Dear GNE Myopathy Patient Community,

We announced very disappointing news from our Phase 3 study of UX001 (Ace-ER) which failed to demonstrate efficacy in treatment of GNE myopathy. We did not confirm the benefit in maintaining the arm strength of subjects treated with Ace-ER as we had expected from our Phase 2 study. If there was any effect, it was small and the other endpoints did not provide any supporting evidence for efficacy. Safety was acceptable as previously observed. We can tell that the patients were taking the drug by their serum sialic acid levels. I believe the Ultragenyx clinical team designed and conducted a high-quality study but the treatment effect was unfortunately, not confirmed.

We have been looking at why it did not work and there is no perfect answer. It is clear that the patients included in this study were stronger at baseline but this is what we planned by our inclusion criteria to include people with more muscle to lose, based on our Phase 2 data. These Phase 3 patients did not decline quite as fast as expected but they did still decline in arm strength and Ace-ER had no significant effect. There may be other smaller differences between the studies, but those differences alone cannot fully account for the lack of efficacy in stabilizing the patients. The phase 2 study was small and the Phase 3 study much larger, so it is a better dataset to make conclusions. Without a pathway forward for the product to approval and no positive results, we had to terminate the program and focus on other things at the company.

For patients in our studies or on compassionate use, we are most heartbroken that we cannot offer even a modest therapy for them and that their future now depends on other research work that is ongoing. We will manage this transition graciously to avoid a precipitous stop. We know this is a shocking moment for patients on our studies and for those who feel the drug is helping them. For patients not already on Ace-ER, we cannot initiate new therapy. Whether on Ace-ER or not, the GNE myopathy patient community needs to not lose faith in research but participate in other clinical studies to help get an effective treatment approved. Patients will likely have to be off Ace-ER to participate in other clinical studies.

While we were unable to get Ace-ER to approval, we did contribute to the field and this is very important in the development of any therapy. GNE myopathy is a more widely known disease now among people other than doctors and patients. It is being diagnosed more often with the diagnosis program we supported. We established and made available new methods and endpoints for measuring muscle strength and GNE myopathy patient function as well as gained acceptance for those endpoints from a regulatory standpoint. FDA and EMA know the disease now and a regulatory pathway now exists. Our DMP natural history study data are very valuable and as planned, all of our data will be available for others doing research on the disease through our relationship with TREAT-NMD. Finally, we will continue our research work to develop a better replacement therapy in our sialic acid prodrug program. If we can demonstrate it has substantial efficacy in animal models then perhaps we can come back to the clinic at some point in the future. We don't know when that will be but the work is ongoing. In the meantime, we are hoping to see patients participate in other clinical programs and fight this disease everywhere, every day, and all the time, until a solution is found.

Thank you for all you do.

Emil