Deventer, M.D., Ph.D., chief scientific officer at uniQure. “We are particularly encouraged by the broad potential of AMT-180 in treating both patients with and without inhibitors, and the unique approach of AMT-180 that potentially circumvents durability issues because of its hepatocyte-friendly profile.”

AMT-190 for Fabry Disease

Fabry disease is an X-linked genetic disorder resulting from a deficiency of α-galactosidase A (α-gal or GLA). The current standard of care for Fabry disease is bi-weekly infusions of enzyme replacement therapy, a treatment that has shown not to be effective in many patients due to poor targeting of target organs such as the kidney and heart. In addition, a significant number of patients develop antibodies to the enzyme, α-gal or GLA.

AMT-190 is a novel AAV5 gene therapy approach for Fabry disease that comprises a recombinant AAV5 vector incorporating a proprietary, exclusively licensed, modified NAGA (ModNAGA) variant. AMT-190 provides expression of ModNAGA, which shows a high structural resemblance to α-gal. This approach may have several advantages over α-gal therapies, including higher stability in blood, better biodistribution in the target organs, secondary toxic metabolite reduction and improved cross-correction of neighboring cells. ModNAGA is also effective in the presence of α-gal antibodies.

Data from *in vitro* and *in vivo* studies show that AMT-190 has the potential to become a one-time treatment option that improves upon the enzyme replacement standard of care with more efficient uptake in the kidney and heart and an improved immunogenicity profile.

AMT-190 Preclinical Data Findings

Proof-of-concept for AMT-190 was established through multiple studies in wild-type and Fabry mice. The oral presentation at ASGCT features the following data:

- Preclinical *in vitro* studies demonstrated that the expression of ModNAGA results in GLA activity in cells and suggest that uptake of ModNAGA is mediated by the Mannose-6-phosephase (M6P) receptor.
- *In vivo* studies in wild-type mice show that a single intravenous administration of AMT-190 resulted in a ten- to twenty-fold higher GLA activity in the plasma compared to the control group, suggesting that AMT-190 has the potential to provide therapeutically relevant GLA activity in plasma and in target organs.
- These results were underscored by a study in GLA knock-out mice, demonstrating significantly increased GLA activity in plasma and significantly reduced Lyso-Gb3 in the target organs after a single dose of AMT-190. *In silico* and *in vitro* studies also show that the

modifications introduced into NAGA pose a very low immunogenicity risk.

“These data show that AMT-190 has the potential to be a differentiated, one-time treatment option that could be used by all Fabry patients,” added Dr. van Deventer. “We will continue to advance our preclinical research toward our goal of developing a best-in-class gene therapy for Fabry disease.”

An overview of the AMT-180 and AMT-190 preclinical data presented at ASGCT can be found on the Investor section of uniQure’s corporate website.

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 risk of cessation, delay or lack of success of any of our ongoing or planned clinical studies, our ability to advance our pipeline programs in hemophilia A and Fabry disease, our ability to move closer to providing potentially transformative therapies to patients and further demonstrate the importance of our industry leading technology platform and AAV manufacturing capabilities, and/or the development and regulatory approval of our product candidates in the United States or in Europe, whether AMT-180 proves to be hepatocyte-friendly or non-thrombogenic, or to reduce or prevent bleedings in hemophilia A patients with and without inhibitors, whether AMT-180 is able to provide clinically meaningful Factor VIII-independent activity after a one-time administration, whether AMT-180 is able to successfully treat patients with and without inhibitors, whether AMT-180 circumvents durability issues or proves to have a hepatocyte-friendly profile, whether AMT-190 has advantages over α-gal therapies including higher stability in blood, better biodistribution in the target organs, secondary toxic metabolite reduction or improved cross-correction of neighboring cells, whether ModNAGA is effective in the presence of α-gal antibodies or in patients both with and without inhibitors, whether AMT-190 becomes a one-time treatment option, improves upon enzyme replacement, proves to be superior to the current standard of care, has more efficient uptake in the kidney or heart, or has an improved immunogenicity profile, whether the uptake of ModNAGA is mediated by the Mannose-6-phosephase (M6P) receptor, whether AMT-190 provides therapeutically relevant GLA activity in plasma or in target organs, whether AMT-190 proves to be a differentiated, one-time treatment option that could be used by all Fabry patients, and whether we are able to achieve our goal of developing a best-in-class gene therapy for Fabry disease. 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, 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 Quarterly Report on Form 10-Q filed on April 29, 2019. 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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