Ultragenyx Announces the Publication of a Successful 96-Week Randomized, Placebo-Controlled Trial with Crossover Treatment of GENGLYCOS™ (also known as DTX401) AAV Gene Therapy in GSDIa in The Journal of Inherited Metabolic Disease

September 1, 2026

At Week 96, participants across treatment and crossover groups experienced mean reduction in daily cornstarch intake of 61% while maintaining glycemic control, with most participants achieving reduction of at least 50%

Complete elimination of nighttime cornstarch dosing observed in 33% of DTX401 treatment group and 42% of crossover group, while maintaining glycemic control

Analyses at Week 48 showed that 83% of DTX401-treated participants met or exceeded their own expectations for meaningful cornstarch reduction

NOVATO, Calif., Sept. 01, 2026 (GLOBE NEWSWIRE) -- Ultragenyx Pharmaceutical Inc. (NASDAQ: RARE) today announced the publication of 96-week data from its Phase 3 study of GENGLYCOS™ AAV gene therapy (pariglasgene brecaparvovec-opnr), also known as DTX401, for the treatment of glycogen storage disease type Ia (GSDIa) in *The Journal of Inherited Metabolic Disease*. GENGLYCOS was recently approved by the U.S. Food and Drug Administration (FDA) in patients ages eight and older with GSDIa.

“These results demonstrate the potential of gene therapy to provide greater stability in day-to-day life for patients with GSDIa and may help guard against the risk of severe hypoglycemia associated with missed doses of raw cornstarch," said Dr. John Mitchell, scientist in the Child Health and Human Development Program at the Research Institute of the McGill University Health Centre (The Institute), pediatric endocrinologist at the Montreal Children’s Hospital, lead author of the publication and an investigator on the study. “For me, the reduction in overnight cornstarch dosing will have the most meaningful impact by reducing sleep disruption, with patient-reported outcomes included in the publication underscoring the profound impact that cornstarch reductions may have on daily life. I view long-term outcomes from the 96-week period showing continued improvements as particularly important, offering valuable insight into how post-treatment management may continue to evolve and improve as clinical experience grows."

“The complete results from this Phase 3 study more fully capture the benefits of this gene therapy and the importance of providing patients the ability to breakdown glycogen to provide a source of glucose during fasting or times of increased metabolic demands,” said Eric Crombez, M.D., chief medical officer at Ultragenyx. “Most patients achieved cornstarch reductions that met or exceeded their own expectations, with substantially less overnight treatment burden and reduced dependence on the around-the-clock cornstarch need that defines life with this disease. Importantly, reducing cornstarch dependence while maintaining glycemic control indicates the establishment of the liver’s ability to regulate glucose production on its own, giving us confidence that the therapy is directly addressing the underlying cause of disease and offering protection from the risk of life-threatening hypoglycemia.”

Authors emphasize statistically significant and clinically meaningful reductions in cornstarch while maintaining glycemic control

As previously reported, the study met its primary endpoint with patients treated with DTX401 (n=20) experiencing a mean reduction in cornstarch of 41% at Week 48 compared to 10% reduction in the placebo group (n=24) ($p < 0.0001$). Data at Week 96 showed even greater improvements, with both the DTX401 group (n=20) and the crossover group (n=19) achieving a mean reduction in daily cornstarch intake of 61% from baseline. Participants in both groups also experienced statistically significant improvements in other cornstarch-related endpoints.

Additionally, 72% of participants in the crossover-DTX401 group and 67% of participants in the original DTX401 group achieved reductions of at least 50% in daily cornstarch intake by Week 96. In the manuscript, the authors noted that reductions within the crossover period are particularly meaningful, as that period more closely approximates anticipated patient management in a real-world setting.

Importantly, participants maintained low levels of hypoglycemia and improved levels in euglycemic range (70-120 mg/dL) throughout the second year of the study despite substantial reductions in daily cornstarch intake. Participants dosed with DTX401 also experienced improved normalized fasting tolerance in a controlled fasting challenge (CFC) through year 2 of the study, supporting the potential for protection from severe hypoglycemia (< 54 mg/dL).

Publication offers additional insights into nighttime treatment burden

The publication provides detailed analyses of nighttime cornstarch use, one of the most burdensome aspects of current GSDIa management.

