30 October 2023

Dear members of the World Duchenne Organization,

As part of our ongoing partnership and following your request to receive timely updates about Roche Duchenne muscular dystrophy (DMD) research efforts, we are writing to share that topline results of Part 1 (1-year data) of the EMBARK Phase 3 study have been announced.

- The study did not meet its primary endpoint of showing a difference in a change on the North Star Ambulatory Assessment (NSAA) total score after treatment with delandistrogene moxeparvovec (Elevidys™) gene therapy, compared with placebo. The NSAA measures motor function abilities in DMD. Participants treated with delandistrogene moxeparvovec did show an improvement in motor function abilities, compared with placebo-treated participants; however, that difference was not statistically significant.
- Clinically meaningful and statistically significant improvements were observed in both key pre-specified secondary functional endpoints (time to rise from the floor and 10-metre walk test). Improvements were also seen on other secondary functional endpoints. Results were consistent across age groups treated with delandistrogene moxeparvovec, compared with placebo.
- The safety of delandistrogene moxeparvovec was consistent with other studies, and no new safety signals were observed.

The findings are from an analysis after one year observation of 125 ambulatory boys (those who can walk unassisted) with DMD aged 4-7 years who received treatment or placebo.

Detailed data analysis is starting
At this time, only topline data and safety information from the study are available - they represent the first look at EMBARK study findings. We are currently assessing the full body of data. Detailed data are planned to be presented at an upcoming scientific congress and requested community forums.

What happens now?
Study participants who have already received treatment will continue to be followed for at least five years to monitor for safety and clinical outcomes. Families involved with delandistrogene moxeparvovec trials should reach out to their clinical trial site directly for questions and further support.

As we continue to analyse EMBARK Part 1 results, learnings may be applied to ongoing/planned delandistrogene moxeparvovec clinical trials, including:

- The EMBARK study is ongoing and Part 2 is expected to complete in late 2024. Part 2 will provide additional data (2-year data) about the safety and efficacy profile of delandistrogene moxeparvovec.
- The Phase 3 ENVISION study in older ambulatory/non-ambulatory individuals is fully enrolled in the US and we plan to start enrolment outside the US by the end of 2023.
- The planned Phase 2 ENVOL study in children under 4 years of age has not yet started.

About regulatory activities:

- At this time, delandistrogene moxeparvovec is approved in the US, United Arab Emirates (UAE) and Qatar for ambulatory children aged 4 through 5 years with DMD and have a confirmed mutation in the *DMD* gene. The UAE and Qatar approvals are based on the US Food and Drug Administration (FDA) accelerated approval of delandistrogene moxeparvovec.
- Our partner in the US (Sarepta Therapeutics) is in discussion with the FDA on potentially expanding the label in the US, based on these EMBARK results.
- Roche will maintain applications for approval it has already submitted in Bahrain, Brazil, Israel, Kuwait, Oman, Saudi Arabia and Switzerland. These countries accept applications based on Phase 1 and 2 data.
- Roche will discuss EMBARK Part 1 results with EMA and other health and reimbursement authorities to explore the path forward.

Notification of sites and trial families

As a publicly traded company, Roche is legally obligated to share EMBARK results first via a public press release, which you can view here. After which, we are allowed to notify clinical trial investigators, health authorities, and partners like yourself.

Per international clinical trial guidelines, Roche is not able to contact trial participants and families directly. However, we have notified all clinical trial investigators and they are now starting the process of informing study participants and families. Because our clinical trials are global with sites in several countries spanning many time zones, we acknowledge that trial families and members of the community will find out at different times and in different ways.

Thank you to the community

Our sincere gratitude goes out to the community, especially all those who are taking part in the trials - participants, families, investigators and trial site staff. Today's data are the first-ever results from a global Phase 3 study of a gene therapy in DMD, and this was only possible thanks to the community commitment, engagement and partnership. We greatly appreciate the ongoing commitment to clinical trial participation to further the understanding of delandistrogene moxeparvovec in DMD.

We are keenly aware of the urgent medical need in DMD for treatment that addresses the underlying cause of the disease. We are encouraged by the totality of data and consistent results seen across secondary functional endpoints. We look forward to discussing the data with health authorities and the scientific and family community.

Please do not hesitate to reach out if you or your community have immediate questions. Individuals and families looking for further information on delandistrogene moxeparvovec should speak to their physician. Additionally, individuals outside the US can contact Roche Medical Information in their respective country via MedInfo.Roche.com, while people in the US can contact Sarepta at SareptAlly@Sarepta.com.

Sincerely,

Fani Petridis, on behalf of the Roche Global Duchenne Team
Global Patient Partnership

About the EMBARK study
EMBARK (Study SRP-9001-301; NCT05096221) is a multinational, Phase 3, randomised, double-blind (neither participants nor investigators know if treatment or placebo is being given), placebo-controlled study assessing the safety and efficacy of delandistrogene moxeparvovec in ambulatory boys with a confirmed mutation in the *DMD gene*, aged between 4 and 7 years. The total study duration is two years (108 weeks).

EMBARK is a two-part, crossover trial, meaning in Part 1, participants received a one-time intravenous (IV) infusion of delandistrogene moxeparvovec or placebo and were monitored for one year. In Part 2, they cross over - meaning those who received delandistrogene moxeparvovec in Part 1 are given a placebo, and those who received a placebo receive delandistrogene moxeparvovec. All participants are monitored for an additional year.

The primary analyses took place after the study's first 52 weeks. The primary outcome is change in total score from baseline to week 52, as measured by the NSAA.

About the ENVISION study
ENVISION (Study SRP-9001-303; NCT05881408) is a multinational, Phase 3, randomised, double-blind, placebo-controlled study that aims to evaluate the safety and efficacy of delandistrogene moxeparvovec in non-ambulatory boys of any age and older ambulatory boys aged 8-18 years.

About the ENVOL study
ENVOL (Study 302; 2022-000691-19) is a multinational, open-label Phase 2 clinical study to evaluate the safety and expression of delandistrogene moxeparvovec in boys under 4 years of age, including newborns.