ultragenyx

**Going beyond every day.™**

May 31, 2024

Dear AGSD UK,

To meet your request for ongoing updates about DTX401, our investigational AAV8 gene therapy for the potential treatment of GSDIa, Ultragenyx would like to share that yesterday we announced positive top-line results from the ongoing Phase 3 *GlucoGene* study (2020-004184-2). The randomized, double-blind, placebo-controlled study has dosed 46 participants aged eight years and older with DTX401 or placebo.

Summary of the top-line announcement includes:

- The primary endpoint of the study was achieved, showing that treatment with DTX401 resulted in a statistically significant and clinically meaningful reduction in daily cornstarch intake compared with placebo at Week 48.
- All of the participants treated with DTX401 have been able to reduce their daily intake of cornstarch while maintaining their glucose control, and at Week 48 the mean percent reduction was 41.4% in the DTX401 group compared with 10.1% in the placebo group.
- The safety profile was acceptable and consistent with Phase 1/2 study results. Anticipated effects on the liver from AAV gene therapy were all non-serious and manageable with a prophylactic corticosteroid regimen.
- As with all experimental drugs, it is important to remember that at this time, the safety and efficacy of DTX401 have not yet been established.

What happens next?

- We plan to present the data at an upcoming scientific conference later this year.
- Continued participation by all patients enrolled in this study remains critical to its success. As we know from our Phase 1/2 study, reduction in cornstarch intake can continue over time and long-term data will be essential as we work to gain regulatory approval.
- The safety profile of DTX401, including AAV8 class effects and risks, will continue to be monitored in the study and through long-term follow-up.
- We are preparing to hold discussions with global regulatory authorities to support a marketing application in 2025. Once a marketing application is submitted, regulatory agencies carefully review it to determine whether an experimental drug is considered of good quality, safe and effective, has a positive benefit/risk profile, and can be approved for use outside of a clinical trial.

On behalf of Ultragenyx, I want to thank the GSDIa community for championing this gene therapy program. From your early support to start the research years ago, to the patients and families participating in the DTX401 studies and the clinicians and researchers contributing to this research, we are humbled to work alongside you to rapidly move the development of DTX401 forward.

While we still have a lot of work ahead of us, we recognize that this is an important milestone for the community. We remain committed to sharing timely information as the program progresses.

Sincerely,

Kristin Voorhees

Kristin Voorhees, MA
Senior Director, Patient Advocacy