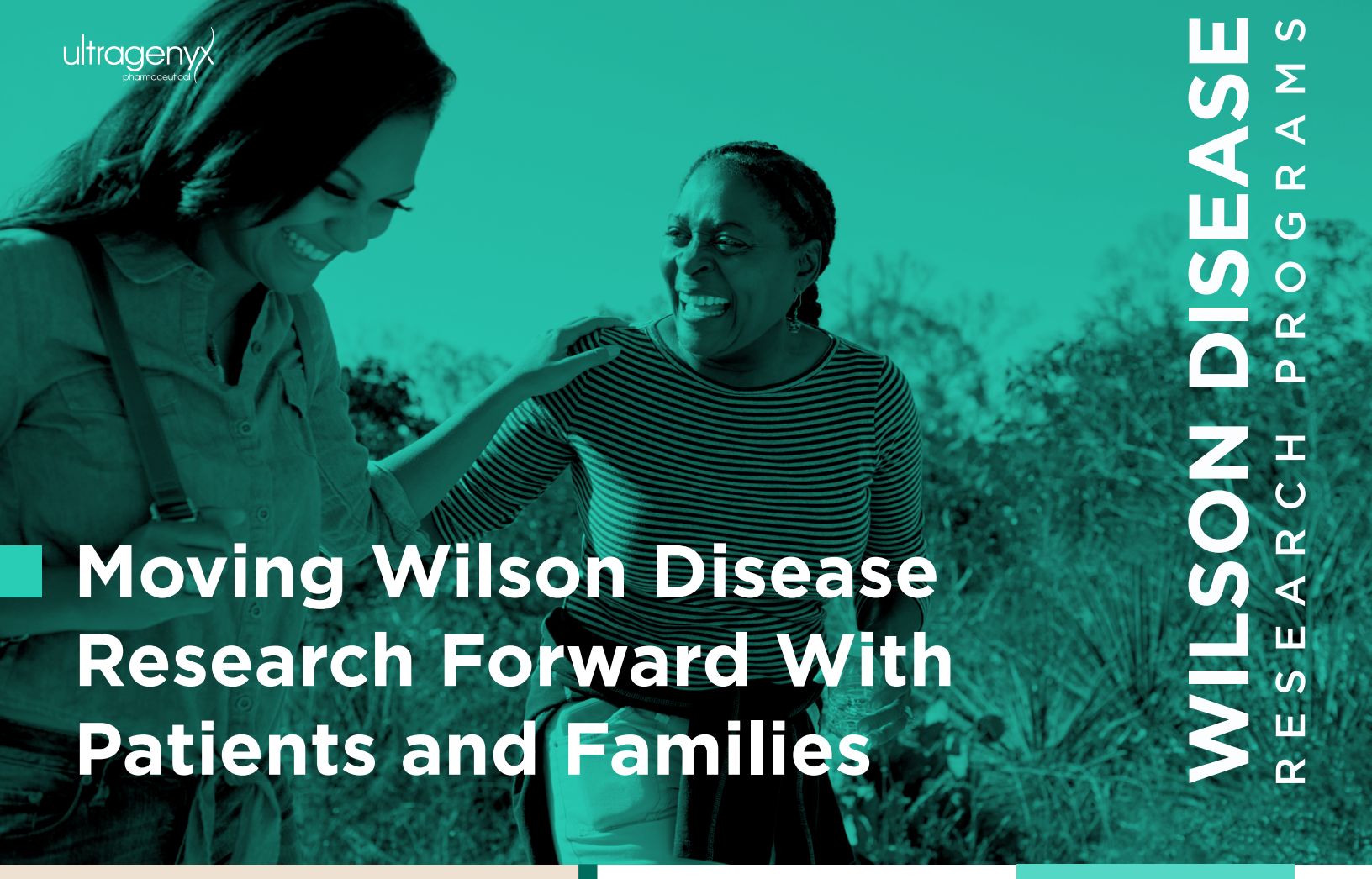


Moving Wilson Disease Research Forward With Patients and Families

WILSON DISEASE
RESEARCH PROGRAMS

ultragenyx pharmaceutical

At Ultragenyx, we're intentional in how **we listen to and learn from people living with Wilson disease.** Your insights and experiences help drive our research programs forward. Follow the path below to better understand where we started and where we are headed. Learn about how we hope to continue to support the Wilson disease 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 Rare Disease Community**
- **Ensure Access**
- **Address Unmet Need**

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 Wilson disease community**, in addition to healthcare providers, as partners in advancing research. Community feedback is critical to how we design both our interventional and observational studies.

Interventional Studies
evaluate the safety and efficacy of a particular investigational treatment.