Among participants requiring nighttime cornstarch at baseline:

- At Week 48, 50% of DTX401-treated participants eliminated at least one nighttime cornstarch dose compared with 7% of placebo-treated participants (p=0.031).
- At Week 96, 67% of participants in both treatment groups eliminated at least one nighttime cornstarch dose.
- By Week 96, 33% of original DTX401 participants and 42% of crossover-DTX401 participants had completely eliminated nighttime cornstarch dosing.

Despite substantial reductions in daily and nighttime cornstarch use, participants maintained glycemic control throughout the study, without inducing severe hypoglycemic episodes. These findings build upon previously reported reductions in nighttime cornstarch requirements and provide additional insight into the impact of DTX401 on overnight disease management.

Patient-reported outcomes support treatment effect as clinically meaningful

Authors detailed findings of a patient-centered analysis that showed the average reduction in daily cornstarch intake considered meaningful by participants at baseline was 45%. At Week 48, 83% of DTX401-treated participants met or exceeded their own baseline expectations for meaningful

reduction in cornstarch use, with continued improvements through Week 96.

At Week 48, 79% of DTX401-treated participants reported improvement in GSDIa on the Patient Global Impression of Change compared with 52% of placebo-treated participants (p=0.131); at Week 96, improvement was reported by 95% of crossover-DTX401 participants and 83% of original DTX401 participants.

The publication further characterizes how reducing cornstarch requirements affected overall nutritional management. At baseline, cornstarch accounted for nearly 50% of study participants' total caloric intake. Following treatment with DTX401, participants were able to transition to a more balanced, food-based diet closer to the U.S. Dietary Guidelines for the general population.

DTX401 was generally well tolerated with an acceptable safety profile

Consistent with previously reported findings, the authors concluded that DTX401 demonstrated an acceptable and manageable safety profile. The most common treatment-related adverse events were transient elevations in liver enzymes, which were generally nonserious and managed with prophylactic corticosteroids.

No AAV8 class effects of dorsal root ganglion toxicity, malignancy, or thrombotic microangiopathy were observed in the study through Week 96. Hypertriglyceridemia was observed in all study groups but more frequently following DTX401 treatment.

INDICATION

GENGLYCOS (pariglasgene brecaparvovec-opnr) is indicated to reduce daily cornstarch intake as an adjunct to nutritional management in adult and pediatric patients 8 years of age and older with glycogen storage disease type Ia (GSDIa).

This indication is approved under accelerated approval based on reduction in daily cornstarch intake. Continued approval for this indication may be contingent upon verification of clinical benefit in confirmatory trial(s).

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS
GENGLYCOS is contraindicated in patients with known severe hepatic fibrosis or cirrhosis.

WARNINGS AND PRECAUTIONS

Hypersensitivity and Infusion Reactions (IRs)

- Hypersensitivity reactions including anaphylaxis and IRs have occurred with GENGLYCOS treatment. Severe reactions have been reported. Monitor for signs and symptoms of hypersensitivity and IRs, including urticaria, flushing, hypotension, bronchospasm, dyspnea, chest tightness, nausea, vomiting, headache, abdominal pain, lightheadedness, flu-like symptoms, shivering, rash, and hypertension.
- Premedicate with acetaminophen and non-sedating antihistamines and administer GENGLYCOS according to recommended infusion rates. Monitor patients during and after completion of GENGLYCOS infusion as clinically indicated. If anaphylaxis or severe IR occurs, pause GENGLYCOS infusion immediately and initiate medical treatment as clinically indicated, monitoring as needed. For mild to moderate IRs, consider slowing or temporarily interrupting the infusion, and administer symptomatic treatment as clinically indicated. The infusion may be restarted at half the prior rate upon resolution of symptoms.
- Medical support measures, including cardiopulmonary resuscitation equipment and medications for the treatment of anaphylaxis (e.g., epinephrine, antihistamines, corticosteroids), should be available during GENGLYCOS administration.

