Ultragenyx Receives Complete Response Letter from FDA for UX111 AAV Gene Therapy to Treat Sanfilippo Syndrome Type A (MPS IIIA)

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Complete Response Letter (CRL) cited specific chemistry, manufacturing and controls (CMC) related observations that are resolvable

FDA clinical reviews acknowledged that the clinical data are robust and biomarker data are supportive

NOVATO, Calif., July 11, 2025 (GLOBE NEWSWIRE) -- Ultragenyx Pharmaceutical Inc. (NASDAQ: RARE), today announced that the U.S. Food and Drug Administration (FDA) has issued a Complete Response Letter (CRL) for its Biologics License Application (BLA) for UX111 (ABO-102) AAV gene therapy as a treatment for patients with Sanfilippo syndrome type A (MPS IIIA).

“Our goal is to get UX111 to patients as quickly as possible knowing how critical this first therapy is to the Sanfilippo community. We have been diligently responding to the recent CMC observations and our priority is to resolve them so that we can resubmit the BLA as soon as possible,” said Emil D. Kakkis, M.D., Ph.D., chief executive officer and president of Ultragenyx. “We believe the CMC observations are readily addressable and many have already been addressed. While the CRL will delay the potential approval of UX111 to 2026, we are working with urgency to respond and resubmit.”

In the CRL, the FDA requested that the company provide additional information and improvements related to specific aspects of CMC and observations from the recently completed manufacturing facility inspections. The company believes that these observations are readily addressable, related to facilities and processes, and are not directly related to the quality of the product. The company will be working with the FDA over the next few months to resolve the observations. Once resolution is achieved, the company expects to resubmit the BLA and anticipates up to a 6-month review period to follow the resubmission.

Clinical review had been ongoing and the FDA has acknowledged that the neurodevelopmental outcome data provided to date are robust and the biomarker data provide additional supportive evidence. The CRL did not note any review issues related to the clinical data package nor clinical inspections, and asked that updated clinical data from current patients be included in the resubmission.

About UX111
UX111 is a novel in vivo 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 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 produce the enzyme and secrete it to be taken up by other brain cells, cross-correcting the enzyme deficiency. 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. If approved, the product will be commercialized with Ultragenyx’s existing metabolic disease team seeing the same biochemical genetics doctors.

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. MPS IIIA is estimated to affect approximately 3,000 to 5,000 patients in commercially accessible geographies with a median life expectancy of 15 years. 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 glycosaminoglycans, which accumulate in cells throughout the body resulting in the observed rapid neurodegeneration that is associated with the disorder.

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 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 resubmission of the BLA 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 potential Type A meeting, the outcome of any 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 May 7, 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-/).

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