Moving Research Forward with Patients and Families Affected by OTC Deficiency

OTC DEFICIENCY
RESEARCH PROGRAMS

ultragenyx

At Ultragenyx, we're intentional in how **we listen to and learn from people living with Ornithine Transcarbamylase (OTC) deficiency**. Your insights and experiences drive our research programs forward. Learn about how we hope to continue to support the OTC community with our research, and how you can stay informed.

Founded in 2010

Ultragenyx has a long-standing commitment to developing novel treatments for rare and ultra-rare diseases—providing treatments where none previously existed.

Support the Rare Disease Community

Ensure Access

Address Unmet Needs

Designed for Rare Diseases

We recognize that people living with rare diseases and their families are the experts on their conditions. That's why we engage **the OTC community**, in addition to healthcare providers, as partners in advancing research. Community feedback is critical to how we design our interventional or non-interventional studies.

OTC Deficiency and Gene Therapy

OTC deficiency

OTC deficiency is a genetic disease that results from variants in the *OTC* gene that lead to enzyme deficiency. Liver cells do not produce enough of the OTC enzyme, which is responsible for breaking down ammonia.

Gene therapy

Gene therapies are treatments that provide fully functioning copies of the gene that isn't working correctly in patients with rare diseases. Gene therapies are designed to treat genetic disorders by introducing, removing, or changing DNA within cells to compensate for genes that carry mutations and do not function correctly. For example, gene therapy could deliver a gene that instructs a cell to produce a missing protein or enzyme.

How does gene therapy work?

The gene therapies Ultragenyx is developing use a modified virus called the adeno-associated virus, or AAV, that is designed to deliver fully functioning copies of genes to the cells and organs that need the gene to function correctly. These investigational gene therapies are given by a single intravenous (IV) infusion and travel to the target cells and tissues where the modified virus, which is called a vector, delivers the gene with the goal of producing the needed protein. AAV gene therapy is the most common method of delivery being explored in clinical research today, with two FDA-approved therapies. In a patient with OTC deficiency, the goal is that the new functional gene can allow the cell to produce OTC enzymes that will break down ammonia.

Phase 3 Study Overview

Now Open!

Enh$_3$ance™ Gene Therapy for the Treatment of OTC Deficiency

About Enh$_3$ance:

- A Phase 3 study designed to evaluate the efficacy and confirm the safety of DTX301, an investigational gene therapy for the treatment of OTC deficiency
- DTX301 is a one-time IV infusion investigational gene therapy designed to provide a functional *OTC* gene that will work properly in cells
- DTX301 was granted orphan drug designation in both the US and Europe. Whether or when DTX301 will receive regulatory approval is not known

Learn more ▶

Who:

- The study will enroll approximately 50 patients (12 years and older) who have late-onset OTC deficiency and require daily treatment to control their disease

Where:

- US, Canada, Europe, South America, Australia, and Japan. In the US, approximately 10 study sites will participate in the study

What's involved:

- Patients will receive a single IV infusion of either DTX301 or placebo
- After the initial 15-month analysis period, patients who received placebo will receive an infusion of DTX301

Study duration:

- Primary efficacy analysis period: 15 months
- Screening period: 8 weeks
- Follow-up period: about 4 or 5 years, depending on when the patient receives DTX301
- This long-term follow-up is important for patients receiving investigational gene therapy products and is consistent across gene therapy trials

Study visits:

- Patients will have lab tests, clinical assessments, and reviews of their electronic study diary at inpatient and outpatient clinic visits throughout the study. The number of visits a patient will have depends on when they receive DTX301

Phase 1/2 Study Overview

CAPtivate Phase 1/2 OTC Deficiency Gene Transfer Trial

Ultragenyx has completed a Phase 1/2 study of DTX301 and has presented results at several medical conferences, including the International Congress of Inborn Errors of Metabolism and the European Society of Gene and Cell Therapy.

The latest results were presented at the American Society of Gene and Cell Therapy (ASGCT) conference.

To learn more about the study, contact our Medical Information team at **medinfo@ultragenyx.com** or **1-888-756-8657.**

Learn more ▶

Enrollment Complete!

About the study:

- CAPtivate, a global, multicenter, open-label Phase 1/2 dose escalation trial, evaluated the safety and preliminary efficacy of a single IV infusion of DTX301 in adults with late-onset OTC deficiency
- The purpose of the study was to evaluate the safety of DTX301 and to determine the optimal dose to move forward with in a larger Phase 3 study
- Patients were followed for 52 weeks after dosing. After completion, patients were asked to enroll in a 4-year extension study to evaluate the long term (a total of 5 years) safety and efficacy of DTX301
- Nine patients were treated in the first 3 dose finding groups and an additional 2 patients were enrolled to receive prophylactic steroids at the highest-dose

Antibody Study

Now Open!

Antibody Study

- Observational study of anti-AAV antibodies in people with OTC deficiency
- AAVs are naturally occurring viruses that are used in gene therapy. People who have been exposed to AAV naturally and have antibodies to the virus may not be able to take AAV-based gene therapies

Who:

- Adults (18 years and older) with a diagnosis of OTC deficiency

Study objective:

- To better understand how many people have been exposed to a virus that is used in gene therapy

Results could help understand:

- How common it is for patients with OTC deficiency to have antibodies to certain types of AAVs

During a single visit either at home or at the clinic:

- A blood sample will be taken to test whether patients have antibodies to the AAV8 serotype of the AAV virus
- A blood sample will be taken to study the patient's *OTC* gene

What patients can expect during the study:

- Agreement to participate
- Medical questionnaires
- Genetic testing
- Lab tests

Learn more ▶

Our collective understanding will grow as research evolves

Ultragenyx is committed to ongoing conversations with the OTC community. We will share findings from our OTC deficiency studies at an appropriate time after the trials are completed. Research takes time, so we expect it may be a while until we have information to report.

Help move OTC deficiency research forward

Learn more about OTC deficiency studies

Phase 3 Enh$_3$ance Study ▶ Antibody Study ▶ Phase 1/2 CAPtivate Study ▶

Connect with Patient Advocacy at Ultragenyx

Visit www.UltraRareAdvocacy.com or email PatientAdvocacy@Ultragenyx.com to stay in touch with the Patient Advocacy team and access further information about OTC deficiency and gene therapy

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