Ultragenyx Announces Positive Longer-Term Data Demonstrating Treatment with UX111 Gene Therapy Results in Sustained, Significant Reductions in CSF-HS and Continued Meaningful Improvements in Clinical Function Across Multiple Developmental Domains in Children with Sanfilippo Syndrome (MPS IIIA)

February 3, 2026

Data represents up to 8.5 years of follow-up and are consistent across age, dose, and genotype

BLA resubmitted to U.S. FDA in January 2026; Company expects up to six-month review period per FDA guidelines

NOVATO, Calif., Feb. 03, 2026 (GLOBE NEWSWIRE) -- Ultragenyx Pharmaceutical Inc. today announced new long-term data from clinical studies evaluating UX111 (rebisufligene etisparvovec), an investigational AAV9 gene therapy for Sanfilippo syndrome Type A (MPS IIIA), a fatal neurodegenerative lysosomal storage disorder. The results demonstrate substantial and durable biomarker improvements and meaningful functional benefits compared with natural history, with consistent and highly statistically significant results across age and disease severity. UX111 was well-tolerated and the safety profile remains favorable.

“These data continue to demonstrate a remarkable and unprecedented separation from the natural history of Sanfilippo syndrome through more than eight years of follow-up, with children in their teens retaining skills at an age when many of their untreated peers have sadly lost their most basic abilities and succumbed to this disease,” Emil D. Kakkis, M.D., Ph.D., chief executive officer and president of Ultragenyx. “Our studies consistently show that reductions in heparan sulfate are associated with meaningful clinical benefits across multiple domains, underscoring the urgency to bring forward a treatment for families who currently have no options to stop or delay the heartbreaking and inevitable progression and loss of function associated with this disease.”

The data will be delivered in an oral presentation, *Treatment with UX111 Reduced Cerebrospinal Fluid (CSF) Heparan Sulfate (HS) Exposure and Stabilized or Improved Functioning across Dose, Age, and Stage of MPS IIIA*, at the WORLD*Symposium* ™ 2026 on Friday, February 6 at 8 a.m. PST.

Clinical Improvements in Functional Abilities Compared to Natural History
Cognitive function, expressive and receptive communication, and fine and gross motor skills were measured using Bayley-III and compared to natural history data from untreated patients with reported rapid progressor phenotypes. Children under two years of age or with earlier stage disease at the time of treatment (n=17) demonstrated a +23.2 point ($p<0.0001$) treatment effect in the mean Bayley-III cognitive raw score compared to natural history data during 24-60 months of age.

In addition to cognitive function, clinical improvements were also observed across the other four subtests compared to natural history:

- Receptive communication (8.1-point improvement; p=0.0076)
- Expressive communication (11.1-point improvement; p=0.0008)
- Fine motor (9.0-point improvement; p=0.0026)
- Gross motor (3.9-point improvement; p=0.070)

On separate caregiver-reported outcome utilizing Vineland 2, there were comparable improvements in the communication, motor, and personal subdomains.

“There is an unmet clinical need for a therapy for this devastating disease,” said Kevin Flanigan, M.D., director of the Center for Gene Therapy at Nationwide Children’s Hospital in Columbus, Ohio, and a principal investigator on the study. “These results provide evidence of benefit from this gene transfer therapy, especially when delivered early.”

Eight children reached a 36-month cognitive developmental age, enabling higher-level testing—none of the natural history patients reached this milestone.

Functional Skill Retention in Later-Stage Children
Patients with older age or having more advanced disease at the time of treatment (n=10), showed retention of functional abilities in at least one of three areas at the time of last assessment that exceed typical decline patterns in untreated children with Sanfilippo syndrome Type A. Specifically:

- All retained communication (verbal or non-verbal) at last assessment, with a median age of 9.70 years (5.7, 15.8); median age of loss in untreated patients is ~7.6 years of age.
- 9/10 retained independent ambulation at last assessment, with a median age of 9.05 years (5.7, 15.8); median age of loss in natural history is ~11.3 years.
- 9/10 maintained the ability to eat by mouth and/or self-feed, with a median age of 9.05 years (5.7, 15.8 max).

These findings are clinically relevant as these functions progressively worsen and are eventually lost in late childhood and early adolescence.

Significant and Durable Reduction in CSF Heparan Sulfate
Levels of CSF-HS decreased within the first month following treatment with UX111 ($3x10^{13}$ vg/kg) in the overall efficacy set (N=27), regardless of age or stage of disease progression at the time of treatment. As of the September 2025 cutoff date, the median reduction in CSF-HS exposure was

63.98% (p<0.001). The majority of children treated (88.2% of younger patients and 81.5% of the overall efficacy set) achieved a 50% or greater reduction.

Safety profile remains favorable

UX111 was generally well tolerated across all doses (N=33), including the highest dose of $3x10^{13}$ vg/kg, with a median follow-up 4.8 years (range 0.6–8.5). The most frequently reported treatment-emergent adverse events (TEAEs) were elevations in liver enzymes. Treatment-related adverse events were mostly mild or moderate and resolved spontaneously. No participants experienced infusion-related hypersensitivity or anaphylaxis, and no incidences of thrombotic microangiopathy (TMA), myocarditis, dorsal root ganglion (DRG) toxicity, or malignancy were associated with treatment.

