MAVRIX BIO

Frequently Asked Questions

1. How does a gene therapy work and how is it used in Angelman syndrome (AS)?

Gene therapy is an approach to treating genetic disorders. With gene therapy the goal is to address the root cause of the condition by repairing or replacing faulty or missing genes. It can involve adding a working copy of a gene, modifying a disease-causing gene, or changing how a gene works in an attempt to correct the underlying genetic problem. Generally, a healthy copy of a specific gene is carried into cells of the body by a virus (e.g. Adeno-Associated Virus or AAV) that has been changed to remove the parts that cause illness in people. This virus acts as a delivery vehicle. In the case of AS, a healthy copy of the missing or non-functional *UBE3A* gene is packaged inside this virus and is injected into the fluid that surrounds the brain, called the cerebrospinal fluid (CSF). Once in the fluid, the virus and gene should reach important cells of the brain, called neurons, with the goal of replacing the *UBE3A* gene involved in AS.

2. What is MVX-220?

MVX-220 is an investigational gene therapy designed to deliver the human *UBE3A* gene to neurons of the brain by a single injection into a small area at the base of the skull called the "cisterna magna" which contains CSF. MVX-220 uses an adeno-associated virus to carry a healthy copy of the *UBE3A* gene to the brain. Once injected into the fluid, the virus and gene should reach important cells of the brain, called neurons, with the goal of replacing the missing healthy copy of the *UBE3A* gene.

3. What does a cleared IND mean?

An investigational new drug application or IND is an application submitted to the US Food and Drug Administration (FDA) to run a clinical trial of an investigational therapy in humans. A cleared IND means that the FDA has reviewed the IND application submitted by the study Sponsor (MavriX Bio) and indicated that the planned clinical study may proceed.

4. Has gene therapy been used in patients with other diseases?

Yes, gene therapy has been used in patients with many other diseases such as spinal muscular atrophy, Duchenne muscular dystrophy, Hemophilia, etc. In the US, there are over 20 approved gene therapy treatments and over 200 clinical trials have studied an AAV-based gene therapy.

5. When do you expect to start this clinical trial?

We plan to start this trial in the second half of this year (2025). We will provide more information in the coming months through a webinar jointly hosted by the Foundation for

Angelman Syndrome Therapeutics (FAST) and the Angelman Syndrome Foundation (ASF). We will also provide study details on clinicaltrials.gov as soon as they become available.

6. Which study sites will be included?

We are still in the process of selecting sites for this study. We will provide more information in the coming months through a webinar jointly hosted by FAST and ASF. We will also provide study details on clinicaltrials.gov as soon as they become available, which will include a list of study sites as they are added to the trial.

7. How can I get my child enrolled in this study?

As the Sponsor, MavriX Bio is not involved in the selection of patients for enrollment in the study. Enrollment in the study is the responsibility of the Investigator at each study site. We will provide study site details on clinicaltrials.gov as soon as they become available, which will include a list of study sites and contact information as individual sites are added to the trial.

8. How is MVX-220 administered?

MVX-220 is administered by a one-time intra cisterna magna (ICM) injection. The cisterna magna is a space at the base of the skull in the back of the neck that contains a small pocket of the CSF that bathes the brain. MVX-220 is injected through the skin into the cisterna magna space using a needle. The injection of MVX-220 will be performed by a doctor specially trained in this delivery technique. This is done under general anesthesia and with imaging, like a CT scan. The study involves a one-time administration of MVX-220.

9. Are there risks of ICM delivery?

There are risks from the ICM injection that are similar to what might occur with other injections into the CSF such as lumbar puncture. These risks include leaking of CSF, bleeding, infection, pain, increased pressure under the skull, headache after the procedure, and vomiting. With ICM injection, there is also a very small risk of brain injury during the procedure, but this is minimized by using imaging (like MRI and CT scan) to screen each patient and to guide the needle during the one-time injection. The injection of MVX-220 will be performed by a doctor specially trained in this delivery technique.

10. What are the eligibility criteria?

The study will include adults and children with AS with a variety of genotypes including uniparental disomy (UPD) and imprinting center disorders (ID). Detailed eligibility criteria will be posted on clinicaltrials.gov closer to the time of study start in the second half of 2025. We

will provide more information in the coming months through a webinar jointly hosted by FAST and ASF.

11. If my child is in another clinical trial of an investigational treatment, can they join this one too?

No. If your child is participating in another clinical trial of an investigational drug they cannot enroll in the clinical study of MVX-220 at the same time.

12. If my child is/was on an antisense oligonucleotide (ASO) can they enroll in this trial of MVX-220?

If your child is participating in another clinical trial of an investigational ASO they cannot enroll in the clinical study of MVX-220 at the same time.

If your child was previously enrolled in a clinical trial of an ASO but no longer receives treatment with an ASO they *might* be eligible for the study for MVX-220 if it has been more than 1 year since they were last treated with an ASO. Detailed eligibility criteria will be posted on clinicaltrials.gov closer to the time of study start in the second half of 2025.

13. Where can I get more information about the study?

We will provide more information in the coming months through a webinar jointly hosted by FAST and ASF. We will also provide study details on clinicaltrials.gov as soon as they become available.

14. Will there be reimbursement for travel?

Reimbursement for reasonable expenses related to travel (such as parking, mileage, meals, etc.) will be provided.

15. How long is the study?

The primary phase of the study will last 2 years. After this time, there will be a less frequent visit schedule (1-2 clinic visits per year) for 3 years. The total duration is 5 years because FDA requires long-term follow-up for investigational gene therapy products to better assess how long their effects last.

16. Is there a placebo or a control group?

No. There is no control group in the study and all patients enrolled will receive a single-dose of MVX-220.

17. Can my child take seizure medications during the study?

If your child receives treatment with anti-seizure medications, they may remain on those same medications during the study.