

# ForPatients

by Roche

## Angelman Syndrome

### **A 12-week study to investigate how the body handles alogabat once it is swallowed, how safe it is, and whether it could be effective in treating the symptoms of AS.**

Study to Investigate the Pharmacokinetics and Safety and to Provide Proof of Mechanism of Alogabat in Children and Adolescents Aged 5-17 Years With Angelman Syndrome (AS) With Deletion Genotype.

**Trial Status**  
Recruiting

**Trial Runs In**  
6 Countries

**Trial Identifier**  
NCT05630066 2022-501844-14-00  
BP41315

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*The source of the below information is the publicly available website ClinicalTrials.gov. It has been summarised and edited into simpler language.*

#### ***Trial Summary:***

This is a two-part, Phase IIa, multicenter, 12-week, open-label study. Up to 56 participants with deletion Angelman Syndrome (AS) aged 5-17 years (inclusive) will be enrolled in the study.

**Hoffmann-La Roche**  
Sponsor

**Phase 2**  
Phase

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**NCT05630066 2022-501844-14-00 BP41315**  
Trial Identifiers

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#### ***Eligibility Criteria:***

**Gender**  
All

**Age**  
>=5 Years & <= 17 Years

**Healthy Volunteers**  
No

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#### **1. Why is this clinical study needed?**

Alogabat (Study Drug) is being developed as a possible treatment for Angelman syndrome (AS). The loss of a certain brain enzyme (UBE3A) is responsible for AS. In the most common and most severe form of AS, known as "deletion AS", additional genes are partially lost, including those coding for proteins that are necessary to build the GABAA #5 receptor. This receptor plays a major role in our body e.g., in brain development, learning, sleep, and seizure control, among others.

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Alogabat is designed to help the remaining receptors to perform their function and thus could potentially make up for their reduced number. This may improve various symptoms of AS.

Scientific studies found that brain activity is altered a lot in deletion AS. We know that alogabat changes brain activity in the correct direction in healthy adults, and this study will start to help us find out whether it does so in children and teenagers with AS. This would allow us to decide early on whether it might work. In previous adult studies in healthy volunteers was found to be safe., It is necessary to also evaluate its safety in children.

## **2. How does the clinical study work?**

This clinical study is recruiting people who have Angelman Syndrome and have the “deletion AS” subtype. If your child has the clinical diagnosis of AS, you probably will also have genetic results available. Your clinician will help you review them and tell you whether your child has this specific type of AS.

The main purposes of this clinical study are:

- to understand the way the body processes alogabat
- to test the safety of alogabat at different doses
- to measure how alogabat impacts brain activity (using EEG) within AS participants.

We will do some tests to confirm if your child and the study are good fit. If your child is eligible for the study and you agree for your child to participate, it will be given daily doses of alogabat for 12 weeks. In total, the time commitment for you both is approximately 24 weeks

- 6 weeks to assess eligibility,
- 12 weeks of treatment,
- 6 weeks of observation following the last treatment.

Over this time period, we will need you and your child to visit the study site up to 9 times; 4 of these visits could be performed at your home instead if you prefer (this also depends on local regulations).

These study site visits will include checks to see how your child is responding to the treatment and any side effects they may be having. You are free to leave the clinical study at any time.

## **3. What are the main endpoints of the clinical study?**

The main clinical study endpoint (the main results that are measured in the study to see if Alogabat works as expected) are

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- levels of the study drug in the blood at different time points after taking it
- brain activity measurement (EEG), which allows us to review changes in brain waves after taking Alogabat
- side effects, if there are any, how often, how bad they are and why they might have occurred
- blood and urine results, we review these for trends to see if Alogabat is causing changes in your child's body
- vital signs (pulse rate, blood pressure, pulse oximetry) and electrocardiogram (ECG, measurements of the heart rhythm), we review these for trends in changes after Alogabat has been taken.

The other clinical trial endpoints are measuring your child's clinical symptoms before and after taking Alogabat (movement, communication, thinking, behavior, seizures, sleep...).

## **4. Who can take part in this clinical study?**

Your child can take part in this study if they:

- are aged 5 to 17 years, inclusive.
- have the "deletion" type of Angelman syndrome
- are able to undergo blood draws, ECG and EEG assessments
- have a stable caregiver who can accompany them to hospital visits, answer questions about health and behavior, etc.

