These Clinical Study Results are provided for informational purposes only.

This lay summary is a brief summary of the main results from a clinical study. The study listed may include approved and non-approved uses, formulations or treatment regimens. It is not intended to promote any product or indication and is not intended to replace the advice of a healthcare professional. The results reported in any single clinical trial may not reflect the results obtained across the full clinical development program. Only a physician can determine if a specific product is the appropriate treatment for a particular patient. If you have questions, please consult a health care professional. Before prescribing any product, healthcare professionals should consult the regional approved product labeling for indications and proper use of the product.

Clinical study results

A study to learn about the safety of GTX-102 in children with Angelman syndrome (AS)

Thank you!

Thank you to the participants and caregivers who took part in the clinical study for GTX-102. Ultragenyx, the sponsor of this study, is grateful and believes it is important to share the results with the participants and their families.

By taking part in this study, the participants helped the researchers learn more about using GTX-102 in people with AS.

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Why was this study needed?

Researchers designed this study, **GTX-102-001**, to learn about the safety of different doses of GTX-102 in children with Angelman syndrome (AS). Because this study was the first time that people received GTX-102, the main goal was not to learn how well GTX-102 worked on AS symptoms.

What causes AS?

AS is caused by a non-working or missing (deletion) gene called ubiquitin protein ligase E3A, or ***UBE3A***, which makes a protein that helps the brain develop. People usually have 2 copies of *UBE3A*:

- A **maternal** copy from the mother that is turned on to make the protein
- A **paternal** copy from the father that is turned off in the brain, or inactive, and does not make the protein

In AS, people have a non-working or missing maternal copy of *UBE3A*, which causes very little or none of the needed protein. There is no approved medicine for AS. Currently, people with AS manage their symptoms with treatments like physical therapy, speech therapy, and medicines to prevent or treat seizures.

What is AS?

AS is a rare, genetic condition that affects the brain. It can cause developmental delays, such as lack of speech, seizures, trouble walking or moving and sleeping. It can also cause cognitive impairment, such as problems with learning new tasks, problem solving, focus, and attention. Symptoms may change over time.

What is GTX-102?

GTX-102, also called apazunersen, is a type of study treatment called an antisense oligonucleotide (ASO). An **ASO** gives instructions to cells to stop or start making a certain protein. GTX-102 is designed to "turn on" the inactive paternal copy of *UBE3A*, so the paternal copy can tell cells to make the protein to support brain development.

As a possible treatment, GTX-102 is designed to be administered on a regular schedule as an intrathecal (IT) injection. An **IT injection** means that doctors insert a thin needle in the lower part of the spine to inject GTX-102 into the fluid around the spinal cord. This allows the treatment to get into the **cerebrospinal fluid (CSF)** to reach the brain. CSF surrounds the brain and spinal cord.

Where did GTX-102 get its name from?

The name comes from GeneTx Biotherapeutics, which was the company that developed GTX-102. Ultragenyx partnered with GeneTx in 2019 and then bought GeneTx, including GTX-102, in 2022.

Who was in this study?

This study included 74 children with AS from these countries:

- Australia
- Canada
- France
- Germany
- Israel
- Spain
- United Kingdom
- United States of America

All children in the study had a missing maternal copy of *UBE3A* causing AS. Everyone in the study was ages 4 to 17 years when they joined the study. Their average age was 8 years old.

What happened during this study?

The study started in February 2020 and finished in January 2025. Each participant was in the study for about 3 years.

Before treatment

The study doctors checked each participant's health to make sure they were healthy enough to join the study.

During treatment

At the start of treatment, each child received a smaller dose of GTX-102 with less time between doses (called a **loading phase**). Then, the dose of GTX-102 went up until it reached the planned dose. For the rest of treatment, each child received the planned dose of GTX-102 with more time between doses (called the **maintenance phase**).

Participants received GTX-102 for about 3 years during this study.

Study doctors gave GTX-102 into the lower back as an IT injection. If needed, each participant could receive medicine to help them sleep, stay still, or relax, which is called anesthesia or sedation.

First, a few participants were given the planned dose of GTX-102. The study doctors checked them for safety concerns before giving GTX-102 to more participants. Based on early results from the first few participants, researchers adjusted the planned doses of GTX-102.

After treatment

At the end of this study, participants were invited to join a long-term extension study, **GTX-102-CL302**. If they chose not to join, the study doctors checked the participants' health for up to 2 months after their last IT injection of GTX-102.

The long-term extension study, GTX-102-CL302, that participants were invited to join is designed to look at the safety of GTX-102 and how well it works in participants with AS over a longer period of time. In an **extension study**, researchers invite participants from another study to join, so the participants can continue to take the study treatment and the researchers can continue to learn about the study treatment.

