Delandistrogene Moxeparvovec Micro-Dystrophin Expression and Safety in 3–4-year-olds with Duchenne Muscular Dystrophy in ENDEAVOR and ENVOL Studies

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*At the time of the studies (currently employed by Sarepta Therapeutics, Inc.)

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Disclosures

- JRM received study funding from Sarepta Therapeutics, while at Nationwide Children's Hospital at the time of the study and is currently an employee of Sarepta Therapeutics. JRM is a co-inventor of AAVrh74.MHCK7.micro-dys technology.
- EMM has received fees from AveXis, Biogen, and F. Hoffmann-La Roche Ltd.
- AG served on advisory boards for Italfarmaco and has received fees from F. Hoffmann-La Roche Ltd and Sarepta Therapeutics.
- AN has received fees from AveXis, Biogen, and F. Hoffmann-La Roche Ltd.
- CMM reports grants from Capricor Therapeutics, Catabasis, Edgewise Therapeutics, Epirium Bio, Italfarmaco, Pfizer, PTC Therapeutics, Santhera Pharmaceuticals, and Sarepta Therapeutics; and has a consultancy/advisory role with Biomarin, Capricor Therapeutics, Catalyst, Edgewise Therapeutics, Italfarmaco, PTC Therapeutics, F. Hoffmann-La Roche Ltd, Santhera Pharmaceuticals, and Sarepta Therapeutics. He has received honoraria from PTC Therapeutics and Sarepta Therapeutics.
- ID has nothing to disclose.
- CMZ has received research support from Biogen and Novartis and has served on an advisory board for Sarepta Therapeutics.
- LS serves on advisory boards for Novartis Gene Therapies (formerly AveXis), Biogen, Biophytis, Cytokinetics, Dynacure, F. Hoffmann-La Roche Ltd, GeneTx Biotherapeutics, REGENXBIO, Santhera Pharmaceuticals, and Sarepta Therapeutics; has consulted for Pfizer, Affinia Therapeutics, and Sysnav; conducts research funded by Novartis Gene Therapies (formerly AveXis), Biogen, and F. Hoffmann-La Roche Ltd; and holds part of the patent WO2017129890A1 with no financial interest.
- PT, MV, and KD are employees of Sarepta Therapeutics and may have stock options.
- APM is an employee of Roche Products Ltd and may have stock options in F. Hoffmann-La Roche Ltd.
- BBZ, KW, and PP are employees of F. Hoffmann-La Roche Ltd and may have stock options.
- LRR-K is an employee of Sarepta Therapeutics and may have stock options.
  In addition, she is a co-inventor ofAAVrh74.MHCK7.micro-dys technology.

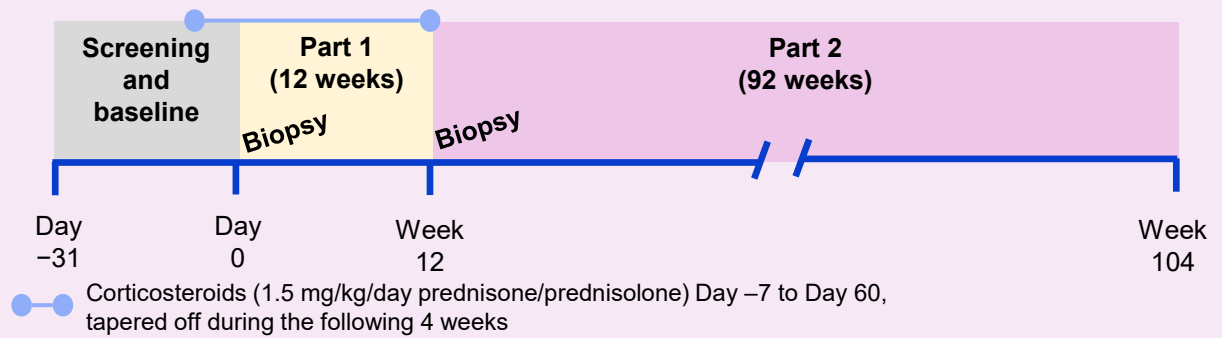
Background and study designs

- Delandistrogene moxeparvovec is an rAAVrh74 vector-based gene transfer therapy that delivers a transgene encoding delandistrogene moxeparvovec micro-dystrophin, which has shown to stabilize or slow progression in ambulatory patients with DMD[1–4]
- Approved in the USA and other select countries; not approved in Austria[5–13]

