Angelman Syndrome

A Phase 2 Study of GTX-102

AURORA

Angelman Syndrome Clinical Research

To learn more about this study, please email TrialRecruitment@ultragenyx.com

AURORA study overview

What is GTX-102?

GTX-102 is an investigational antisense oligonucleotide (ASO) therapy designed to address the root cause of Angelman syndrome (AS). An ASO is a small lab-made piece of DNA, RNA, or a combination of both that is intended to restore specific genetic instructions (mRNA) in the body. Because GTX-102 needs to reach the brain, it is injected directly into the cerebrospinal fluid surrounding the spinal cord (intrathecal injection) via the lower back (lumbar puncture).

DNA=deoxyribonucleic acid; mRNA=messenger ribonucleic acid; RNA=ribonucleic acid.

Why are we doing the AURORA study?

In combination with the ASPIRE study—which included children with deletion-genotype AS ages 4 years through 17 years old—Ultragenyx will research the safety of GTX-102 and the effects it may have for people with AS ages 1 year through 64 years old and across all genotypes.

The AURORA study includes 4 different groups of participants with AS

Click on the study group you would like to learn more about.

Study Group A

Ages: 1 year through 3 years

AS genotypes:

Deletion

SELECT

Study Group B

Ages: 4 years through 17 years

AS genotypes:

ICD UPD

SELECT

Study Group C

Ages: 18 years through 64 years

AS genotypes:

Deletion ICD Mutation UPD

SELECT

Study Group D

Ages: 4 years through 17 years

AS genotypes:

Mutation

SELECT

ICD=imprinting center defect; UPD=uniparental disomy.

If a child or loved one does not fit into one of the AURORA study groups, please email TrialRecruitment@ultragenyx.com to stay informed

For more information about the AURORA study on ClinicalTrials.gov, click here

AURORA study details

Who is eligible to participate?

Anyone with AS who meets the following requirements:

- 1 year through 64 years of age
- AS diagnosis confirmed with genetic testing
- Qualifying blood test results
- Able to receive magnetic resonance imaging (MRI) and lumbar puncture procedure
- Can tolerate anesthesia without intubation

We plan to enroll a total of **60** **INDIVIDUALS** in the AURORA study

Additional eligibility requirements for each AURORA study group are included in its specific section.

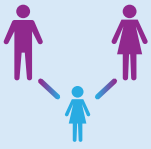
If previously treated with an ASO or gene therapy, a child or loved one is ineligible for the study. Please discuss any other previous treatment with their doctor to see if they may be able to participate. Email TrialRecruitment@ultragenyx.com for more information on eligibility.

What effects will be studied in people with AS?

- Behavior
- Cognitive function
- Communication
- Motor function
- Sleep

What AS genotypes will be studied in AURORA?

- Deletion
- ICD
- Mutation
- UPD



What is a genotype?

Your genotype is the specific combination of genes you inherit from your parents that acts like your body's instruction manual for many traits. It also refers to the specific change in a gene that causes a genetic condition.

Caregivers are encouraged to confirm their loved one's AS genotype with the doctor or geneticist if unsure.

To learn more about this study, please email TrialRecruitment@ultragenyx.com

AURORA study for young children with AS

STUDY GROUP A

Select a tab | Eligibility and goals | What to expect | Study overview

Who is eligible?

To be eligible for study participation, children with AS will need to meet these requirements:

- 1 year through 3 years of age
- Confirmed deletion of the maternal copy of the *UBE3A* gene
- Weight of at least 8 kg (17.6 pounds) at screening
- Qualifying blood test results
- Able to receive MRI and lumbar puncture procedure
- Can tolerate anesthesia without intubation

AS genotypes in Study Group A

Deletion

Check with the child's doctor or geneticist to see which genotype of AS they have if you aren't sure.

If previously treated with an ASO or gene therapy, children are ineligible for the study.
Please discuss any other previous treatment with their doctor to see if they may be able to participate.
Email TrialRecruitment@ultragenyx.com for more information on eligibility.

Why are we doing this study?

