

February 17, 2022

Dear Members and Friends of WDA,

First and foremost, we hope this update finds you and your families continuing to stay safe and healthy. Enclosed is an important update about the CYPRUS²⁺ study on behalf of the Ultragenyx Wilson disease study team.

Ultragenyx is pleased to announce that the first patient has been dosed in the CYPRUS²⁺ study, a one-time intravenous (IV) infusion of UX701, an investigational gene therapy for the treatment of Wilson disease. Ultragenyx is sponsoring this global study to determine if UX701 gene therapy is a safe and effective treatment for adults with Wilson disease. This adeno-associated virus (AAV) gene therapy has the potential to restore ATP7B function, which may improve copper metabolism and distribution.

CYPRUS²⁺ is a study to assess safety, tolerability and efficacy of a one-time intravenous (IV) infusion of UX701, an investigational gene therapy for the treatment of Wilson Disease. CYPRUS²⁺ utilizes an innovative seamless Phase 1/2/3 clinical trial design for UX701 that allows us to progress through the phases of drug development more efficiently. UX701 has been granted Orphan Drug Designation in the United States and the European Union, as well as Fast Track Designation in the United States, however this type of research takes time, so it will be a while before we know whether or when UX701 will receive regulatory approval.

The CYPRUS²⁺ study continues to enroll adults living with Wilson disease, currently well-managed on standard of care. We will be enrolling across multiple sites in the United States, Canada, Latin America, Europe and Japan. Please find a full summary of the study at this [link](#). In addition, you are invited to email PatientAdvocacy@Ultragenyx.com for more information, as well as request educational resources for gene therapy.

We would like to express our sincere gratitude to those individuals and families who have helped us deepen our understanding of Wilson disease. We will continue to work with a sense of urgency and purpose on your behalf and are committed to providing updates as information becomes available to share.

Warm regards,



Kristin Smith
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