What did researchers learn from this study?

This is a **summary** of the main results from this study. Each participant's individual results might be different and are not in this summary. If you or your child took part in this study and have questions about this results summary, please contact the study site.

The results from several studies are needed to decide if treatments are safe and work to treat a condition. Other studies may give new information or different results. Always talk to a doctor before making any treatment changes.

This study was designed to answer this **main question:**

- **How safe is GTX-102 in participants with AS?**

To answer this question, researchers looked at:

- How many participants had medical problems called adverse events during the study
- What possible side effects happened during the study - a possible side effect is an adverse event that doctors thought might be caused by the study treatment or study procedure

How many participants had medical problems called adverse events during the study?

All participants (74 of 74) had adverse events, and 30 of them had serious adverse events.

What is an adverse event?

An **adverse event** is an unwanted or unexpected sign or symptom that happens after taking the study treatment.

A lot of research is needed to know if a treatment causes an adverse event. Adverse events **may or may not be caused by the study treatment**, other drugs taken while in the study, the participants' medical history, or procedures performed in the study.

What is a serious adverse event?

An adverse event is considered **serious** when it:

- Is considered medically important by a doctor
- Requires hospitalization
- Causes a disability or birth defect
- Is life-threatening
- Causes death

This section is a summary of **all adverse events** that happened during the study, even if the doctors thought they might not be caused by the study treatment.

The table below shows the number of participants who had adverse events during the study.

Number of participants who had **at least 1**:	
Adverse event, including serious and other adverse events	**74 of 74 participants** (100%)
Serious adverse event	**30 of 74 participants** (41%)
Adverse event of special interest (AESI)	**8 of 74 participants** (11%)

An **adverse event of special interest (AESI)** is a specific adverse event that doctors carefully watch participants for during a study. An AESI is based on adverse events that happened in past studies and help researchers better understand possible safety risks. AESIs are important because they may be related to the study treatment or could be signs of a health issue. In this study, the AESI was leg pain or weakness from an irritated nerve in the spine (radiculopathy).

The next section is a summary of the possible side effects.

What's the difference between a possible side effect and an adverse event?
A **possible side effect** is an adverse event that the doctors thought **might be caused by the study treatment or study procedure.**
Not all adverse events are side effects.

What possible side effects happened during the study?

31 of 74 participants had possible side effects.

What serious possible side effects did participants have during this study?

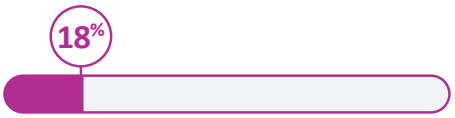
8 participants had a serious possible side effect during this study, which resolved. The serious possible side effects were:

Leg pain or weakness from an irritated nerve in the spine
Radiculopathy
7 of 74 participants

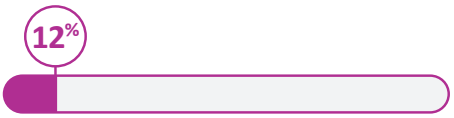
Muscle weakness
Muscular weakness
1 of 74 participants

What other possible side effects did the participants have during this study?

Below are the common possible side effects that happened in more than 10% (8 or more) of participants in this study. There were other possible side effects that happened in fewer participants.



Higher level of protein in cerebrospinal fluid (CSF), which may be a sign of infection or bleeding, or might be related to treatment with GTX-102
CSF protein increased
13 of 74 participants



Problems controlling muscle movements
Ataxia
9 of 74 participants

How has this study helped participants and researchers?

Overall, these results helped researchers decide the doses of GTX-102 that may be safe and work for use in other AS studies.

Ultragenyx has ongoing studies of GTX-102 for AS. These studies will continue to help researchers learn if the possible benefits for people with AS are greater than the risks.

Where can I learn more about this study?

You can find more information about this study on these websites:

- https://clinicaltrials.gov/study/NCT04259281
- https://www.clinicaltrialsregister.eu/ctr-search/trial/2021-001793-36/DE

Official Study Title: A phase 1/2 open-label, multiple-dose, dose-escalating clinical trial of the safety and tolerability of GTX-102 in pediatric patients with Angelman syndrome (AS)

National Clinical Trial number: NCT04259281

EudraCT number: 2021-001793-36

If you have questions about the results, please speak with a doctor or staff at the study site.

Thank you!

At Ultragenyx, our focus is developing medicines for people who live with rare and ultra-rare diseases. But it takes more than scientific knowledge and research to develop medicines. Your involvement is essential and ensures that the research process moves forward. Thank you for your participation in this study and commitment to research.

Ultragenyx is a biopharmaceutical company committed to bringing to patients products for the treatment of rare and ultra-rare diseases, with a focus on serious, debilitating genetic diseases.

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