October 15, 2020

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

First and foremost, we hope this note finds you and your families safe and healthy in light of this year of many unexpected and unprecedented challenges.

We continue to work diligently to help address the unmet needs of patients and families impacted by creatine transporter deficiency (CTD) and are pleased to provide you with several important updates following our letter in February.

Earlier this year, we shared that Ultragenyx was focused on crafting the clinical development plan for UX068, our investigational treatment for CTD. We were excited to share preclinical results at this summer's CCDS Virtual Conference and we continue to pursue the mandatory safety activities which the U.S. Food and Drug Administration requires in order for us to move into the clinic. The UX068 program is a priority for Ultragenyx and, at this time, we plan to file an Investigational New Drug (IND) application in 2021, pending the results of the safety studies.

The Vigilan study continues to progress well, despite some challenges imposed by COVID-19. To those new to Vigilan, it is an observational study focused on understanding the natural history of CTD, which means there is no treatment involved at this time. The study includes nine active sites, with 49 patients currently enrolled, and is still open for enrollment. During the height of the COVID-19 pandemic, all sites were closed for non-interventional studies such as Vigilan, to ensure the safety of patients. We have been in frequent communication with the sites and are monitoring their individual reopening plans based on state and institutional policies. Based on a recent evaluation of study information gathered to date, we do not expect COVID-19 to have any major impact on Vigilan.

In addition, we continue to make progress on our goal of better understanding the experiences of patients, caregivers and families living with CTD through two unique global initiatives: an online burden of disease survey and a virtual advisory board.

Our Clinical Outcomes Research and Evaluation (CORE) team concluded its caregiver burden of disease survey this summer. CORE is responsible for conducting research, like this survey, to understand patients' experiences, perspectives, needs, and priorities and subsequently ensuring that these data are incorporated into Ultragenyx's drug development programs. CORE will use this information to help ensure that the assessments selected for any future Ultragenyx CTD clinical studies are relevant to patients and their caregivers. A total of 40 caregivers from the United States, Canada, Australia, the United Kingdom, the Netherlands, and Germany participated in this survey over the course of 14 months. We are now analyzing the data and expect to share a high-level summary of results with the ACD community in early 2021. Ultragenyx also plans to publish the full results of the survey in the future.

In addition, the Patient Advocacy team convened a virtual advisory board meeting in July to understand the journey of patients and families living with CTD, gain insights into their treatment experiences and preferences, and identify opportunities to engage with and educate the community. A group of nine caregivers provided Ultragenyx with

deep insight into topics such as challenges with testing and diagnosis, how their loved one's symptoms have changed over time, and opportunities to support and advance the CTD field. These insights complement the burden of disease survey and will also be used to inform Ultragenyx's CTD program.

Ultragenyx is excited about the progress we have made this year and look forward to sharing future updates with you as new information becomes available. As always, thank you for your contributions to the CCDS community and all that you and others do to advance the CCDS field. In addition, thank you to all of the families who participated in the advisory board, survey, and those that are participating in the Vigilan study – you are helping to shape Ultragenyx's understanding of CTD and inform the patient, caregiver, scientific and medical communities through future publications that will result from these efforts.

Sincerely,

Camille L. Bedrosian, MD
Chief Medical Officer and Executive Vice President