22 June 2023

Dear Parent Project APS,

Following your request for regular updates, it is a great pleasure to share the news that the US Food and Drug Administration (FDA) has approved delandistrogene moxeparvovec-rokl (also known as SRP-9001) for the treatment of ambulatory children (those who are able to walk unassisted) aged 4 through 5 years with Duchenne muscular dystrophy (DMD) and a confirmed mutation in the *DMD* gene.[1] Delandistrogene moxeparvovec-rokl is contraindicated in patients with any deletion in exons 8 and/or 9 in the *DMD* gene. In the US, delandistrogene moxeparvovec-rokl will be marketed as Elevidys™ (Ah-LEV- ah-dis) and is the first gene therapy approved for Duchenne.

Duchenne is characterised by mutations in the dystrophin gene that result in the lack of dystrophin protein. In the absence of dystrophin, which is required to strengthen and protect muscles, muscles become weakened and damaged.[2] Delandistrogene moxeparvovec addresses the root genetic cause of the disease by delivering a gene that codes for a functional shortened form of the dystrophin protein to muscle cells known as Elevidys micro-dystrophin. Delandistrogene moxeparvovec is given as a one-time intravenous (IV) infusion. Roche is developing delandistrogene moxeparvovec in partnership with Sarepta Therapeutics and is responsible for bringing this treatment to patients across the rest of the world (excluding the US).

The Biologics License Application (BLA) submitted to the FDA included safety and efficacy data from three Phase 1 and Phase 2 studies for delandistrogene moxeparvovec:[3] Study 101 (NCT03375164), Study 102 (NCT03769116), Study 103 (also known as ENDEAVOR, NCT04626674) and an integrated analysis across these three clinical studies comparing functional results to a propensity-score-weighted external control*.[4,5,6] Delandistrogene moxeparvovec-rokl was approved under the FDA's Accelerated Approval pathway**.

To qualify for this approval pathway, a confirmatory trial to verify the results of the studies submitted for a BLA must be completed. The fully enrolled, global Phase 3 EMBARK study (NCT05096221) will serve as the confirmatory study for delandistrogene moxeparvovec-rokl. This means that, if the trial meets its objectives, the FDA will assess conversion to traditional approval and the results will inform its decisions moving forward regarding the potential for a broader indication. Sarepta will work as quickly as possible to share data from EMBARK with the FDA. The top-line results are expected at the end of this year.[8]

Following this announcement, we deeply appreciate that many families, caregivers and people living with Duchenne will be seeking to understand if and when this medicine is likely to receive approval in their country.

We know that time is muscle, and time has incredible value for every family touched by Duchenne. At Roche, our unwavering focus remains on working with urgency to file regulatory applications with health authorities around the world to ensure delandistrogene moxeparvovec reaches eligible children as quickly as possible. An overview of our regulatory application plans is below, based on the latest information we have available. (Please do note that the status of our applications may change, depending on the requirements of health authorities.)

- In countries that can accept applications based on Phase 1 and Phase 2 data for delandistrogene moxeparvovec, we are already engaging with health authorities and plan to submit applications as soon as possible. These countries include Bahrain, Brazil, Israel, Kuwait, Oman, Qatar, Saudi Arabia, Singapore and the United Arab Emirates.

- The European Medicines Agency (EMA) have indicated that the inclusion of clinical trial data from the Phase 3 EMBARK study for delandistrogene moxeparvovec are vital for their assessment. If the EMBARK data are supportive, we expect to submit marketing authorisation applications to the EMA and to other health authorities as soon as possible.

The FDA approval is the first of what we hope will be many more encouraging updates to the Duchenne community as delandistrogene moxeparvovec continues its journey to reach those who need it. Our sincere gratitude and appreciation goes out to the families who are participating in Duchenne research and the tireless efforts of patient groups, clinical trial sites and staff - achievements like these that benefit the entire community would not be possible without you. We are humbled to be part of this resilient community.

Sincerely,

Enrico Mazza, on behalf of the Roche Rare Conditions Team

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**Propensity-score-weighted external control* is a statistical method used to estimate the effectiveness of a medical treatment or intervention when a large enough placebo controlled group is not feasible, using real-world data as an external control.*

***The FDA Accelerated Approval* programme allows treatments for serious conditions that fill an unmet medical need to be approved based on a surrogate endpoint, or biomarker data that are likely to be predictive of clinical benefit. Pharmaceutical companies are still required to conduct studies to confirm the anticipated clinical benefit. If the confirmatory trial shows that the treatment actually provides a clinical benefit, then the FDA grants traditional approval.*

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