To help researchers learn more about the safety of GTX-102* and the effects it may have on:

- Cognitive function
- Communication
- Motor function

*This is an investigational ASO therapy that is not currently approved by any health authority. However, it has been given to children and adolescents in a prior study.

To learn more about this study, please email TrialRecruitment@ultragenyx.com

AURORA study for young children with AS

STUDY GROUP A

Select a tab | Eligibility and goals | What to expect | Study overview

What will participants need to do in this study?

- Receive GTX-102 injections by lumbar puncture (with possible use of anesthesia)
- Take medication to help manage possible side effects
- Complete health assessments
- Brain activity measurements and video assessments (for some participants)

What will the caregiver need to do in this study?

- Bring their child to study visits
- Tell the study team about any changes in their child's health
- Complete virtual study visits
- Potentially record videos of their child doing activities at home
- Complete questionnaires related to their child's condition
- Make sure their child takes medication as instructed by the study doctor
- Keep experiences in the study private between them and the study team

What will happen at study visits?

9 clinic visits

Assessments, testing, and investigational treatment

11 phone/virtual visits

Discussions about changes in the child's health and other medications or therapies

At study visits, assessments and procedures will be done to check the child's health, which may include:

- AS assessments
- Neurological exams
- Physical exams
- Vital sign measurements
- Blood, urine, and cerebrospinal fluid sample collections
- Heart testing (electrocardiogram [ECG])
- Brain-wave testing (electroencephalogram [EEG])
- Questionnaires
- Assessments for adverse events (side effects)

To learn more about this study, please email TrialRecruitment@ultragenyx.com

AURORA study for young children with AS

STUDY GROUP A

Select a tab | Eligibility and goals | What to expect | Study overview

What is involved?

Study participation lasts approximately 1 year
Includes 9 clinic visits between screening and treatment

Screening	Treatment with GTX-102 (11 months)
Screening Period: Evaluations are completed at screening visits and include medical history, lab tests, and in-clinic examinations.	**Baseline Visit:** Assessments and testing will be done at the start of the study to compare with results taken throughout the study. **Loading Period:** If eligible, the child will initially receive 1 low dose of study treatment (GTX-102) each month for 3 consecutive months for a total of 3 doses. At all treatment visits, they will receive a lumbar puncture to collect spinal fluid for monitoring, followed by an injection of GTX-102 into the spinal fluid. **Maintenance Period:** After completion of the Loading Period, the child may continue receiving study treatments for a total of at least 11 months of treatment through the final study visit. In this period, the GTX-102 dose will be given every 2 months and gradually increased each time until the target dose is reached. The target dose will then be given every 3 months for the rest of the study. **Monitoring:** Phone/virtual appointments will be conducted after each treatment to monitor safety before proceeding with additional study visits.

Option to enroll in separate long-term study

After the final study visit, the caregiver may decide to enroll their child in a separate study that will allow them to continue receiving GTX-102 under close monitoring by AS specialists.

Learn more about this long-term follow-up study at ClinicalTrials.gov.

AURORA study for children and adolescents with AS

STUDY GROUP B

Select a tab | Eligibility and goals | What to expect | Study overview

Who is eligible?

To be eligible for study participation, children and teenagers with AS will need to meet these requirements:

- 4 years through 17 years of age
- Confirmed ICD of the maternal copy of the *UBE3A* gene or UPD of the *UBE3A* gene
- Qualifying blood test results
- Able to receive MRI and lumbar puncture procedure
- Can tolerate anesthesia without intubation
- Able to use contraception or practice sexual abstinence during the study and for a period of time after the final dose of GTX-102 (at least 3 months for males and at least 6 months for females of childbearing age)

AS genotypes in Study Group B

ICD UPD

Check with the child's doctor or geneticist to see which genotype of AS they have if you aren't sure.

ICD=imprinting center defect; UPD=uniparental disomy.

If previously treated with an ASO or gene therapy, children are ineligible for the study.
Please discuss any other previous treatment with their doctor to see if they may be able to participate.
Email TrialRecruitment@ultragenyx.com for more information on eligibility.

Why are we doing this study?

