July 21, 2022

Dear Members and Friends of the Association for Creatine Deficiencies (ACD),

First and foremost, we hope this update finds you and your families safe and healthy.

We wanted to inform you of a decision to close the Vigilan Natural History study early and ahead of schedule in September 2022. This study has been a success and we look forward to sharing the data with you in upcoming publications and plain language summaries. Ultragenyx remains steadfast in our commitment to advancing creatine transporter deficiency (CTD) research and we continue to work diligently on our small molecule CTD development program (UX068). This research is progressing as planned.

A bit of history: Ultragenyx assumed the sponsorship of Vigilan, the first observational natural history study focused on understanding CTD, from Lumos Pharma in 2019. We successfully met our target of enrolling 50 patients into the study in September 2021. Since reaching this milestone, the Joint Steering Committee team of Ultragenyx and academic Principal Investigators has been evaluating data to be included in the study's first manuscript, which is anticipated to be published sometime in 2023.

Thank you!
Ultragenyx is extremely grateful to the patients and families who are currently participating and those who have completed participation in Vigilan. You and your children have helped to establish an understanding of disease manifestations over time, data that will shape research today and in the future. Participation in a study requires a significant investment of time and resources for families and your commitment and contributions have made a substantial impact. This research would not be possible without you.

We have been in communication with Vigilan study sites and have reminded them that it is the responsibility of the study investigators and sites to promptly inform patients and families participating in Vigilan of this news. It's important that families participating in the study be informed first, and at the same time we also recognize that the CTD community is small, and we understand the importance of communicating to the broader community as well. We thank you for your patience as this news is disseminated. If you are enrolled in Vigilan and have questions, please contact your study site directly.

The decision is guided by two factors: The decision to complete Vigilan ahead of schedule comes after a thorough analysis of the data, and has been informed by the following:

1. ***Robust and sufficient data collection*.**
    - A significant amount of information has been collected since Lumos initiated the study in 2016. As we near closure in September 2022, the majority of patients will have contributed close to four years of data and fully completed the study.
    - The constructs measured in Vigilan include cognition, behavior, communication (receptive and expressive language), motor function, and activities of daily living. This data shows that

patients demonstrate a very consistent pattern in their assessments over time. This has helped us identify both the constructs to measure and the tests that are most feasible to administer in a future clinical trial. Combined with other sources of data collection, including surveys and interviews, the Vigilan data will inform our endpoint development and strategy. Vigilan data will also be valuable in supporting future regulatory interactions.

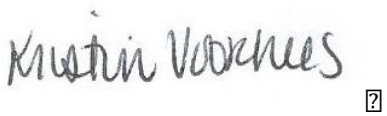
2. ***Focusing on pre-clinical and clinical development***. The decision to complete Vigilan ahead of schedule will enable us to focus our efforts and resources on the future direction of the UX068 program as we prepare for key milestones, including an Investigational New Drug (IND) submission to the FDA and first in human clinical trial. Key activities include advancing non-clinical and Chemistry, Manufacturing and Controls (CMC) research, which are typical at this stage of pre-clinical development. Our regulatory interactions related to UX068 are unaffected by the study's early completion and we will share updated timelines with you when the UX068 program has advanced to the next stage.

Addressing your questions: We understand that you may have questions about this decision. As part of our commitment to providing the community with the timely updates you have requested, we are planning a webinar with ACD and look forward to expanding on this information and further discussing key learnings from Vigilan. As we plan this webinar, we will ask that you submit your questions in advance to ACD so that we can prepare a comprehensive presentation. Please look out for more information from ACD in the coming weeks.

Another research opportunity: We are currently conducting an interview study among caregivers of individuals living with CTD in the United States. The one-on-one interviews will explore caregiver perceptions and the experiences of individuals living with CTD, including the symptoms and daily impacts of CTD. This research will inform both our long-term strategy for developing endpoints and selecting clinical assessments to measure change in future clinical trials and the development of a CTD Conceptual Model. The CTD Conceptual Model will support our interactions with regulatory agencies and include all of the important concepts in CTD related to signs, symptoms and physical, social and emotional impacts to daily living that are discovered through the literature and discussions with clinical experts and families living with CTD. If you are interested in learning more about the interview study and to see if you are eligible to participate, please contact Natasha at 520-325-9510 or natasha.schumacher@clinoutsolutions.com.

We look forward to engaging with you in the upcoming webinar in partnership with ACD. In the meantime, you can access and download rare disease education and tools on our Patient Advocacy website at UltraRareAdvocacy.com and follow us on Facebook at Facebook.com/Ultragenyx.

Sincerely,



Kristin Voorhees
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