Ultragenyx Announces U.S. FDA Approval of GENGLYCOS™ Gene Therapy, the First-Ever FDA-Approved Treatment Designed to Treat the Underlying Cause of Glycogen Storage Disease Type Ia (GSDIa)

August 19, 2026

GENGLYCOS is the first gene therapy approval, and fifth FDA approval overall, for the company

Approval provides a long-awaited first-ever option to reduce the burden of care associated with GSDIa

Ultragenyx received a Priority Review Voucher upon approval

Ultragenyx to host conference call on 8/19/26 at 6:00 p.m. Eastern Time

NOVATO, Calif., Aug. 19, 2026 (GLOBE NEWSWIRE) -- Ultragenyx Pharmaceutical Inc. (NASDAQ: RARE) today announced that the U.S. Food and Drug Administration (FDA) granted accelerated approval for GENGLYCOS™ (pariglasgene brecaparvovec-opnr), also known as DTX401, in adult and pediatric patients eight years and older with glycogen storage disease type Ia (GSDIa).

“The approval of GENGLYCOS fulfills our commitment to provide the first therapy that directly targets the root cause of GSDIa. The reduced reliance on cornstarch, experienced by patients in our clinical studies, demonstrates this gene therapy’s ability to establish the normal breakdown of glycogen to produce glucose during fasting or episodes of metabolic stress. This ability to regulate glucose has alleviated the disease burden and has the potential to mitigate the risk of severe or life-threatening hypoglycemia for these patients,” said Eric Crombez, M.D., chief medical officer at Ultragenyx. “As our first gene therapy approval, GENGLYCOS represents an important achievement for our company and the realization of the promise of a powerful new tool to deliver transformative medicines for people living with rare diseases.”

GSDIa is an ultra-rare genetic metabolic disorder caused by a deficiency of the enzyme needed to release glucose from the liver to the bloodstream. The deficiency reduces the liver’s ability to control glucose levels and is associated with potentially life-threatening hypoglycemia episodes and other serious complications, requiring rigorous nutritional management that involves a burdensome, around-the-clock regimen of raw cornstarch intake as an oral glucose replacement therapy. Glucose control with cornstarch is crude with large swings in glucose, and patients instead end up spending a large fraction of their day significantly hyperglycemic to avoid hypoglycemic episodes. GSDIa affects 1,500-2,500 patients in the U.S. and 6,000-8,000 worldwide within commercially accessible geographies.

“Day-to-day management of GSDIa requires a relentless regimen of raw cornstarch and strict dietary management that can be extraordinarily demanding for patients and families. Even with meticulous adherence to this regimen, patients must be perfect. Any missed cornstarch puts patients at risk of severe hypoglycemia, seizures, and even death,” said David Weinstein, M.D., MMSc, one of the world's leading GSDIa experts. “The approval of GENGLYCOS represents a major step forward for the GSDIa community and reflects almost 30 years of work and scientific progress aimed at improving safety and the quality of life of people living with this disease.”

“For families affected by GSDIa, every day revolves around strict schedules, overnight vigilance, and the constant worry that a missed meal or dose of cornstarch could trigger life-threatening hypoglycemia,” said David and Wendy Feldman, co-founders and current Board members at The Children’s Fund for Glycogen Storage Disease Research. “This approval is an incredibly meaningful milestone for a community that has spent decades hoping, advocating, and helping advance the research for new treatment options that could ease the burdens of this disease.”

Clinical Program and Post-Marketing Study Requirements Supporting Accelerated Approval of GENGLYCOS

The approval of GENGLYCOS is based on positive data from the 48-week randomized, double-blind, placebo-controlled Phase 3 GlucoGene study which treated 46 participants aged eight years and older with DTX401 (1.0 x 10^13 GC/kg dose) or placebo, showing a reduction in the cornstarch requirements in the treated group ($p<0.001$). 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.