To help researchers learn more about the safety of GTX-102* and the effects it may have on:

Behavior | Cognitive function | Communication | Motor function | Sleep

*This is an investigational ASO therapy that is not currently approved by any health authority. However, it has been given to children and adolescents in a prior study.

To learn more about this study, please email TrialRecruitment@ultragenyx.com

AURORA study for children and adolescents with AS

STUDY GROUP B

Select a tab | Eligibility and goals | What to expect | Study overview

What will participants need to do in this study?

- Receive GTX-102 injections by lumbar puncture (with possible use of anesthesia)
- Take medication to help manage possible side effects
- Complete health assessments
- Brain activity measurements and video assessments (for some participants)

What will the caregiver need to do in this study?

- Bring their child to study visits
- Tell the study team about any changes in their child's health
- Complete virtual study visits
- Potentially record videos of their child doing activities at home
- Complete questionnaires related to their child's condition
- Make sure their child takes medication as instructed by the study doctor
- Keep experiences in the study private between them and the study team

What will happen at study visits?

9 clinic visits

Assessments, testing, and investigational treatment

11 phone/virtual visits

Discussions about changes in the child's health and other medications or therapies

At study visits, assessments and procedures will be done to check the child's health, which may include:

- AS assessments
- Neurological exams
- Physical exams
- Vital sign measurements
- Blood, urine, and cerebrospinal fluid sample collections
- Heart testing (electrocardiogram [ECG])
- Brain-wave testing (electroencephalogram [EEG])
- Questionnaires
- Assessments for adverse events (side effects)

To learn more about this study, please email TrialRecruitment@ultragenyx.com

AURORA study for children and adolescents with AS

STUDY GROUP B

Select a tab | Eligibility and goals | What to expect | Study overview

What is involved?

Study participation lasts approximately 1 year
Includes 9 clinic visits between screening and treatment

Screening	Treatment with GTX-102 (11 months)
Screening Period: Evaluations are completed at screening visits and include medical history, lab tests, and in-clinic examinations.	**Baseline Visit:** Assessments and testing will be done at the start of the study to compare with results taken throughout the study. **Loading Period:** If eligible, the child will initially receive 1 low dose of study treatment (GTX-102) each month for 3 consecutive months for a total of 3 doses. At all treatment visits, they will receive a lumbar puncture to collect spinal fluid for monitoring, followed by an injection of GTX-102 into the spinal fluid. **Maintenance Period:** After completion of the Loading Period, the child may continue receiving study treatments for a total of at least 11 months of treatment through the final study visit. In this period, the GTX-102 dose will be given every 2 months and gradually increased each time until the target dose is reached. The target dose will then be given every 3 months for the rest of the study. **Monitoring:** Phone/virtual appointments will be conducted after each treatment to monitor safety before proceeding with additional study visits.

Option to enroll in separate long-term study

After the final study visit, the caregiver may decide to enroll their child in a separate study that will allow them to continue receiving GTX-102 under close monitoring by AS specialists.

Learn more about this long-term follow-up study at ClinicalTrials.gov.

To learn more about this study, please email TrialRecruitment@ultragenyx.com

AURORA study for adults with AS

STUDY GROUP C

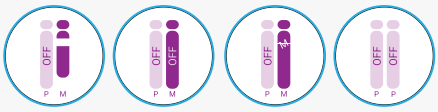
Select a tab | Eligibility and goals | What to expect | Study overview

Who is eligible?

To be eligible for study participation, adults with AS will need to meet these requirements:

- 18 years through 64 years of age
- Confirmed to have one of the following genotypes: deletion, mutation, ICD of the maternal copy of the *UBE3A* gene, or UPD of the *UBE3A* gene
- Qualifying blood test results
- Able to receive MRI and lumbar puncture procedure
- Can tolerate anesthesia without intubation
- Able to use contraception or practice sexual abstinence during the study and for a period of time after the final dose of GTX-102 (at least 3 months for males and at least 6 months for females of childbearing age)

AS genotypes in Study Group C



Deletion ICD Mutation UPD

Check with the study participant's doctor or geneticist to see which genotype of AS they have if you aren't sure.

ICD=imprinting center defect; UPD=uniparental disomy.

