These Clinical Study Results are provided for informational purposes only.

This lay summary is a brief summary of the main results from a clinical study. The study listed may include approved and non-approved uses, formulations or treatment regimens. It is not intended to promote any product or indication and is not intended to replace the advice of a healthcare professional. The results reported in any single clinical trial may not reflect the results obtained across the full clinical development program. Only a physician can determine if a specific product is the appropriate treatment for a particular patient. If you have questions, please consult a health care professional. Before prescribing any product, healthcare professionals should consult the regional approved product labeling for indications and proper use of the product.

Clinical study results

A Long-Term Follow-Up Study for DTX401 in People With Glycogen Storage Disease Type Ia (GSDIa)

Thank you!

Thank you to the participants and caregivers who took part in the long-term follow-up clinical study, **401GSDIA02**. Ultragenyx, the sponsor of this study, is grateful and believes it is important to share the results with the participants and their families.

By taking part in this study, the participants helped the researchers learn more about using **DTX401** in people with **GSDIa**.

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Why was this study needed?

Researchers designed this Phase 1/2 long-term follow-up study, **[401GSDIA02]**, to continue to learn about the long-term safety of DTX401 and how well it worked in participants with **GSDIa**.

What is GSDIa?

GSDIa is a rare, **genetic condition** that prevents the body from keeping blood sugar levels normal between meals. This leads to low blood sugar (hypoglycemia) that can be life-threatening.

A **genetic condition** is passed on from parent to child through genes that do not work properly. Genes are small pieces of DNA that provide instructions for making proteins that are needed for your body to grow and work.

What causes GSDIa?

GSDIa is caused by changes (known as variants) in the gene *G6PC*, which makes an enzyme called G6Pase. In people with **GSDIa**, changes in *G6PC* lead to a missing or nonworking type of G6Pase so the glycogen stored in liver cannot change into glucose. Glycogen can build up and damage certain organs, like the liver and kidneys.

There is currently no medicine for **GSDIa**. Currently, people with **GSDIa** manage their symptoms by closely watching their physical activity and blood sugar levels, following a special meal plan, avoiding certain types of sugar, and taking cornstarch between meals. Cornstarch is a type of carbohydrate that is broken down into glucose over a longer period of time. The slow release of glucose can help keep blood sugar levels from dropping to dangerous low between meals.

How does the body usually keep blood sugar levels normal?

When the body does not need to use blood sugar **(glucose)** for energy right away, it stores it as **glycogen** in the muscles and liver.

When the body needs energy between meals, the enzyme called **G6Pase** turns glycogen back into glucose for the body to use as energy and keep blood sugar levels normal.

What is DTX401?

DTX401, also called pariglasgene brecaparvovec or AAV8G6PC, is a **gene therapy** designed to treat **GSDIa** by adding a healthy copy of the *G6PC* gene to make a working type of G6Pase. The treatment is given one time, through a vein as an intravenous (IV) infusion.

A **gene therapy** is a type of treatment that is designed to change a disease-causing gene or add a working copy of a gene to help the body function better.

Who was in this study?

This study included only participants from the previous dose finding study, 401GSDIA01. This 401GSDIA02 long-term follow-up study included the same **12 participants** with **GSDIa** from Canada, the Netherlands, Spain, and the United States.

DTX401 was only given during the 401GSDIA01 study.

The participants included **8 men and 4 women** who were between **18-57 years old** when they joined the previous 401GSDIA01 study. The average age of participants in this study was 32 years old.

What happened during this study?