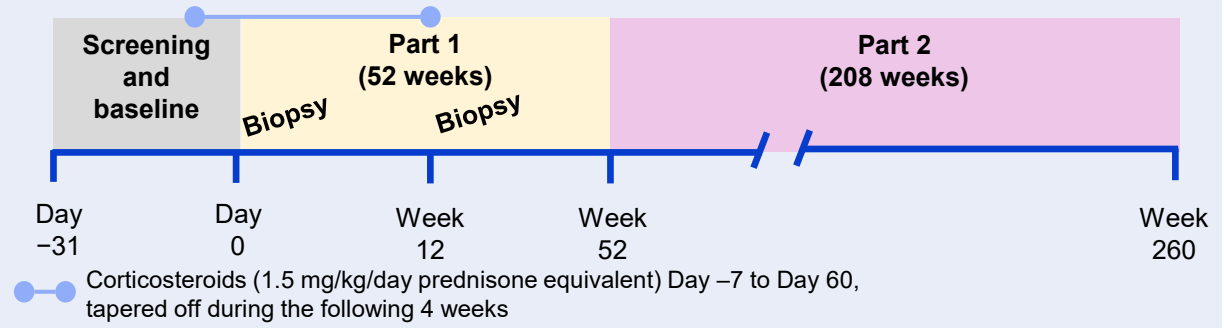
ENDEAVOR: Multi-cohort, open-label, Phase 1b (NCT04626674)[14]
Cohort 4 enrolled ambulatory patients aged ≥3 to <4 years

ENVOL: Multi-cohort, open-label, Phase 2 (NCT06128564)[15]
Cohort A enrolled ambulatory patients aged ≥3 to <4 years

ENDEAVOR



ENVOL



Patients were treated with a **single IV infusion of 1.33×10^{14} vg/kg** (by linear qPCR) of delandistrogene moxeparvovec

Patients in ENDEAVOR Cohort 4 and ENVOL Cohort A were **not receiving corticosteroids at time of screening**

DMD, Duchenne muscular dystrophy; IV, intravenous; qPCR, quantitative polymerase chain reaction; rAAVrh74, recombinant adeno-associated virus rhesus isolate serotype 74; SD, standard deviation.

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13. Japan Ministry of Health, Labour and Welfare Update. 13 May 2025. Roche data on file; 14. ClinicalTrials.gov. NCT04626674 (Accessed October 2025); 15. ClinicalTrials.gov. NCT06128564 (Accessed October 2025).

Baseline characteristics in the 3–4-year-old patient population

Characteristics Mean (SD) (min, max)	ENDEAVOR Cohort 4 (N=7)	ENVOL Cohort A (N=10)
Age, years*	3.5 (0.2) (3.2, 4.0)	3.4 (0.2) (3.1, 3.7)
Dosing weight, kg	15.2 (1.6) (12.5, 16.5)	15.4 (2.2) (12.0, 18.9)
BMI, kg/m^2	17.6 (1.8) (14.8, 20.5)	17.5 (1.7) (15.8, 20.2)
Time since DMD diagnosis, months	15.8 (16.8) (0.7, 38.8)	21.7 (12.3) (3.6, 37.9)
LVEF, %†	63.9 (5.0) (56.4, 72.0)	64.6 (6.9) (56.0, 75.0)

*Age at screening. †Measured by ECHO.
BMI, body mass index; DMD, Duchenne muscular dystrophy; ECHO, echocardiogram; LVEF, left ventricular ejection fraction; SD, standard deviation.

Delandistrogene moxeparvovec transduction efficiency, micro-dystrophin expression, and sarcolemmal localization

Week 12 Mean (SD) (min, max)	ENDEAVOR Cohort 4 (N=7)	ENVOL Cohort A (n=9*)
Vector genome copies, number per nucleus	3.0 (1.3) (1.1, 4.8)	4.8 (2.2) (2.0, 7.7)
Western blot, % control	99.6 (52.0) (46.9, 197.3)	108.9 (56.3) (33.6, 190.7)
PDPF, %†	73.2 (16.0) (54.4, 96.0)	80.5 (19.6) (42.2, 98.3)

Muscle biopsies showed **robust transduction efficiency** at Week 12

Delandistrogene moxeparvovec micro-dystrophin expression was demonstrated at Week 12

Localization to the sarcolemma was observed in both cohorts

*A Week 12 biopsy was not available from one patient. The patient's family consented to biopsy at another timepoint. †Different methodologies were used to measure PDPF in ENDEAVOR Cohort 4 and ENVOL Cohort A.
PDPF, percent dystrophin-positive fibers; SD, standard deviation.