If previously treated with an ASO or gene therapy, adults with AS are ineligible for the study.
Please discuss any other previous treatment with their doctor to see if they may be able to participate.
Email TrialRecruitment@ultragenyx.com for more information on eligibility.

Why are we doing this study?

To help researchers learn more about the safety of GTX-102* and the effects it may have on:

Behavior Communication Motor function

*This is an investigational ASO therapy that is not currently approved by any health authority. However, it has been given to children and adolescents in a prior study.

To learn more about this study, please email TrialRecruitment@ultragenyx.com

AURORA study for adults with AS

STUDY GROUP C

Select a tab | Eligibility and goals | What to expect | Study overview

What will participants need to do in this study?

- Receive GTX-102 injections by lumbar puncture (with possible use of anesthesia)
- Take medication to help manage possible side effects
- Complete health assessments
- Brain activity measurements and video assessments (for some participants)

What will the caregiver need to do in this study?

- Bring their loved one to study visits
- Tell the study team about any changes in their health
- Complete virtual study visits
- Potentially record videos of their loved one doing activities at home
- Complete questionnaires related to their condition
- Make sure they take medication as instructed by the study doctor
- Keep experiences in the study private between them and the study team

What will happen at study visits?

9 clinic visits

Assessments, testing, and investigational treatment

11 phone/virtual visits

Discussions about changes in the loved one's health and other medications or therapies

At study visits, assessments and procedures will be done to check your loved one's health, which may include:

- AS assessments
- Neurological exams
- Physical exams
- Vital sign measurements
- Blood, urine, and cerebrospinal fluid sample collections
- Heart testing (electrocardiogram [ECG])
- Brain-wave testing (electroencephalogram [EEG])
- Questionnaires
- Assessments for adverse events (side effects)

To learn more about this study, please email TrialRecruitment@ultragenyx.com

AURORA study for adults with AS

STUDY GROUP C

Select a tab | Eligibility and goals | What to expect | Study overview

What is involved?

Study participation lasts approximately 1 year
Includes 9 clinic visits between screening and treatment

Screening	Treatment with GTX-102 (11 months)
Screening Period: Evaluations are completed at screening visits and include medical history, lab tests, and in-clinic examinations.	**Baseline Visit:** Assessments and testing will be done at the start of the study to compare with results taken throughout the study. **Loading Period:** If eligible, the study participant will initially receive 1 low dose of study treatment (GTX-102) each month for 3 consecutive months for a total of 3 doses. At all treatment visits, they will receive a lumbar puncture to collect spinal fluid for monitoring, followed by an injection of GTX-102 into the spinal fluid. **Maintenance Period:** After completion of the Loading Period, the study participant may continue receiving GTX-102 for a total of at least 11 months of treatment through the final study visit. In this period, the GTX-102 dose will be given every 2 months and gradually increased each time until the target dose is reached. The target dose will then be given every 3 months for the rest of the study. **Monitoring:** Phone/virtual appointments will be conducted after each treatment to monitor safety before proceeding with additional study visits.

Option to enroll in separate long-term study

After the final study visit, the caregiver may decide to enroll their loved one in a separate study that will allow them to continue receiving GTX-102 under close monitoring by AS specialists.

Learn more about this long-term follow-up study at ClinicalTrials.gov.

To learn more about this study, please email TrialRecruitment@ultragenyx.com

AURORA study for children and adolescents with AS

STUDY GROUP D

Select a tab | Eligibility and goals | What to expect | Study overview

Who is eligible?

To be eligible for study participation, children and teenagers with AS will need to meet these requirements:

- 4 years through 17 years of age
- Confirmed mutation of the maternal copy of the *UBE3A* gene
- Qualifying blood test results
- Able to receive MRI and lumbar puncture procedure
- Can tolerate anesthesia without intubation
- Able to use contraception or practice sexual abstinence during the study and for a period of time after the final dose of GTX-102 (at least 3 months for males and at least 6 months for females of childbearing age)

AS genotypes in Study Group D

Mutation

Check with the child's doctor or geneticist to see which genotype of AS they have if you aren't sure.