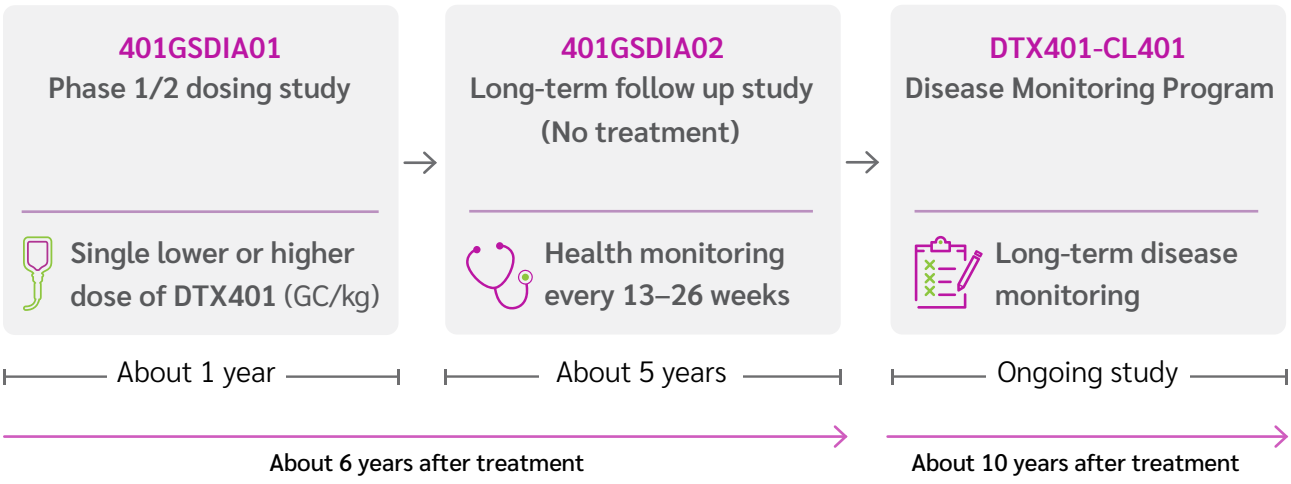
The long-term follow-up study started in **July 2019** and ended in **February 2025**. Participants were in the study **about 5 years**. This was a **long-term follow-up** study, which means researchers invited participants from the Phase 1/2 dosing study, [401GSDIA01] to join, so that the researchers could continue to learn about the study treatment.

Long term Follow-up

- Participants joined this study from the 401GSDIA01 study, where they had received a single low or high dose of DTX401. Most participants were also given medicines, called **steroids**, taken by mouth.

DTX401	DTX401
Lower dose ($2x10^{12}$ GC/kg)	**Higher dose ($6x10^{12}$ GC/kg)**
3 participants	9 participants

- The DTX401 dose was measured in **genome copies (GC)**, which are tiny units of the treatment, per kilogram of body weight (GC/kg).
- No treatment was given during the 401GSDIA02 follow-up study. Researchers continued to check each participants' health about every 13 weeks during the first year and then about every 26 weeks throughout this study.
- At the end of this study, participants were invited to join the DTX401-CL401 **Disease Monitoring Program (DMP)** for further follow-up. A **DMP** is a study that collects data from a larger group of participants over a long period of time. The data from a DMP helps researchers and people better understand the disease, how treatments work over time and how treatments work in real life.



What did researchers learn from this study?

This is a **summary** of the key results from the **401GSDIA02** study. Earlier results from the **401GSDIA01** study are available in a separate summary. Each participant's individual results might be different and are not in this summary. If you took part in these studies and have questions about the results, please contact the study site where you participated.

The results from several studies are needed to decide if treatments are safe and work to treat a condition. Other studies may give new information or different results. Always talk to a doctor before making any treatment changes.

This study was designed to answer the **main questions:**

- **What is the long-term safety of DTX401 in participants with GSDIa?**
- **How well does DTX401 work to keep blood sugar levels normal during fasting?**

This study also wanted to explore:

- **Could DTX401 lower the participants' use of daily cornstarch?**

To answer these questions, researchers looked at:

- How many participants had medical problems, called **adverse events**, during the study?
- What **possible side effects** happened during the study?
- Could participants go for longer between meals before getting low blood sugar?
- Was there a change in the participants' average daily use of cornstarch?

How many participants had medical problems called adverse events during the study?

All participants (12 of 12) had adverse events, and **7 of them** had serious adverse events in this study. No participants died during the study.

What is an adverse event?

An **adverse event** is an unwanted or unexpected sign or symptom that happens after taking the study treatment.

A lot of research is needed to know if a treatment causes an adverse event. Adverse events **may or may not be caused by the study treatment**, other drugs taken while in the study, the participants' medical history, or procedures performed in the study.

What is a serious adverse event?

An adverse event is considered **serious** when it:

- Is considered medically important by a doctor
- Requires hospitalization
- Causes a disability or birth defect
- Is life-threatening
- Causes death

This section is a summary of **all adverse events** that happened during the **401GSDIA02** study, even if the doctors thought they might not be caused by the study treatment.

The table below shows the number of participants who had adverse events during the study.

