

31 October 2023

Dear UK Duchenne community organisations,

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 the topline results of Part 1 (1-year data) of the EMBARK Phase 3 study have been announced<sup>1,2,3</sup>.

- 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<sup>4</sup>. 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 to 7 years (inclusive) 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 the EMBARK study findings. We are currently assessing the full body of data. Detailed data are planned to be presented at an upcoming international scientific congress.

### 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.

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<sup>1</sup> Roche press release, *Roche announces EMBARK trial in Duchenne muscular dystrophy (DMD) did not reach primary endpoint, but shows positive efficacy outcomes on all timed functional key endpoints*. Published 30 October 2023

<sup>2</sup> Roche Data on File M-GB-00014506.

<sup>3</sup> *A Gene Transfer Therapy Study to Evaluate the Safety and Efficacy of Delandistrogene Moxeparvovec (SRP-9001) in Participants With Duchenne Muscular Dystrophy (DMD) (EMBARK)*. Available at: <https://clinicaltrials.gov/study/NCT05096221?cond=Duchenne%20Muscular%20Dystrophy&term=embark&intr=delandistrogene%20moxeparvovec&rank=1>. Last accessed: 30 October 2023

<sup>4</sup> Mercuri E, Coratti G, Messina S, et al. *Revised North Star Ambulatory Assessment for Young Boys with Duchenne Muscular Dystrophy*. PLoS One. 2016; 11:e0160195.

\* 126 patients were enrolled in EMBARK<sup>3</sup> but the primary data analysis was carried out on 125 patients. This is based on timing reasons only - the last patient who was enrolled was too late for inclusion in this primary analysis.

As we continue to analyse EMBARK Part 1 results, learnings may be applied to ongoing/planned delandistrogene moxeparovec 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 moxeparovec<sup>5</sup>.
- 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<sup>6</sup>.
- The planned Phase 2 ENVOL study in children under 4 years of age has not yet started<sup>7</sup>.

### **What does this mean for patients and families in the UK?**

All medicines in the UK require a licence (also known as a marketing authorisation) from the Medicines and Healthcare products Regulatory Agency (MHRA). Achieving a licence is only the first step. Further assessments of clinical and cost-effectiveness by other bodies, such as the National Institute for Health and Care Excellence (NICE) and the Scottish Medicines Consortium (SMC) must also be undertaken before a medicine is available to patients on the NHS.

Licensing decisions are ordinarily reliant on the primary endpoint of a clinical trial being met. Whilst EMBARK did not meet its primary endpoint, we remain committed to discussing these results with the relevant authorities in the UK. We are not able to speculate on the outcomes of these discussions, and we are keenly aware of the urgent medical need in DMD for treatments that address the underlying cause of the disease.

### **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. After which, we are allowed to notify clinical trial investigators, health authorities, and patient organisations such as 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.

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<sup>5</sup>A Gene Transfer Therapy Study to Evaluate the Safety and Efficacy of Delandistrogene Moxeparovec (SRP-9001) in Participants With Duchenne Muscular Dystrophy (DMD) (EMBARK). Available at: <https://clinicaltrials.gov/study/NCT05096221?cond=Duchenne%20Muscular%20Dystrophy&term=embark&intr=delandistrogene%20moxeparovec&rank=1>. Last accessed: 30 October 2023

<sup>6</sup>A Gene Transfer Therapy Study to Evaluate the Safety and Efficacy of Delandistrogene Moxeparovec (SRP-9001) in Non-Ambulatory and Ambulatory Participants With Duchenne Muscular Dystrophy (DMD) (ENVISION). Available at: <https://classic.clinicaltrials.gov/ct2/show/NCT05881408?term=delandistrogene+moxeparovec&draw=2>. Last accessed: 30 October 2023

<sup>7</sup>EU Clinical Trials Register. ENVOL. Available at: <https://www.clinicaltrialsregister.eu/ctr-search/trial/2022-000691-19/DE>. Last accessed: 30 October 2023



## 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. These 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 moxeparvec in DMD.

Please do not hesitate to reach out if you or your community have immediate questions. Individuals and families looking for further information on delandistrogene moxeparvec should speak to their physician. They can also contact Roche UK Medical Information on [medinfo.uk@roche.com](mailto:medinfo.uk@roche.com).

Sincerely,  
The Roche UK DMD team

## About the EMBARK study

EMBARK (Study SRP-9001-301; [NCT05096221](https://clinicaltrials.gov/study/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 moxeparvec in ambulatory boys with a confirmed mutation in the *DMD* gene, aged from 4 to 7 years (inclusive). The total study duration is two years (108 weeks)<sup>8</sup>.

EMBARK is a two-part, crossover trial, meaning in Part 1, participants received a one-time intravenous (IV) infusion of delandistrogene moxeparvec or placebo and were monitored for one year. In Part 2, they cross over - meaning those who received delandistrogene moxeparvec in Part 1 are given a placebo, and those who received a placebo receive delandistrogene moxeparvec. All participants are monitored for an additional year<sup>9</sup>.

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.

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<sup>8</sup>A Gene Transfer Therapy Study to Evaluate the Safety and Efficacy of Delandistrogene Moxeparvec (SRP-9001) in Participants With Duchenne Muscular Dystrophy (DMD) (EMBARK). Available at: <https://clinicaltrials.gov/study/NCT05096221?cond=Duchenne%20Muscular%20Dystrophy&term=embark&intr=delandistrogene%20moxeparvec&rank=1>. Last accessed: 30 October 2023

<sup>9</sup>A Gene Transfer Therapy Study to Evaluate the Safety and Efficacy of Delandistrogene Moxeparvec (SRP-9001) in Participants With Duchenne Muscular Dystrophy (DMD) (EMBARK). Available at: <https://clinicaltrials.gov/study/NCT05096221?cond=Duchenne%20Muscular%20Dystrophy&term=embark&intr=delandistrogene%20moxeparvec&rank=1>. Last accessed: 30 October 2023



### **About the ENVISION study**

ENVISION (Study SRP-9001-303; [NCT05881408](https://clinicaltrials.gov/ct2/show/study/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<sup>10</sup>.

### **About the ENVOL study**

ENVOL (Study 302; [2022-000691-19](https://clinicaltrialsregister.eu/ctr-search/trial/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<sup>11</sup>.

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<sup>10</sup>A Gene Transfer Therapy Study to Evaluate the Safety and Efficacy of Delandistrogene Moxeparvovec (SRP-9001) in Non-Ambulatory and Ambulatory Participants With Duchenne Muscular Dystrophy (DMD) (ENVISION). Available at:

<https://classic.clinicaltrials.gov/ct2/show/NCT05881408?term=delandistrogene+moxeparvovec&draw=2>. Last accessed: 30 October 2023

<sup>11</sup>EU Clinical Trials Register. ENVOL. Available at: <https://www.clinicaltrialsregister.eu/ctr-search/trial/2022-000691-19/DE>. Last accessed: 30 October 2023