Observational Studies
collect information about individuals with a particular condition to better understand the experiences and challenges associated with the condition; treatment is not provided.

Interventional Study

Now Open!

Cyprus^{2+} Gene Therapy for the Treatment of Wilson Disease

Behind the study name

Various aspects of the disease and the trial were thoughtfully integrated into the name and design for Cyprus^{2+}

- Wilson disease is a disorder that causes copper, or **Cu**, to accumulate in the body
- In Greek, the name for copper comes from the word **Cyprus**, a Mediterranean island known for copper mining
- The **2+** corresponds to both the element symbol and the 2 main stages of the overall trial design
- The colors of the logo are **copper**, and the **green** color of oxidized copper

About Cyprus^{2+}:

- A Phase 1/2/3 study designed to assess the safety and effectiveness of a **one-time intravenous (IV) infusion gene therapy**, UX701
  - Phase 1/2 (Stage 1) will evaluate 3 different doses of UX701 to **select a dose** for further evaluation
  - Phase 3 (Stage 2) will evaluate the **safety and effectiveness of UX701 using the dose selected** in Phase 1/2
  - UX701 is an investigational adeno-associated virus (AAV) gene therapy that has the potential to restore ATP7B function, which would improve copper metabolism and distribution
  - UX701 has been granted Orphan Drug Designation in the US and European Union, as well as Fast Track Designation in the US. Whether and when UX701 will receive regulatory approval is not known

Who:

- Adults (18+) living with Wilson disease currently being well managed on copper chelator and/or zinc therapy

Where:

- US, Canada, Latin America, Europe, and Japan

What's involved:

- Patients will receive a single IV infusion of either UX701 or placebo, followed by ~2 months of oral corticosteroids or placebo
- Patients who received placebo will receive UX701 in the long-term follow-up portion of the study if still eligible, followed by ~2 months of oral corticosteroids

Home health and clinic visits
There are 3 to 4 in-person clinic visits and 1 home health visit for screening. Home health visits may be conducted via telephone or video. Once eligible, there is 1 overnight clinic stay for dosing, 5 clinic visits, and 14 home health visits

Long-term follow-up
All patients will undergo long-term follow-up for 5 years

Support is provided for travel costs to clinic visits

Learn more ▸

Engaging the Wilson disease community to understand additional research opportunities

Ultragenyx studies put the people who live with Wilson disease at the center of our research process.

Burden of Wilson Disease Survey | Online survey of adult patients and caregivers to quantify the burden of living with Wilson disease

Impact on quality of life
48% of patients reported that Wilson disease has an overall **negative impact on their quality of life**

Most bothersome aspect of Wilson disease
- Medication regimen (19%)
- Financial burden (19%)

Biggest concern about the future related to Wilson disease
- Liver problems (19%)
- Lack of access to medication (19%)

Highlights From Survey Results

- 21 adults and 4 caregivers of children with Wilson disease took the survey
- Adults rated their emotional state as being the impact most negatively affected by Wilson disease
- Caregivers most frequently reported that "uncertainty about the future" was the most challenging aspect of living with someone with Wilson disease

Results were used to design other research, including Cyprus^{2+}

We would like to acknowledge and thank those who participated in this survey

Observational Studies

Our studies for Wilson disease are approved by an independent third-party Institutional Review Board (IRB).
Please discuss the risks and benefits of participating in any clinical trial with your healthcare provider.

Odyssey Study

Now Open!

- Research study to centralize medical records for patients and create an anonymized dataset for researchers to better understand Wilson disease
- Sponsored by Ultragenyx in partnership with PicnicHealth, a digital health company
- People with Wilson disease who enroll will get access to their complete medical history via the PicnicHealth timeline

Who:

- Adults and children who live in the US with Wilson disease, on any treatment, including those who have undergone a liver transplant

Study objectives:

- Understanding the natural history of Wilson disease, disease progression and how this may change over time
- Understanding how Wilson disease is managed in the real world
- Exploring the disease burden of Wilson disease

Results could help understand:

- How Wilson disease is managed in the real world
- Opportunities to diagnose Wilson disease earlier
- Opportunities to help patients better navigate the healthcare system

How does Odyssey work?

- Sign up, share the names of all your doctors in less than 10 minutes, and complete an initial survey
- PicnicHealth compiles and de-identifies your medical records
- Researchers use your de-identified data to improve their understanding of Wilson disease to help improve future quality of care

Learn more ▸

Antibody Study

Now Open!