Safety overview in the 3–4-year-old patient population

ENDEAVOR Cohort 4: 6 patients (85.7%) experienced **21 TR-TEAEs**

ENVOL Cohort A: 6 patients (60.0%) experienced **23 TR-TEAEs**

TR-TEAEs	ENDEAVOR Cohort 4 (N=7)	ENVOL Cohort A (N=10)
	Patients, n (%)	
Vomiting	3 (42.9)	4 (40.0)
Decreased appetite	3 (42.9)	2 (20.0)
Hepatic enzyme increased or GLDH increased or LFT increased	3 (42.9)	2 (20.0)
Fatigue	-	1 (10.0)
Diarrhea	1 (14.3)	-
Gastric dilation	1 (14.3)	-
Lethargy	1 (14.3)	-
Hepatotoxicity	-	1 (10.0)†
Aggression	-	1 (10.0)
Cough	-	1 (10.0)
Flushing	-	1 (10.0)
Hypersensitivity	-	1 (10.0)
Hypophagia	-	1 (10.0)
Nausea	-	1 (10.0)
Swelling face	-	1 (10.0)

- **Mean (SD) (range) follow-up:**
  - ENDEAVOR Cohort 4: **105.9 (2.6) (101.2 to 110.1) weeks** (safety data cutoff: July 2, 2024)
  - ENVOL Cohort A: **20.8 (10.7) (12.0 to 46.7) weeks** (safety data cutoff: October 21, 2024)

- Most TR-TEAEs were **mild to moderate in severity**
  - First occurrence of most TR-TEAEs was within 60 days from delandistrogene moxeparvovec infusion*
- There were **no TR-SAEs, treatment-related deaths, or study discontinuations due to AEs**
  - Outside of the ENDEAVOR and ENVOL trials, to date, there have been two treatment-related deaths due to acute liver failure approximately 3 months post-infusion in non-ambulatory patients (one in the ENVISION trial and one in the commercial setting) at 15 and 16 years of age and in the advanced stage of DMD (Data on file)

- †This event of hepatotoxicity in ENVOL qualified as an AESI of hepatotoxicity (GGT or GLDH >8× ULN, grade 3 and severe) and was managed with IV methylprednisolone and tacrolimus
- This patient was steroid-naïve at screening and received 1.0 mg/kg of prophylactic corticosteroids instead of 1.5 mg/kg per the study protocol from baseline to Week 2

*One TR-TEAE of GLDH increased occurred on Day 119.

AE, adverse event; AESI, adverse event of special interest; DMD, Duchenne muscular dystrophy; GGT, gamma-glutamyl transferase; GLDH, glutamate dehydrogenase; IV, intravenous; LFT, liver function test; SAE, serious adverse event; SD, standard deviation; TR-TEAE, treatment-related treatment-emergent adverse event; ULN, upper limit of normal.

Conclusions in the 3–4-year-old patient population

- **Robust delandistrogene moxeparvovec transduction**, **micro-dystrophin expression**, and **sarcolemmal localization** were observed 12 weeks post-delandistrogene moxeparvovec infusion
- **Higher overall mean and higher minimum delandistrogene moxeparvovec micro-dystrophin expression** were **observed in the 3–4-year-old population** compared with previously observed results in ambulatory patients ≥5 years of age and non-ambulatory patient populations[1,2]

- Safety was **manageable with appropriate monitoring**, with **no new signals**, and was **consistent with the known safety profile** of delandistrogene moxeparvovec in other age groups of ambulatory patients (≥4-year-olds)

- Additional cohorts in ENDEAVOR and ENVOL will further evaluate the **impact of early screening and treatment** on outcomes for patients aged <4 years[3,4]

1. Mendell JR, et al. *Nat Med*. 2025; 31:332–341; 2. Proud C, et al. Presented at WMS 2024; Poster #424P; 3. ClinicalTrials.gov. NCT04626674 (Accessed October 2025); 4. ClinicalTrials.gov. NCT06128564 (Accessed October 2025).

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