Hepatotoxicity

- Immune-mediated hepatotoxicity, with elevated alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) levels, has occurred with GENGLYCOS. Avoid use in patients with preexisting hepatic impairment or acute hepatic viral infection.
- Prior to GENGLYCOS infusion, evaluate liver-related medical history and assess liver function by clinical examination and laboratory testing. Advise patients to immediately report signs and symptoms of hepatotoxicity, including fatigue, jaundice, dark urine, nausea, vomiting, and right upper quadrant pain. Administer corticosteroids to all patients after GENGLYCOS infusion in order to mitigate hepatic reactions. Elevated transaminases may require adjustment of the corticosteroid treatment regimen, including increased dose or prolongation of the corticosteroid taper.
- Monitor transaminase levels for the first 6 months after GENGLYCOS administration. Continue to monitor transaminases in all patients who develop transaminase elevations, until transaminases return to baseline or as clinically indicated.

Adrenal Insufficiency

- Adrenal insufficiency, including serious events, has been reported in patients receiving GENGLYCOS during corticosteroid use and tapering.
- Signs and symptoms of adrenal insufficiency include fatigue, weakness, anorexia, nausea, vomiting, hypotension, hyponatremia, and hypoglycemia. Adrenal crisis may present as severe hypotension, acute abdominal pain, or loss of consciousness.
- Monitor patients for signs and symptoms of adrenal insufficiency and adrenal crisis after GENGLYCOS administration during and after corticosteroid therapy and tapering. Taper corticosteroid therapy gradually. Do not abruptly discontinue corticosteroid therapy.

AAV Vector Integration and Risk of Tumorigenicity

- There is a theoretical risk of tumorigenicity due to integration of AAV vector DNA into the genome.
- GENGLYCOS is composed of a recombinant, non-replicating AAV8 vector whose DNA persists largely in episomal form. Random integration of recombinant AAV-vector DNA into human DNA has been reported with AAV gene therapies. The clinical relevance of individual integration events is unknown, but it is acknowledged that individual integration events could potentially contribute to a risk of tumorigenicity. If a tumor develops in a patient receiving GENGLYCOS, health care providers should contact and report the tumor to Ultragenyx Pharmaceutical Inc. at 1-888-756-8657.

Adverse Reactions

- Seven serious adverse events were observed in the Primary Efficacy Analysis Period (PEAP) of Study 1 (Weeks 1-48), including

anaphylaxis/infusion reaction (2), adrenal insufficiency (2), high lactate level (2) and hypoglycemia (1).
- The most common adverse reactions during the PEAP of Study 1 (occurring in ≥10% of patients) with higher frequency in GENGLYCOS compared to placebo were ALT/AST Enzyme elevated (71%), Nausea (38%), Headache (24%), Hypertriglyceridemia (29%), Adrenal Insufficiency (24%), Constipation (19%), Hyperglycemia (14%), Acne/Dermatitis Acneiform (19%), Cushingoid Features (14%), and Anaphylaxis (10%).

DRUG INTERACTIONS

Vaccinations

- Vaccine schedules may need to be adjusted for immunosuppressive therapy, and vaccines should be avoided 1 month prior to GENGLYCOS administration.

USE IN SPECIFIC POPULATIONS

Pregnancy

- GENGLYCOS should not be used during pregnancy. There are no data on the use of GENGLYCOS in pregnant women. It is unknown whether GENGLYCOS can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity.

Contraception

- Women of childbearing potential should use effective contraception for at least 12 months after administration of GENGLYCOS.
- For 6 months after administration of GENGLYCOS, men must not donate semen, and men of reproductive potential and their female partners must prevent or postpone pregnancy using an effective form of contraception.

ADDITIONAL PATIENT COUNSELING INFORMATION
Vector Shedding

- Inform patients/caregivers that vector distribution in blood and vector shedding in urine, stool, and saliva can occur after GENGLYCOS infusion. Advise patients/caregivers on proper hygiene when handling patient body waste. These precautions should be followed for 3 months after GENGLYCOS infusion.

Report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088. You may also report side effects to Ultragenyx Pharmaceutical Inc. at 1-888-756-8657.

Please see the full Prescribing Information for GENGLYCOS.

About the Phase 3 GlucoGene study
The 48-week randomized, double-blind, placebo-controlled study treated 46 participants aged eight years and older with DTX401 (1.0 x 10^13 GC/kg dose measured by ddPCR) or placebo. There were 44 participants in the modified intention-to-treat (mITT) population providing efficacy data within the Week 48 analysis period following treatment with DTX401 (n=20) or placebo (n=24). At Week 48, eligible participants crossed over and received the alternate treatment. After crossover, participants continued to be followed with analyses conducted at Week 96 and Week 144. After study completion, participants will be offered enrollment into the GSDIa Disease Monitoring Program (DMP) where they will be followed for 10 years post-DTX401 infusion.