- Observational study of anti-AAV antibodies in people with Wilson disease
- Adeno-associated viruses (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+) with a diagnosis of Wilson disease

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 Wilson disease 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 you have antibodies to the AAV9 serotype of the AAV virus
- A blood sample will be taken to study your *ATP7B* gene

What to expect during the study:

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

Learn more ▸

Clinical Survey Study

Now Open!

- Observational clinical survey study open to adults and children 12 and older with Wilson disease, including those who have undergone a liver transplant

Study objective:

- Determine the relevance and appropriateness of outcome assessments, including biomarkers, within the Wilson disease population

Results could help understand:

- Study design and endpoint selection for future clinical studies

Learn more ▸

Study design:

Daily Diary

Day 1
In-office Assessment
Includes:
- Medical history
- Patient-reported outcome (PRO) and clinician-reported outcome (CRO)
- Motor function and joint pain
- Blood sample

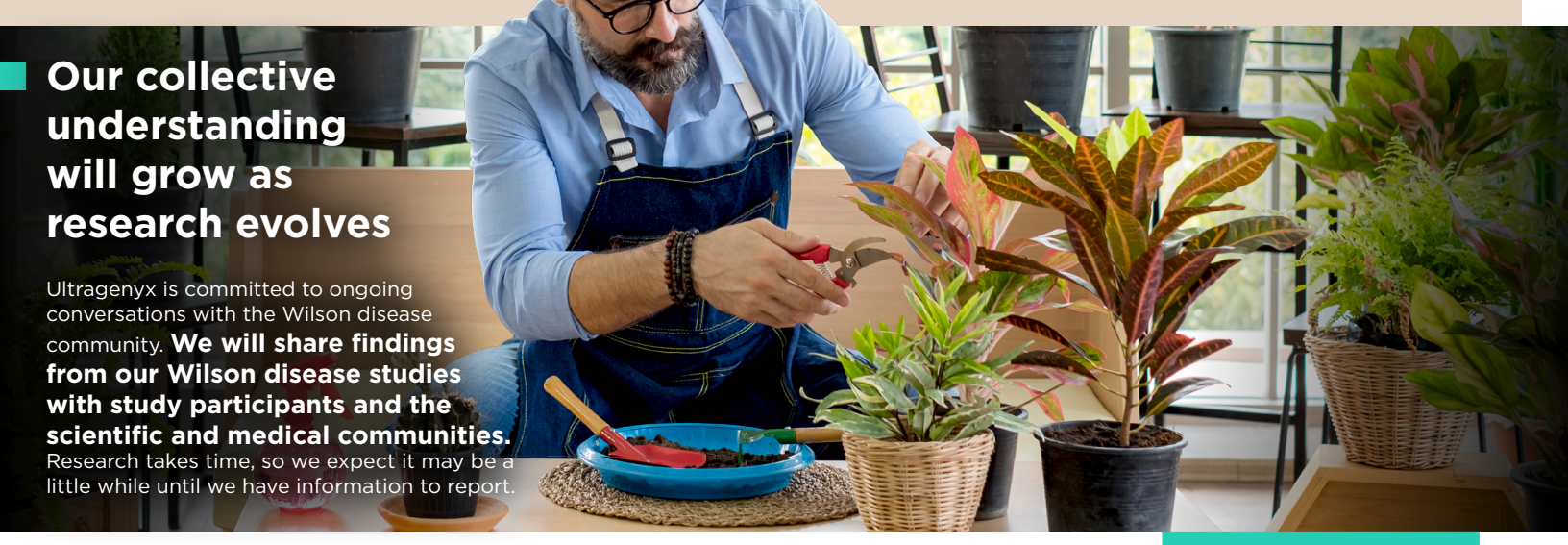
Day 15 (±3 Days)
At-home Assessment by a Home-infusion Nurse
Includes:
- Blood sample
- Urine sample
- PRO
- Daily diary

Day 30 (±7 Days)
At-home Assessment by a Home-infusion Nurse
Includes:
- Blood sample
- Urine sample
- PRO
- Daily diary
- Cognitive debrief interview (US only)

3 to 5 days after last assessment

Follow-up Call
- Collect information on medications, nutritional supplements, and adverse events

Compensation and travel will be provided for participants



Our collective understanding will grow as research evolves

Ultragenyx is committed to ongoing conversations with the Wilson disease community. **We will share findings from our Wilson disease studies with study participants and the scientific and medical communities.** Research takes time, so we expect it may be a little while until we have information to report.

Help move Wilson disease research forward

Learn more about Wilson disease studies

Cyprus^{2+} ▸ | Antibody Study ▸ | Odyssey ▸ | Clinical Survey 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 Wilson disease and gene therapy

WILSON DISEASE
RESEARCH PROGRAMS

MRCM-UX701-00061
December 2021