Your child may not be able to take part in this trial if they:

- have any other type of Angelman syndrome other than deletion AS
- are frequently taking certain medications that could interfere with Alogabat
- have active or uncontrolled infections, including exhibiting symptoms consistent with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) within 6 weeks prior the start of the participation in the study.
- have certain kinds of heart disease
- have a history of cancer within 5 years prior to Screening.
- have any illness or major diseases that in the Doctor's judgment may affect interpretation of study results or patient safety.

## **5. What treatment will participants be given in this clinical study?**

### **PART 1 OF THE STUDY**

In this study, a range of different dose levels of the alogabat are planned to be tested, one per cohort. Everyone who joins this clinical trial will be given daily doses of alogabat over the course of 12 weeks. After each cohort has completed 2 weeks of treatment, the results will be reviewed. Initially, teenagers and older children will be enrolled. Once Alogabat has been shown to be safe and well tolerated in these participants, younger children will be enrolled.

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The planned doses for participants in part 1 of the study are as follows:

- For ages 15–17 years, the adult dose of 60 mg will be given (adult dose).
- For ages 10–14 years, this dose is adjusted to 40 mg because they are smaller and younger (age-adjusted dose).
- For ages 5–9 years, a lower dose of 7 mg is planned (age-adjusted dose).

## **PART 2 OF THE STUDY**

For part 2 of the study, doses will be chosen based on results of part 1, again adjusted for age. We plan starting participants on a lower dose, and then switching them to a higher dose after 2 weeks (if possible). We are expecting to assess age-adjusted doses of up to 100 mg. The design is flexible – based on the findings of these cohorts, we will select the most suitable dose.

## **HOW IS ALOGABAT TAKEN?**

Alogabat will be given as tablets. You may need to combine two or more tablets to get the right dose for your child. Alogabat can be swallowed whole, dissolved in (preferably) water (though apple and orange juice may also be used), or given with soft food (e.g., yoghurt).

## **6. Are there any risks or benefits in taking part in this clinical study?**

The safety or effectiveness of the Study Drug in Angelman syndrome patients is not known at the time of the trial. Most studies involve some risks to the participant, although they may not be greater than the risks related to routine medical care or the natural progression of the health condition.

You will be told about any risks of taking part in the clinical study, as well as any additional procedures, tests, or assessments your child will be asked to undergo. These will be described in an informed consent document (a document that provides people with the information they need to make a decision to volunteer for a clinical study). Caregivers of potential participants should also discuss these with members of the research team at the study site and with their usual health care provider. Anyone interested in taking part in a clinical study should know as much as possible about the trial and feel comfortable asking the research team any questions about the study.

## **RISKS ASSOCIATED WITH THE CLINICAL TRIAL STUDY DRUG**

Your child may have side effects (an unwanted effect of a drug or medical treatment) from the Study Drug used in this clinical study. Side effects, should they happen, can be mild to severe and even life threatening, and can vary from person to person.

## **ALOGABAT (RO7017773)**

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Alogabat has been tested mostly in healthy adult volunteers so far (total number = 159), with doses up to 375 mg. Some adult subjects with Autism Spectrum Disorder have also received the drug. So far, alogabat was safe and well tolerated. The most common side effects were sleepiness and dizziness. A slight effect on electric conductivity in the heart was observed. Some subjects felt unwell; roughly 1 in 40 had slight changes in liver markers. None of these problems were permanent. This will be the first study of alogabat in children, and the first study in AS; some risks for young subjects with AS may thus be unknown.

Your child will be observed regarding all possible side effects. We will monitor the heart using ECG, the liver through blood tests, and provide you with diaries where you can write down sleepiness and other possible problems.

If needed because of side effects, alogabat treatment can be stopped, or your child may be switched to a lower dose.

## **POTENTIAL BENEFITS ASSOCIATED WITH THE CLINICAL TRIAL**

There is no guarantee that your child will receive any benefits from this study and taking part in this study may or may not cause their health to improve. The doses we are investigating in this study are in the range where we expect the drug might be effective.

Information from this study may help doctors learn more about the Study Drug and the treatment of AS. This information may benefit other patients with AS or a similar condition in the future.

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Additional information about this study will be available on [Clinical-Trials](#) within 30 days of the enrolment of the first patient into the study.