If previously treated with an ASO or gene therapy, children are ineligible for the study.
Please discuss any other previous treatment with their doctor to see if they may be able to participate.
Email TrialRecruitment@ultragenyx.com for more information on eligibility.

Why are we doing this study?

To help researchers learn more about the safety of GTX-102* and the effects it may have on:

- Behavior
- Cognitive function
- Communication
- Motor function
- Sleep

*This is an investigational ASO therapy that is not currently approved by any health authority. However, it has been given to children and adolescents in a prior study.

To learn more about this study, please email TrialRecruitment@ultragenyx.com

AURORA study for children and adolescents with AS

STUDY GROUP D

Select a tab | Eligibility and goals | What to expect | Study overview

What will participants need to do in this study?

- Receive GTX-102 injections by lumbar puncture (with possible use of anesthesia)
- Take medication to help manage possible side effects
- Complete health assessments
- Brain activity measurements and video assessments (for some participants)

What will the caregiver need to do in this study?

- Bring their child to study visits
- Tell the study team about any changes in their child's health
- Complete virtual study visits
- Potentially record videos of their child doing activities at home
- Complete questionnaires related to their child's condition
- Make sure their child takes medication as instructed by the study doctor
- Keep experiences in the study private between them and the study team

What will happen at study visits?

Up to 11 clinic visits
Assessments, testing, and investigational treatment

Up to 15 phone/virtual visits
Discussions about changes in the child's health and other medications or therapies

At study visits, assessments and procedures will be done to check the child's health, which may include:

- AS assessments
- Neurological exams
- Physical exams
- Vital sign measurements
- Blood, urine, and cerebrospinal fluid sample collections
- Heart testing (electrocardiogram [ECG])
- Brain-wave testing (electroencephalogram [EEG])
- Questionnaires
- Assessments for adverse events (side effects)

To learn more about this study, please email TrialRecruitment@ultragenyx.com

AURORA study for children and adolescents with AS

STUDY GROUP D

Select a tab | Eligibility and goals | What to expect | Study overview

What is involved?

If eligible, the child will be assigned at random to a GTX-102 study treatment group. For every 3 participants, 2 will enter the group that begins receiving GTX-102 right after the Baseline Visit. One will enter the group that receives no study treatment at first, then receives GTX-102 after the No-Treatment Period ends.

1-year study	1.5-year study
Participants receive GTX-102 immediately after Baseline Visit	Participants receive GTX-102 after a No-Treatment Period (about 5.5 months) following Baseline Visit

Study participation lasts approximately 1 year

Includes 9 clinic visits between screening and treatment

Screening	Treatment with GTX-102 (11 months)
Screening Period: Evaluations completed at screening visits include medical history, lab tests, and in-clinic examinations.	**Baseline Visit:** Assessments and testing will be done at the start to compare with results taken throughout the study. **Loading Period:** If eligible, the child will initially receive 1 low dose of study treatment (GTX-102) each month for 3 consecutive months for a total of 3 doses. At all treatment visits, they will receive a lumbar puncture to collect spinal fluid for monitoring, followed by an injection of GTX-102 into the spinal fluid. **Maintenance Period:** After completion of the Loading Period, the child may continue receiving study treatments for a total of at least 11 months of treatment through the final study visit. In this period, the GTX-102 dose will be given every 2 months and gradually increased each time until the target dose is reached. The target dose will then be given every 3 months for the rest of the study. **Monitoring:** Phone/virtual appointments will be conducted after each treatment to monitor safety before proceeding with additional study visits.

Option to enroll in separate long-term study

After the final study visit, the caregiver may decide to enroll their child in a separate study that will allow them to continue receiving GTX-102 under close monitoring by AS specialists.

Learn more about this long-term follow-up study at ClinicalTrials.gov.

To learn more about this study, please email TrialRecruitment@ultragenyx.com

AURORA study for children and adolescents with AS

STUDY GROUP D

Select a tab | Eligibility and goals | What to expect | Study overview

What is involved?

If eligible, the child will be assigned at random to a GTX-102 study treatment group. For every 3 participants, 2 will enter the group that begins receiving GTX-102 right after the Baseline Visit. One will enter the group that receives no study treatment at first, then receives GTX-102 after the No-Treatment Period ends.