Number of participants who had at least 1:	
Adverse event, including serious and other adverse events	**12 of 12 participants** (100%)
Serious adverse event	**7 of 12 participants** (58%)

This section is a summary of the **possible side effects**.

What's the difference between a possible side effect and an adverse event?

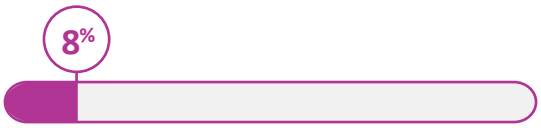
A **possible side effect** is an adverse event that the doctors thought **might be caused by the study treatment or study procedure.**

Not all adverse events are side effects.

4 of 12 participants had possible side effects.

What serious possible side effects did participants have during this study?

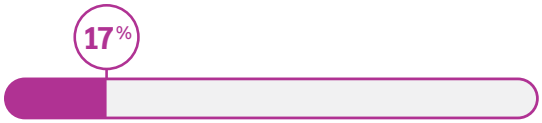
One participant had a **serious** possible side effect of hypertriglyceridemia.



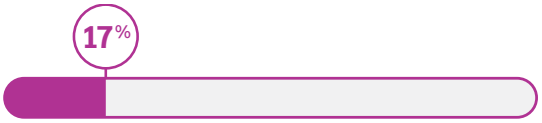
High triglyceride level in the blood
(Hypertriglyceridemia - Serious)
1 of 12 participants

What other possible side effects did participants have during the study?

Other possible events were those that did not meet the criteria to be considered as "serious". Below are other common possible side effects that happened in more than **15% (2 or more) of participants** in the study. There were other possible side effects that happened in fewer participants.



Increased liver enzyme
(alanine aminotransferase [ALT] increased)
2 of 12 participants



High triglyceride level in the blood
(Hypertriglyceridemia)
2 of 12 participants

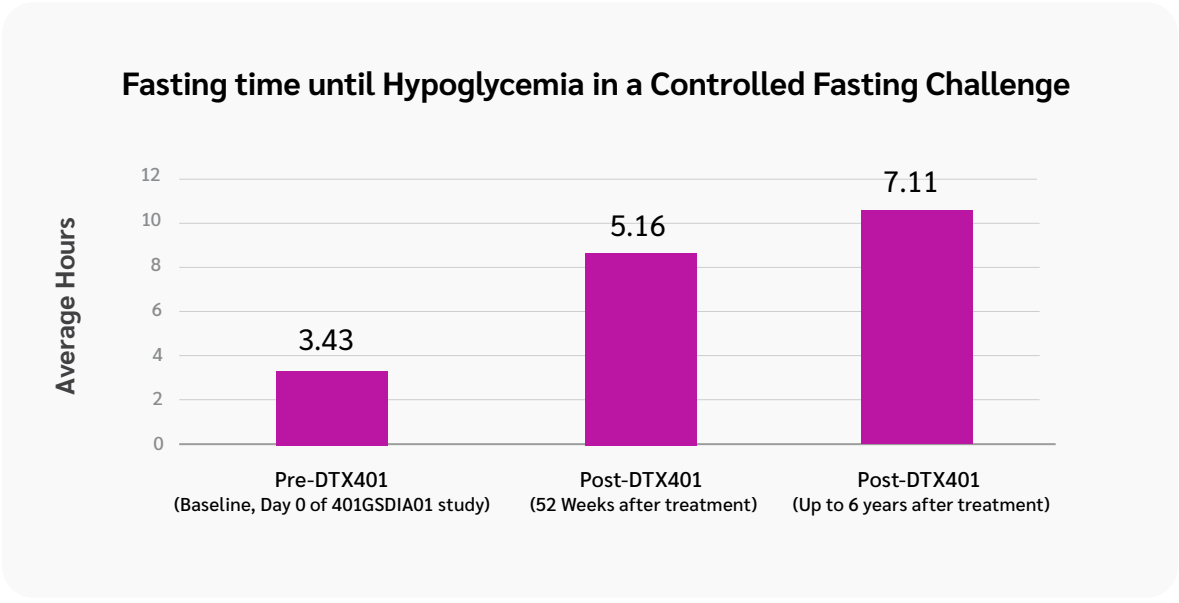
Could participants go for longer between meals before getting low blood sugar?

Overall researchers found that, up to 6 years after receiving DTX401, participants could fast (not eat or drink anything but water) for an average of 3.7 hours longer than before receiving DTX401. Researchers learned this by doing a **controlled fasting challenge**.