About Glycogen Storage Disease Type Ia (GSDIa)
GSDIa is an ultra-rare, serious, and life-threatening disease due to an inborn error of carbohydrate metabolism caused by pathogenic variants of the *G6PC* gene, which encodes G6Pase, an enzyme that is critical for the release of glucose from glycogen and other metabolic sources. Deficiency of G6Pase activity results in severe hypoglycemia during periods of fasting between meals and during the night along with excess hepatic glycogen storage, metabolic derangements and other disease related complications. Cornstarch is critical in the management of GSDIa throughout the day and night in providing an exogenous source of glucose to help avoid sudden and severe drops in plasma glucose levels; however, current management strategies carry a significant burden to patients and families. GSDIa affects approximately 1,500-2,500 patients in the U.S. and 6,000-8,000 worldwide within commercially accessible geographies.

About Ultragenyx
Ultragenyx is a biopharmaceutical company committed to bringing novel products to patients for the treatment of serious rare and ultra-rare genetic diseases. The company has built a diverse portfolio of approved therapies and product candidates aimed at addressing diseases with high unmet medical need and clear biology for treatment, for which there are typically no approved therapies treating the underlying disease.

The company is led by a management team experienced in the development and commercialization of rare disease therapeutics. Ultragenyx's strategy is predicated upon time- and cost-efficient drug development, with the goal of delivering safe and effective therapies to patients with the utmost urgency.

For more information on Ultragenyx, please visit the company's website at: www.ultragenyx.com.

Forward-Looking Statements and Use of Digital Media
Except for the historical information contained herein, the matters set forth in this press release, including statements regarding the interpretation, significance and potential implications of the published 96-week Phase 3 data and analyses for GENGLYCOS (also known as DTX401); the clinical meaningfulness and durability of reductions in daily and nighttime cornstarch requirements; the ability of patients to maintain glycemic control and improve fasting tolerance following treatment; the potential for GENGLYCOS to protect against severe hypoglycemia, reduce treatment burden, improve nutritional management and provide other patient benefits; the safety and tolerability of GENGLYCOS; expectations regarding continued follow-up of study participants and the design, enrollment, timing, conduct and results of the GSDIa Disease Monitoring Program and other post-marketing requirements; Ultragenyx's ability to confirm clinical benefit, satisfy FDA requirements and maintain accelerated approval for GENGLYCOS; and estimates of the prevalence of GSDIa and the potential patient population for GENGLYCOS, are forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. Such forward-looking statements involve substantial risks and uncertainties that could cause actual results to differ significantly from those expressed or implied by the forward-looking statements. Such risks and uncertainties include, among others, the risk that results from a limited number of study participants, including crossover

and other analyses, may not be replicated or predictive of future or real-world results; the risk that longer-term follow-up may not demonstrate sustained efficacy, durability, safety or patient benefit; risks related to serious or undesirable side effects, including risks associated with AAV gene therapy; Ultragenyx's ability to complete post-marketing requirements within required timeframes and confirm clinical benefit; the risk that the FDA may modify the approved indication or impose additional requirements, or may withdraw accelerated approval if clinical benefit is not confirmed or post-marketing requirements are not satisfied; and other matters that could affect the availability or commercial potential of Ultragenyx's products and product candidates. Ultragenyx undertakes no obligation to update or revise any forward-looking statements.

For a further description of the risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, as well as risks relating to the business of Ultragenyx in general, see Ultragenyx's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on August 5, 2026, and its subsequent periodic reports filed with the SEC.

In addition to its SEC filings, press releases and public conference calls, Ultragenyx uses its investor relations website and social media outlets to publish important information about the company, including information that may be deemed material to investors, and to comply with its disclosure obligations under Regulation FD. Financial and other information about Ultragenyx is routinely posted and is accessible on Ultragenyx's Investor Relations website (https://ir.ultragenyx.com/) and LinkedIn website (https://www.linkedin.com/company/ultragenyx-pharmaceutical-inc-/).

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