BLA resubmitted to FDA with PDUFA date expected in Q3

These longer-term data were included in the resubmitted Biologics License Application (BLA) to the U.S. Food and Drug Administration (FDA) seeking accelerated approval for UX111. The company anticipates up to a 6-month review period from the date of resubmission per FDA regulations, with a PDUFA date expected in the third quarter of 2026.

About UX111 (rebisufligene etisparvovec)

UX111 (rebisufligene etisparvovec) is a novel in vivo AAV9 gene therapy in Phase 1/2/3 development for Sanfilippo syndrome type A (MPS IIIA), a rare fatal lysosomal storage disease with no approved treatment that primarily affects the brain. The therapy is designed to address the underlying sulfamidase (SGSH) enzyme deficiency responsible for abnormal accumulation of heparan sulfate, a glycosaminoglycan, in the brain that results in progressive cell damage and neurodegeneration. UX111 is dosed in a one-time intravenous infusion using a self-complementary AAV9 vector to deliver a functional copy of the SGSH gene to cells. These transduced cells then secrete the functional enzyme into the tissue fluid where it can be taken up by surrounding neurons and other cells. The enzyme is taken up efficiently into other cells and is then routed to the lysosome where it can reduce the accumulation of the heparan sulfate HS and prevent the progression of lysosomal storage and consequential injury that occurs in untreated patients. The product was originally developed by Abeona Therapeutics and transferred to Ultragenyx to complete development. The UX111 program has received Regenerative Medicine Advanced Therapy, Fast Track, Rare Pediatric Disease, and Orphan Drug designations in the U.S., and PRIME and Orphan medicinal product designations in the EU.

About the UX111 Clinical Program

The *Transpher A* study (NCT02716246) has enrolled and treated 28 patients across 3 dose Cohorts at 5 sites in 3 countries. The high dose Cohort 3 ($3x10^{13}$ vg/kg) consists of 22 patients, and 17 are in the modified intent-to-treat (mITT) group. The mITT group is defined as patients who were either up to age 2 years old, or patients older than 2 years with a cognitive developmental quotient of 60 or above at time of enrollment. These patients received the highest dose of UX111.

A separate study (NCT04088734) enrolled five patients. All participants received the highest dose of $3x10^{13}$ vg/kg.

Subjects who participated in either clinical study were invited to enroll into a long-term follow-up study (NCT04360265). The *Transpher A* and long-term follow-up studies are ongoing, and patients will continue to be followed for a minimum of 5 years following treatment with UX111.

About Sanfilippo Syndrome Type A (MPS IIIA)

Sanfilippo syndrome Type A (MPS IIIA) is a rare, fatal lysosomal storage disease with no approved treatment that primarily affects the brain and is characterized by rapid neurodegeneration, with onset in early childhood. Children with MPS IIIA present with global developmental delay which eventually leads to progressive cognitive, language and motor decline, behavioral abnormalities and early death with a median life expectancy of 15 years in the rapid progressor form of MPS IIIA. MPS IIIA is estimated to affect approximately 3,000 to 5,000 patients in commercially accessible geographies. MPS IIIA is caused by biallelic pathogenic variants in the *SGSH* gene that lead to a deficiency in the sulfamidase (SGSH) enzyme responsible for breaking down heparan sulfate, a sulfated glycosaminoglycans, which accumulate in cells throughout the body primarily manifesting in the observed rapid neurodegeneration that is associated with the disorder.

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 related to Ultragenyx's ability to provide the requested documentation and address the comments in the CRL to the satisfaction of the FDA, the development, timing and progress of UX111, including the timing of FDA acceptance of the BLA resubmission and the timing of FDA review of any such resubmission, the timing and outcome of any FDA inspections related to UX111, the timing of future regulatory interactions related to UX111, including the outcome of the BLA resubmission, business plans and objectives for UX111, expectations regarding the tolerability and safety of UX111, and future clinical and regulatory developments for UX111 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 our clinical development programs, collaboration with third parties, future results, performance or achievements to differ significantly from those expressed or implied by the forward-looking statements. Such risks and uncertainties include, among others, the uncertainty of clinical drug development and unpredictability and lengthy process for obtaining regulatory approvals, the ability of the company to successfully develop UX111, the company's ability to achieve its projected development goals in its expected timeframes, risks related to adverse side effects, risks related to reliance on third party partners to conduct certain activities on the company's behalf, smaller than anticipated market opportunities for the company's products and product candidates, manufacturing risks, our limited experience in operating our own manufacturing facility, the ability of the company and its third party manufacturers to comply with regulatory requirements, competition from other therapies or products, and other matters that could affect sufficiency of existing cash, cash equivalents and short-term investments to fund operations, the company's future operating results and financial performance, the timing of clinical trial activities and reporting results from same, and the availability or commercial potential of Ultragenyx's products and drug 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 November 4, 2025, 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-/).

Ultragenyx Contacts

Investors
Joshua Higa
ir@ultragenyx.com

Media
Jess Rowlands

media@ultragenyx.com