May 25, 2022

Alexandra Hall
Managing Director
The ISAAC Foundation
5291 County Road 30
Campbellford, Ontario
K0L 1L0, CANADA

Dear Alexandra,

On behalf of Takeda, we are writing to share some disappointing news with the Hunter syndrome community regarding Takeda's investigational intrathecal enzyme replacement therapy (ERT), TAK-609, for the potential treatment of pediatric patients with Hunter syndrome (mucopolysaccharidosis II / MPS II) and cognitive impairment.

After an eight-year journey, Takeda has made the difficult decision to discontinue development of TAK-609 and will not proceed with regulatory submissions to the U.S. Food & Drug Administration (FDA), the European Medicines Agency (EMA) or any other health authorities. We recognize this is not the decision we all hoped for when Shire (acquired by Takeda in 2019) set out to find a treatment that could address the debilitating cognitive effects of this disease. Several members of our Takeda team have been working on this program, alongside the MPS II patient community, since the beginning, so we understand the sadness we all share about this outcome.

As the community likely recalls, we announced that the Phase 3 trial did not meet its primary or key secondary endpoints back in December 2017. Since that time, we continued collecting extensive data, remaining hopeful that we might find a potential path forward. We know the MPS II community has waited since then for an answer and we thank you for your patience. Unfortunately, after several years of extensive review and discussions with health authorities, we are disappointed to share that the data were determined to be insufficient to support a regulatory filing and unable to meet the evidentiary standard for regulatory approval.

This outcome does not change our unwavering commitment to the MPS II community. We are highly sympathetic to the families affected by this rare disease. With patient care continuity as our priority, we will continue to make TAK-609 available to patients who are currently enrolled in the ongoing open-label extension studies until an approved treatment option is available to address the cognitive symptoms of this devastating disease. We also plan to share extensive learnings from the clinical program with external partners/collaborators to help inform future studies for the potential benefit of patients and their families.

To our long-term advocacy partners, we are deeply grateful for everything you do in representing those living with MPS II, and to the support of the families, children, and healthcare professionals in the community throughout this clinical program. There is no doubt that your collective support contributed to elevating our understanding of Hunter syndrome and how we can best support this community in the future.

Please let us know if you have any questions.

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