November 2023

Dear families living with CDKL5 Deficiency Disorder,

Ultragenyx recognizes the CDD community's interest in our ongoing research and we want to ensure that you have access to timely and accurate information. We are writing today to share an update on the timeline for development of UX055, our investigational gene therapy program for the treatment of CDD.

We have been conducting pre-clinical studies in non-human primates to understand how our gene therapy, UX055, affects the expression of CDKL5, the enzyme that is deficient in some cells in patients living with CDD. We are actively engaged in analyzing and understanding the expression data being generated by these studies. As a result, we need additional time before we file an application for review and approval by the US Food and Drug Administration (FDA) or other global regulatory authorities, which will in turn delay the start of our clinical program. We want to be fully confident before we treat patients and believe this is necessary to be absolutely certain that we get it right for families living with CDD.

We have invested time and resources over the last 5+ years to the UX055 program to lay an integral foundation for our clinical development efforts and our commitment remains unchanged. We are working with urgency towards a future regulatory submission and will provide you with an update by March 2024 when new information becomes available. We are also committed to sharing learnings to benefit the CDD research community more broadly. For example, our team will participate in the 2023 CDKL5 Forum this month and Dr. Sharyl Fyffe-Maricich will present non-clinical learnings about the expression/regulation of *CDKL5* that we have accumulated over the course of developing UX055.

We understand this news might disappoint you. We want to assure you that we remain focused and dedicated to the UX055 program and our team is working as quickly as possible to advance it to the next phase. The nature of early pre-clinical research requires flexibility given the number of variables involved at this stage of development, and each team member is working urgently with the knowledge that children and their families are waiting.

As we look ahead, we reflect on remarks made by our CEO Dr. Emil Kakkis during the 2022 CDKL5 Forum: *"The development of new treatments for rare diseases is hard, and we will all be in this together. Many unforeseen challenges will occur that we must solve to advance research and getting to a safe and effective drug will take time, fortitude, and collaboration with the community."*

Our relationship with the CDD community is of the utmost importance, and the Ultragenyx UX055 team would like to express our sincere gratitude to the caregivers, families and CDD patient advocacy organizations who have been strong allies in sharing insights and feedback. We will continue to work together as we prepare for a future clinical trial, and we look forward to additional collaborations and learning from you. Thank you for your partnership on this dynamic journey.

Sincerely,

Kristin Voorhees

Kristin Voorhees
Director, Patient Advocacy and Patient Engagement