ASSOCIATION FOR CREATINE DEFICIENCIES

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Ultragenyx Town Hall Follow-Up Questions

Thank you to Ultragenyx for providing the following answers to questions submitted during ACD's ***October 2022*** *virtual town hall discussion with Ultragenyx. Answers to all other questions submitted before the town hall were addressed during the event which can be viewed on ACD's YouTube channel.*

1. Is there any potential for follow-up studies?

   We received a great deal of information from the Vigilan study. At this time, we are not planning any follow-up NH studies.

2. How many females were enrolled in the NHS (natural history study)? Is there enough info on them to be included in a potential clinical trial?

   Research on females living with CTD is very limited and to our knowledge, the field does not have a good understanding of the prevalence of CTD in females. Lumos Pharma, the company who started Vigilan, did not include females in the study design and Ultragenyx did not make any changes to the study when we took over Vigilan because the study had been ongoing for several years. It would be very helpful to have natural history data on female patients, especially because their clinical presentation is quite variable. All clinical trials have inclusion and exclusion criteria which are specific to that study and the research goals of that study. Future CTD studies could benefit from including females given the lack of research in this population.

3. Considering the vast range of variability amongst study participants {black bars}, has there been/will there be any investigating to see how/rather this gap may be partially attributed to exposure(s) to interventions? IE: physical, occupational, speech, behavior intervention. Was there any difference in development/improvements seen over time in those kids that were receiving intervention in form of speech, physical, occupation therapy and/or taking supplements, versus not?

   These are very good questions and perspectives. It does seem likely that these interventions could impact skill development. However, it is not clear that we have enough patients in each age range, nor enough data on exposure to each therapeutic modality over time to draw significant conclusions.

4. For the enrolled individuals who did not meet the characteristics for Autism Spectrum Disorder- how was that assessment made? Was there any correlation between this finding and their mutation/function associated with their SLC6A8 variant? Was this an age-related finding or does it mean that they have a less severe presentation? How might this impact their enrollment in the trial? More likely/less likely?

   The Autism Spectrum Disorder (ASD) diagnosis was based on caregiver report obtained as part of the Medical History, so it was not validated by testing. We have not done any specific genotype phenotype correlation in this study. We are not at the stage of the drug development process where we are defining enrollment criteria but would not expect the diagnosis of ASD to have an impact on enrollment in a clinical trial.

5. Will you be able to show the data broken down by age range- to differentiate between whether or not there is an age related plateau; rather than data shown only in median ranges?

   This is an interesting concept, but our age group cohorts are too small to make definitive conclusions on this topic.

6. Have animal trials started yet?

   Yes, they are in progress. Ultragenyx continues to pursue preclinical development of UX068, including animal studies, to support a potential IND filing, and looks forward to sharing more details about the program as appropriate.

The recording of the town hall can be found on ACD's YouTube Channel.