ForPatients
by Roche

Angelman Syndrome

A Study To Investigate The Safety Of RO7248824 in Children With Angelman Syndrome And To Understand The Way The Body Processes The Investigational Therapy

A Study to Investigate the Safety, Tolerability, Pharmacokinetics (PK) and Pharmacodynamics (PD) of RO7248824 in Participants With Angelman Syndrome (AS)

Trial Status	Trial Runs In	Trial Identifier
Active, not recruiting	4 Countries	NCT04428281 2019-003787-48 RG6091 BP41674

The information is taken directly from public registry websites such as ClinicalTrials.gov, EuClinicalTrials.eu, ISRCTN.com, etc., and has not been edited.

Official Title:

An Open-label, Multicenter Study to Investigate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of RO7248824 in Participants With Angelman Syndrome

Trial Summary:

This is a phase I, multicenter, non-randomized, adaptive, open-label, multiple ascending, intra-participant, dose-escalation study with a long-term extension (LTE) part and an optional open-label extension (OOE) part. The objective of the study is to investigate the safety, tolerability, PK and PD of RO7248824 administered intrathecally (IT) in participants with AS. Two linked sets of dose escalation cohorts are planned based on two different age groups, namely participants with AS aged # 5 to # 12 years in cohorts A1 to A5 (with at least 2 participants # 8 years old in each cohort) and AS participants aged # 1 to # 4 years in cohorts B1 to B5. The two sets of cohorts will be run in parallel, with each cohort A1 to A5 preceding and gating the linked cohort B1 to B5 (e.g., A1 precedes B1).

Hoffmann-La Roche
Sponsor

Phase 1
Phase

NCT04428281 2019-003787-48 RG6091 BP41674
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers

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All	#1 Year & # 12 Years	No

A clinical study for children with Angelman Syndrome between 1 and 12 years old

This clinical study will test the safety of a new investigational therapy and study the way the body processes the study medication. The study will measure the impact of the investigational therapy using various clinical scales.

Angelman Syndrome (AS) is a rare genetic disease impacting the development of the nervous system. It results in life-long physical and cognitive disability. Standard treatments for AS are designed to treat disease symptoms such as seizures and sleep disturbance.

What is a clinical trial?

Who is eligible to participate?

Children diagnosed with AS between 1 to 12 years old will be evaluated by a hospital healthcare team.

Does this clinical study use placebo?

There is no placebo. All participants in the study will receive the investigational treatment.

Where do I go to get more information about this study?

As a caregiver for a child with AS, we understand your need for up-to-date information about this clinical study. Use the link to Contact us for further information. It may be possible to discuss this clinical study, one-to-one, with a study nurse. Your child's treating physician is also invited to contact us on your behalf.

How is this study set up?

Children participating in this clinical study will receive the investigational therapy at a hospital staffed with teams trained in AS care. Many hospitals will participate in the study and we encourage you to find out if there is a hospital participating in the study that is close to where you live. Tap **Find trial locations** at the top of this page.

This study is set up to measure the effects of taking the investigational therapy. The study will measure changes in AS symptoms, as well as many details of your child’s health and emotional wellbeing.

The study will also consider your treatment journey, as caregivers. This assessment is holistic. We consider fatigue associated with night time care of your child, the impact of your care schedule on everyday life, and how living with AS impacts family relationships.

Children taking sleep medications may be eligible for this study. When studying a new treatment under the conditions of a clinical study, it is important that any existing treatments remain unchanged throughout the study period.

In practical terms, this means that your child must already have taken the sleep medication for at least one (1) month prior to joining the study. In addition, the dose of the sleep medication should be kept constant throughout the study period.

Children on a ketogenic diet may also be eligible for this study. Here, the conditions are that your child needs to stick closely to the ketogenic diet for a period of at least three (3) months prior to joining the study, and remain on it throughout the study period.

Our study has similar conditions around medication for epilepsy. It's worth reaching out to the study team to find out which medications, and which dosing regimens, are compatible with participation in the study.

Global developmental delay. What does this mean?

A child with AS may show recognisable delays in the development of movement, speech and cognitive abilities from an early age, relative to their peers. These delays are global, meaning that they impact many aspects of brain functioning.

The onset of AS coincides with critical phases of early brain development and learning, causing disabilities that remain throughout life. Providing treatment at an early age may reduce the impact of AS on the developing brain.