What is a controlled fasting challenge?

Participants stayed in the hospital overnight. They received dinner, which included a dose of cornstarch and then did not eat or drink anything for up to 15 hours. The researchers tested their blood sugar levels many times until the participant had a low blood sugar or showed symptoms of low blood sugar. **Low blood sugar** was 54 or lower milligrams of glucose per deciliter of blood (mg/dL) or 3.0 or lower millimoles per liter of blood (mmol/L).

The graph below shows the change in fasting time.



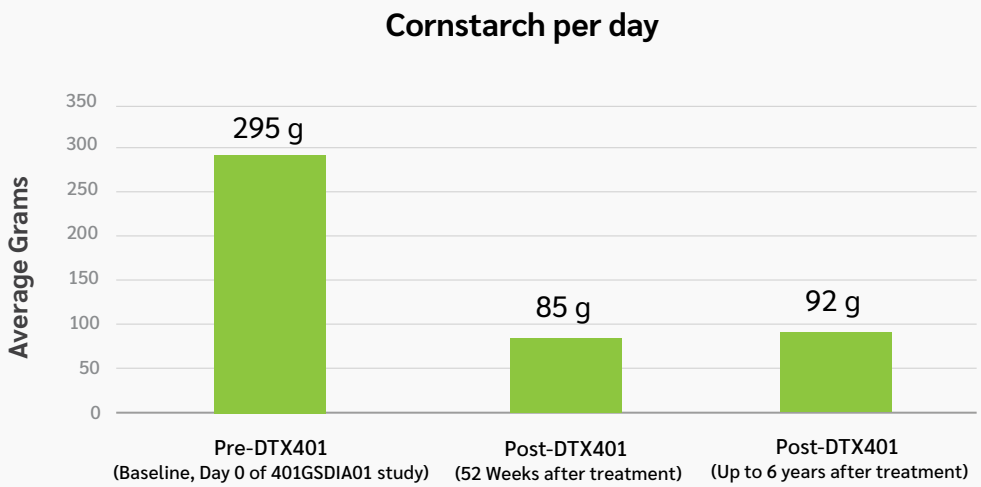
The results in this section were not the main question the study wanted to answer, but the researchers believe they may be interesting to people with GSDIA.

Was there a change in the participants' average daily use of cornstarch?

Overall researchers found that, up to 6 years after receiving DTX401, participants used an average of **69% (92 grams)** less cornstarch per day than before receiving DTX401.

To answer this question, participants reported the amount of cornstarch they used per day throughout the study.

The graph below shows the change in daily cornstarch use.



How has this study helped participants and researchers?

- Researchers found that up to 6 years after treatment with DTX401, participants could take less cornstarch and could fast longer during a controlled fasting challenge (as seen in graphs above).
- Researchers also found the most common side effects thought to be related to the study treatment were high triglycerides in the blood and increased liver enzymes. No new safety concerns were identified during this long-term follow-up study.

Ultragenyx has ongoing studies of DTX401 in participants with **GSDIa**.

Other studies may have new or different results. Always talk to a doctor before making any treatment changes.

Where can I learn more about this study?

You can find more information about this study, including a report with the study's results, on these websites:

- https://clinicaltrials.gov/ct2/show/NCT03970278
- https://euclinicaltrials.eu/search-for-clinical-trials/?lang=en&EUCT=2023-504004-29-00

Official Study Title: A Long-Term Follow-Up Study to Evaluate the Safety and Efficacy of Adeno-Associated Virus (AAV) Serotype 8 (AAV8)-Mediated Gene Transfer of Glucose-6-Phosphatase (G6Pase) in Adults With Glycogen Storage Disease Type Ia GSDIa

National Clinical Trial number: NCT03970278

EU CT number: 2023-504004-29-00

If you have questions about the results, please speak with a doctor or staff at the study site.

Thank you!

At Ultragenyx, our focus is developing medicines for people who live with rare and ultra-rare diseases. But it takes more than scientific knowledge and research to develop medicines. Your involvement is essential and ensures that the research process moves forward. Thank you for your participation in this study and commitment to research.

Ultragenyx is a biopharmaceutical company committed to bringing to patients products for the treatment of rare and ultra-rare diseases, with a focus on serious, debilitating genetic diseases.

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