



Ultragenyx Receives Breakthrough Therapy Designation for GTX-102 in Angelman Syndrome

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Phase 3 Aspire study enrollment on track to complete in 2025

Aurora study to evaluate GTX-102 in other Angelman syndrome genotypes and ages expected to initiate later this year

NOVATO, Calif., June 27, 2025 (GLOBE NEWSWIRE) -- Ultragenyx Pharmaceutical Inc. (NASDAQ: RARE), today announced that it has received Breakthrough Therapy Designation from the U.S. Food and Drug Administration (FDA) for GTX-102 (apazunersen) as a treatment for Angelman syndrome.

"FDA Breakthrough Therapy Designation underscores both the urgent need for an effective treatment for patients and families affected by Angelman syndrome and the clinically meaningful results demonstrated to date with GTX-102," said Eric Crombez, M.D., chief medical officer at Ultragenyx. "Based on the strength of the Phase 2 data and with strong support and interest from the Angelman syndrome community, our Phase 3 *Aspire* study is rapidly enrolling across our global sites. We look forward to advancing GTX-102 through the development process as rapidly as possible to bring this potential treatment to patients."

The FDA's decision is based on preliminary clinical evidence including positive data from the Phase 1/2 study in 74 patients (4-17 years of age) with a full maternal *UBE3A* gene deletion, that showed participants have made consistent developmental gains with rapid, sustained and continuing improvements across multiple symptom domains when treated for up to 3 years. Breakthrough Therapy Designation aims to expedite the development and review of drugs that are intended to treat serious or life-threatening diseases and whose preliminary clinical evidence indicates that the drug may demonstrate substantial improvement on one or more clinically significant endpoints over existing therapies.

Enrollment in the global Phase 3 *Aspire* study ([NCT06617429](https://clinicaltrials.gov/ct2/show/study/NCT06617429)) began in December 2024 and is expected to enroll approximately 120 children ages four to 17 with Angelman syndrome with a genetically confirmed diagnosis of full maternal *UBE3A* gene deletion. The *Aurora* study will evaluate GTX-102 across other Angelman syndrome genotypes and ages and is expected to initiate in the second half of 2025. Families can learn more by visiting www.ultraclinicaltrials.com.

About GTX-102 (apazunersen)

GTX-102 (apazunersen) is an investigational antisense oligonucleotide (ASO) therapy delivered via intrathecal administration and designed to target and inhibit expression of the *UBE3A antisense transcript (UBE3A-AS)* to prevent silencing of the paternally inherited allele of the *UBE3A* gene and reactivate expression of the deficient protein. GTX-102 has been granted Breakthrough Therapy Designation, Orphan Drug Designation, Rare Pediatric Disease Designation, and Fast Track Designation from the FDA and Orphan Designation and PRIME designation from the EMA.

About Angelman Syndrome

Angelman syndrome is a rare, neurogenetic disorder caused by loss-of-function of the maternally inherited allele of the *UBE3A* gene. The maternal-specific inheritance pattern of Angelman syndrome is due to genomic imprinting of *UBE3A* in neurons of the central nervous system (CNS), a naturally occurring phenomenon in which the maternal *UBE3A* allele is expressed and the paternal *UBE3A* is not. Silencing of the paternal *UBE3A* allele is regulated by the *UBE3A-AS*, the intended target of GTX-102. In almost all cases of Angelman syndrome, the maternal *UBE3A* allele is either missing or mutated, resulting in limited to no protein expression. This condition is generally not inherited but instead occurs spontaneously. It is estimated to affect approximately 60,000 people in commercially accessible geographies.

Angelman syndrome is a lifelong neurodevelopmental disorder that causes cognitive impairment, motor impairment, balance issues and debilitating seizures. Some individuals with Angelman syndrome are unable to walk and most do not speak. Anxiety and disturbed sleep can be serious challenges in individuals with Angelman syndrome. Although individuals with Angelman syndrome have a normal lifespan, they require continuous care and are unable to live independently. Angelman syndrome is not a degenerative disorder, but the loss of the *UBE3A* protein expression in neurons results in abnormal communications between neurons. Angelman syndrome is often misdiagnosed as autism or cerebral palsy. There are no currently approved therapies for Angelman syndrome; however, several symptoms of this disorder can be reversed in adult animal models of Angelman syndrome, suggesting that improvement of symptoms can potentially be achieved at any age.

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 expectations and projections regarding its future operating results and financial performance, business plans and objectives for GTX-102, expectations regarding the tolerability and safety of GTX-102, and future clinical and regulatory developments for GTX-102 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 GTX-102, the company's ability to achieve its projected development goals in its expected timeframes, the risk that results from earlier studies may not be predictive of future study results, 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, 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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