1-year study	1.5-year study
Participants receive GTX-102 immediately after Baseline Visit	Participants receive GTX-102 after a No-Treatment Period (about 5.5 months) following Baseline Visit

Study participation lasts approximately 1.5 years

Includes 11 clinic visits from screening to end of treatment

Screening and Baseline Visits

Screening Period: Evaluations completed at screening visits include medical history, lab tests, and in-clinic examinations.

Baseline Visit: Assessments and testing will be done at the start to compare with results taken throughout the study.

No Treatment (safety monitoring for 5.5 months)

No-Treatment Period: This period begins with a Baseline Visit. During the No-Treatment Period, the child will not receive any study drug. Study visits will monitor safety and assess the natural development of the disease. This is designed to help researchers better understand the impacts of mutation-type AS without treatment and compare them with the potential effects of GTX-102. This period ends after about 5.5 months with a final assessment visit that also serves as the first visit of the Treatment Period.

Treatment with GTX-102 (11 months)

Loading Period: This begins when the child receives the first dose of GTX-102. During the Treatment Period, the child will initially receive 1 low dose of study treatment (GTX-102) each month for 3 consecutive months for a total of 3 doses. At all treatment visits, they will receive a lumbar puncture to collect spinal fluid for monitoring, followed by an injection of GTX-102 into the spinal fluid.

Maintenance Period: After completion of the Loading Period, the child may continue receiving study treatments for a total of at least 11 months of treatment through the final study visit. In this period, the GTX-102 dose will be given every 2 months and gradually increased each time until the target dose is reached. The target dose will then be given every 3 months for the rest of the study.

Monitoring: Phone/virtual appointments will be conducted after each treatment to monitor safety before proceeding with additional study visits.

Option to enroll in separate long-term study

After the final study visit, the caregiver may decide to enroll their child in a separate study that will allow them to continue receiving GTX-102 under close monitoring by AS specialists.

Learn more about this long-term follow-up study at ClinicalTrials.gov.

To learn more about this study, please email TrialRecruitment@ultragenyx.com

How AURORA continues research on a potential AS therapy

	Phase 1/2 study	Phase 2 AURORA study	Phase 3 ASPIRE study	Phase 3 long-term extension study*
Age (years)	4-17	1-64	4-17	1-64
AS genotypes	Deletion	Deletion, ICD, mutation, UPD	Deletion	Deletion, ICD, mutation, UPD

*Requires prior participation in a clinical study with GTX-102.

ASPIRE Angelman Syndrome Clinical Research

ASPIRE sought to better understand if this investigational therapy is safe and how well it works in children with AS who are 4 years through 17 years of age. Participants must have confirmed deletion genotypes of AS.

AURORA Angelman Syndrome Clinical Research

AURORA is a study designed to explore the effects of GTX-102 in participants with AS across genotypes (deletion and nondeletion) and age groups (1 year through 64 years). **This will be the first Ultragenyx study to assess this potential therapy in certain populations.**

Why is clinical research important?

Clinical studies are a foundational part of developing new medicines and treatments. People choose to take part in clinical studies for a variety of reasons, such as:

- The chance to receive an investigational drug not available outside the trial
- Close monitoring of a health condition by specialized doctors
- Making a positive contribution to the AS community

Currently, there are no approved medicines for AS

That's why our research team at Ultragenyx continues to study GTX-102 with the urgent goal of bringing this potential treatment forward for families impacted by AS.

To learn more about this study, please email TrialRecruitment@ultragenyx.com

AURORA

Angelman Syndrome Clinical Research

Looking for more information about the AURORA study?

Our Ultragenyx Patient Enrollment Liaison (PEL) team is here to help. Every member of our PEL team has a robust professional background and the clinical expertise and experience to help answer your questions.

To speak with a liaison about current and future medical research opportunities, please email our PEL team at TrialRecruitment@ultragenyx.com.

Scan the QR code to learn about clinical trial opportunities that may help make a meaningful difference, or visit UltraClinicalTrials.com

ultragenyx