As part of accelerated approval, Ultragenyx has agreed to provide two years of safety and efficacy clinical data from open-label commercial treatment of 50 patients and 20 control patients through enhancement of its existing GSDIa Disease Monitoring Program (DMP). The control group will consist of patients who sought commercial treatment but cannot be treated with GENGLYCOS due to the presence of anti-AAV8 antibodies. The study will provide more data to support the reduction in cornstarch clinical burden, fasting tolerance, and other measures in a post-marketing setting where patients can know their immediate glucose levels, and their cornstarch and diet can be managed more promptly by their physician. The DMP will also evaluate previously treated clinical trial participants as well as these new commercial patients for a total of 10 years.

Enabling Access for Eligible Patients

Ultragenyx will provide support to help enrolled patients and caregivers navigate access to treatment through its UltraCare® program, which now includes specially trained UltraCare® Gene Therapy Guides to help understand insurance coverage, assist in obtaining treatment support, and answer questions about the treatment process. Dedicated in-house UltraCare Gene Therapy Guides are available Monday through Friday from 9 a.m. to 8 p.m. Eastern Time at 888-756-8657. More information is available at www.ultracaresupport.com.

GENGLYCOS will be available through a national network of Qualified Treatment Centers (QTCs) with specialized expertise and training to safely administer gene therapy.

GENGLYCOS is manufactured entirely at Ultragenyx’s Gene Therapy Manufacturing Facility (GTMF) in Bedford, Mass., strengthening the Company’s ability to scale production of high-quality gene therapy products and deliver them to patients as efficiently as possible.

More information will be available at www.genglycos.com.

This approval reflects the work of a remarkable team spanning many years and organizations. Ultragenyx is deeply grateful to the patients, families, and clinical investigators who made our clinical studies possible; Dr. David Weinstein, whose scientific and clinical leadership laid critical groundwork across early research and clinical trials; Dr. Janice Chou for her early work at NIH, and the team from Dimension Therapeutics. Their collective commitment and perseverance have transformed a scientific vision into a new therapeutic option for patients.

Investor Conference Call and Webcast Information

Ultragenyx will host a conference call today at 6:00 p.m. Eastern Time / 3:00 p.m. Pacific Time to discuss the approval of GENGLYCOS. The live and replayed webcast of the call will be available through the company's website at https://ir.ultragenyx.com/events-presentations.

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 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 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 therapies to patients for the treatment of serious rare and ultra-rare genetic diseases. The company has built a diverse portfolio of approved medicines and treatment candidates aimed at addressing diseases with high unmet medical need and clear biology, 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 commercial launch, availability and market acceptance of GENGLYCOS; Ultragenyx's ability to manufacture GENGLYCOS at its gene therapy manufacturing facility, scale production and supply GENGLYCOS to Qualified Treatment Centers; patient access to GENGLYCOS, including insurance coverage and reimbursement; the safety, efficacy, durability and potential benefits of GENGLYCOS; estimates of the number of patients with GSDIa and the potential commercial opportunity for GENGLYCOS; the design, enrollment, timing, conduct and results of the post-marketing Disease Monitoring Program and other post-marketing requirements; and Ultragenyx's ability to satisfy FDA requirements and maintain accelerated approval 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, risks and uncertainties related to the commercial launch and market acceptance of GENGLYCOS; the ability to identify eligible patients and establish and support a network of Qualified Treatment Centers; uncertainty related to insurance coverage and reimbursement; risks related to serious or undesirable side effects, including risks associated with AAV gene therapy; manufacturing risks, including Ultragenyx's limited experience operating its own manufacturing facility and the ability to manufacture and supply GENGLYCOS in sufficient quantities and in compliance with regulatory requirements; Ultragenyx's ability to complete the post-marketing Disease Monitoring Program and other post-marketing requirements within required timeframes and to 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; smaller than anticipated market opportunities; competition from other therapies or products; product liability; regulatory scrutiny; 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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