

## **Q and A on the RAINBOW study**

### **What is the RAINBOW study?**

This is a **RA**ndomized, double **bl**IND, place**Bo**-controlled, multicenter, 12-week phase II study to evaluate the safety, tolerability pharmacokinetics, and pharmacodynamics of **O**ral AZ-3102 in patients diagnosed **W**ith GM2 Gangliosidosis or Niemann-Pick Type C disease.

### **What is the aim of the RAINBOW study?**

The RAINBOW study tests two doses of the study drug. The aim is to find out if the two selected doses of AZ-3102 can be safely administered and are well tolerated in adolescents with GM2 gangliosides or Niemann-Pick type C (NPC) disease. We are also investigating the level of AZ-3102 found in the blood and how long it remains in the body (pharmacokinetics). The aim of this is to gain a better understanding of how to optimize the dose in children in order to help with further studies (see below for more details on the Phase III study).

### **What is AZ 3102?**

AZ-3102 is an Investigational Medicinal Product which is being developed for the treatment of Niemann-Pick Type C and GM2 Gangliosidosis. At present, AZ-3102 has not been approved in any country for the treatment of Niemann-Pick Type C and GM2 Gangliosidosis. AZ-3102 belongs to the small molecules drug class. With their ability to pass through cell membranes and the blood-brain barrier, these small molecules offer the opportunity to reach targets inside the cells of the body, as well as in the brain and spinal cord (central nervous system).

In Niemann-Pick Type C and GM2 Gangliosidosis, the lysosomes (components of cells) start to malfunction. This causes certain fats called lipids to accumulate. The storage of these lipids induces the dysregulation of cellular functions and the symptoms of these diseases.

AZ-3102 is designed with the aim of reaching the central nervous system and reducing the accumulation of fats or lipids (known as Substrate Reduction Therapy). Through this mechanism, AZ-3102 is designed with the aim of reducing the impact of the impaired lysosome on cell function.

AZ-3102 comes in capsule form and can be swallowed with fluids, but the capsules cannot be opened.

### **Where will the RAINBOW study be conducted?**

For the latest update on current study centers please click on the following link:  
<https://clinicaltrials.gov/ct2/show/NCT05758922>

### **What can I expect if I participate in the RAINBOW study?**

Participants will need to take small capsules by mouth once a day, for 12 weeks. The study drug will be administered in the morning after a period of fasting (overnight).

RAINBOW is a placebo-controlled study which means that 1 in every 3 participants will receive a placebo (a non-active drug that looks just like AZ-3102) and the other 2 patients will receive one of 2 different doses of the study drug. The decision on whether a patient receives the study drug or the placebo will be determined by a “randomization” procedure. Randomization is similar to tossing a coin. In order to evaluate the results of the study objectively, it is necessary that neither you nor your study doctor knows which substance you are taking (3mg dose, 9mg dose, or placebo). This is called a “double-blind study”. However, if necessary (for safety reasons), the study doctor can find out at any time which substance you have received.

### **Am I eligible to participate in this study?**

Eligibility to participate in the study can only be decided by the study doctor or physician at the study center, in discussion with you and your family. Azafaros employees do not make this decision.

In general terms, you should:

- Have a genetic diagnosis confirmed with either disease (GM2 Gangliosidosis or Niemann-Pick disease type C).
- Be between 12 and 20 years old.
- Be neurologically symptomatic.
- Be able to swallow capsules.
- Not be treated with Miglustat or have stopped at least a month ago because of tolerability issues.
- Not be treated with other investigational drugs or have stopped at least three months ago.

The complete enrollment criteria can be found at [ClinicalTrials.gov](https://clinicaltrials.gov), but please contact your study doctor if you are interested in participating. The study doctor can also explain if the exclusion criteria apply to you.

### **What is the first step if I agree to take part?**

If you decide to take part in this study, you will be asked to sign an informed consent form. You will receive a copy of this form to sign, as well as a patient information sheet for your records. After you have signed the form you will have a screening visit at the study center, during which you will receive medical tests to check if you can take part. Your study doctor will inform you if you are eligible for this study.

**What will be the course of the RAINBOW study?**

The study will take 12 weeks and participants will need to visit the hospital once a month (a total of 4 visits).

At each study visit, you will receive capsules of either the study drug or the placebo in bottles to take home with you. At the same appointment, the study team will carry out certain tests. These are mostly carried out to evaluate if the drug is safe for patients.

After your last visit, a phone interview will be scheduled where the clinical investigator will check on your health.

**If I am currently taking another investigational drug, can I participate in the RAINBOW study when I stop?**

It is generally possible to take part, as long as at least a three-month (or longer if the elimination of the other investigational drug is slow) washout period is observed. Please discuss this with your own physician.

**Do you plan for an open label extension after the 12-week RAINBOW study?**

In Brazil, after the initial 12 weeks, patients in the placebo group will be randomly assigned one of the 2 active doses until the most suitable one is selected. The other patients will remain on the same doses they are receiving. We do not plan for an open label extension in the US.

**After how long the Phase III study will be initiated?**

We cannot yet be sure, as any unexpected findings could delay the start of the Phase III studies. However, if there are no serious delays, the phase III studies could begin as early as 2024.

**Does the timing of the diagnosis influence eligibility?**

The age of the participant at onset of the disease as well as the current age of the patient will influence their eligibility to participate.

**Who can answer my questions about the study?**

You can approach your study doctor if you have any questions about this study.