Why is the AS community so important?

Parents and other caregivers were involved in the design of this study from the very beginning. Patient advocacy groups gathered caregiver's views about the impact of AS symptoms relating to sleep, hyperactivity, seizures, self-care and inappropriate speech.

The study introduces a new measure of your child's communication ability. This measure was developed in collaboration with members of the AS community and reflects the importance of communication to the wellbeing of children living with AS, and to their families.

Caregivers who participate in this clinical study will gain firsthand experience with these measurements. You will be asked to record your experiences, and those of your child, in

special diaries. Insights captured in these diaries will be included in the evaluation of the investigational therapy.

How is treatment given?

The investigational therapy is given in a special injection to the spine. The injection will be made while your child is under general anaesthesia. This procedure will need to be made two(2) or three(3) times during an 8 week period.

The new investigational therapy is given in a special injection to the spine. The procedure is made under general anaesthesia.

Your study healthcare team monitors and follows your child's treatment throughout the clinical study. They are available to answer your questions and are your point of contact if you have any concerns. Your existing healthcare team may also bring questions to the study doctor.

How often will my child be seen in follow-up appointments, and for how long?

The investigational therapy will be given over an eight (8) week period. During that time your child will have up to three(3) overnight stays in hospital following each injection procedure. In order to ensure the safety of your child the study team will schedule eight (8) follow-up visits ending with a final follow-up visit 12 months after treatment began.

The investigational therapy will be given 3 times over an 8 week period. The study team will schedule 8 follow-up visits ending with a final follow-up 12 months after treatment began.

Who has approved this clinical study?

This study is designed by physicians, scientists and the AS community. The study is carefully reviewed by the US Food and Drug Administration (FDA), for studies in the USA. Studies in Europe are reviewed by Regulatory Authorities in each country.

Every study is overseen closely until all participants complete their treatment and treatment follow-up, and until the study findings have been presented for a final review.

Who can answer my questions about this clinical study?

If you have further questions about your participation in the study, we suggest you bring them directly to the study medical team located nearest to you. Study teams have detailed knowledge to support parents and other caregivers participating in the study.

We encourage you to discuss clinical studies with your healthcare team, and with others who can support you to make decisions about care and treatment for your child.

Every clinical study is listed on a public registry.

This study can be found on the ClinicalTrials.gov public registry by searching the registry, using the Trial Identifier NCT04428281.

You can share the Trial Identifier with healthcare workers and with other members of the AS community.

How do I take part in this clinical study?

To join the study, healthcare professionals must carefully evaluate your child.

If your child is eligible to join the study and you give consent for them to enroll, they can join the study.

Tap **Find trial locations** at the top of this page for a list of hospitals nearest to you.

What happens if I am unable to take part in this clinical trial?

If it turns out that your child is not eligible for this study, the ClinicalTrials.gov website may have information about alternative clinical trials for your child.

Thank you for your time and interest in this clinical study.

Date of last medical review: June 2020.

Inclusion Criteria:

- The participant has a parent, caregiver or legal representative (hereinafter "caregiver") who is reliable, competent and at least 18 years of age. The caregiver is willing and able to accompany the participant to clinic visits and to be available to the Investigational Site by phone or email if needed and who (in the opinion of the Investigator) is and will remain sufficiently knowledgeable of participant's ongoing condition to respond to any inquiries about the participant from personnel from the Study Site.
- A caregiver must be able to consent for the participant according to International Council on Harmonisation (ICH) and local regulations.
- Ability to comply with all study requirements.
- Have adequate supportive psychosocial circumstances.
- Able to tolerate blood draws.
- Able to undergo lumbar puncture (LP) and IT injection, under sedation or anesthesia if needed and as determined appropriate by the Investigator.
- Stable medical status for at least 4 weeks prior to Screening and at the time of enrollment.

- Body weight of # 7 kg
- Participant must be # 1 to # 12 years of age at the time of signing of the informed consent by the caregiver.
- Clinical diagnosis of AS confirmed by a molecular diagnosis with genotypic classification of either Ubiquitin-protein ligase E3A (UBE3A) mutation of the maternal allele or deletion on the maternally inherited chromosome 15q11q13 that includes the UBE3A gene and is less than 7 megabyte (Mb) in size.

Reproductive Status:

Some of the provisions that follow may have limited applicability based on the age range of study participants (i.e., up to the age of 12) and the nature of the disease understudy. These provisions are nonetheless included for purposes of completeness in order:

A) Female Participants

A female participant is eligible to participate if she is not pregnant, not breastfeeding, and at least one of the following conditions applies:

- Women of non-childbearing potential.
- Women of childbearing potential who agree to remain abstinent (refrain from heterosexual intercourse) or use acceptable contraceptive methods during the treatment period and for at least 6 months after the final dose of RO7248824 (RG6091). The following are acceptable contraceptive methods: bilateral tubal occlusion/ ligation, male sexual partner who is sterilized, established proper use of hormonal contraceptives that inhibit ovulation, hormone-releasing intrauterine devices and copper intrauterine devices, male or female condom with or without spermicide; and cap, diaphragm, or sponge with spermicide.

B) Male Participants

During the treatment period and for at least 6 months after the final dose of RO7248824 (RG6091), consent has to be provided to:

- Remain abstinent (refrain from heterosexual intercourse) or use contraceptive measures such as a condom, with a female partner of childbearing potential, or pregnant female partner, to avoid exposing the embryo.

The reliability of sexual abstinence for male and/or female enrollment eligibility needs to be evaluated in relation to the duration of the clinical study and the preferred and usual lifestyle of the participant. Periodic abstinence (e.g., calendar, ovulation, symptothermal, or post-ovulation methods) and withdrawal are not acceptable methods of preventing drug exposure.

Inclusion Criteria for OOE Part:

- Current or prior participations in the LTE part of Study BP41674.

Exclusion Criteria:

Diagnostic Assessments

- Clinically-significant laboratory, vital sign or electrocardiography (ECG) abnormalities at Screening

Type of Participants and Disease Characteristics

- Molecular diagnosis of AS with genotypic classification: Paternal Uniparental Disomy (UPD) of 15q11-13; UBE3A Imprinting center defect (ID); A partial molecular diagnosis of AS, that cannot exclude (UPD)or ID despite appropriate genetic testing.
- Clinically relevant hematological, hepatic, cardiac or renal disease or event, in the judgement of the Investigator.
- Any concomitant condition that might interfere with the clinical evaluation of AS and that is not related to AS.
- Known history of human immunodeficiency virus (HIV) or hepatitis B virus (HBV) or hepatitis C virus (HCV).
- Any condition that increases risk of meningitis.
- History of bleeding diathesis or coagulopathy.
- A medical history of brain or spinal disease that would interfere with the LP process, CSF circulation or safety assessment
- History of clinically significant post-lumbar-puncture headache of moderate or severe intensity and/or blood patch
- Malignancy within 5 years of Screening
- Hospitalization for any major medical or surgical procedure involving general anesthesia within 12 weeks of Screening or planned during the study
- Have any other conditions, which, in the opinion of the Investigator, would make the participant unsuitable for inclusion or could interfere with the participant participating in or completing the study, including any contraindication to administration of intrathecal therapy.
- Premature birth with gestational age at birth below 34 weeks.
- History of hypersensitivity to the investigational medicinal product (IMP), antisense oligonucleotides, or any excipients.

Prior Therapy

- Allowed sleep medications have not been stable for 4 weeks prior to screening and at the time of enrollement.
- Allowed medications for treatment of epilepsy have not been stable for 12 weeks prior to screening and at the time of enrollment.
- Use of antiplatelet or anticoagulant therapy for 2 weeks prior to screening and at the time of enrollment.
- Concurrent psychotropic medications have not been stable for 4 weeks prior to screening and at the time of enrollment.

Other Exclusion Criteria: Prior/Concurrent Clinical Study Experience

- Received an investigational drug within 90 days or 5 times the half-life of the investigational drug (whichever is longer) or participation in a study testing an investigational medical device within 90 days prior to first dosing or if the device is still active.
- Concurrent or planned concurrent participation in any clinical study (including observational, non-drug and non-interventional studies) without a signed data sharing agreement in place between the other clinical study and the Sponsor.
- Previous participation in a cellular therapy, or gene therapy, or gene editing clinical study.

Exclusion Criteria for OOE Part:

- Participants who never enrolled in Study BP41674, or who discontinued participation due to safety reasons, are not eligible for the OOE part.