2025 J.P. Morgan Healthcare Conference

NASDAQ: TRDA

entrada THERAPEUTICS

Disclaimer

This presentation has been prepared by Entrada Therapeutics, Inc. (the “Company”) and shall not constitute an offer to sell or a solicitation of an offer to buy securities or an invitation or inducement to engage in investment activity nor shall there be any sale of securities in any jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification of such securities under the securities law of any such jurisdiction. The Company has filed a shelf registration statement (including a prospectus) with the Securities and Exchange Commission (the “SEC”) for the offering to which this presentation relates. Before you invest in any securities of the Company, you should read the prospectus in that registration statement and any other documents the Company has filed with the SEC for more complete information about the Company and the offering. You may get these documents for free by visiting EDGAR on the SEC website at www.sec.gov.

This presentation contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this presentation, including statements regarding the Company's strategy, future operations, prospects and plans, objectives of management, the validation and differentiation of Entrada’s approach and EEV platform and its ability to provide a potential treatment for patients, expectations regarding significant accumulation of exon skipping and dystrophin production in patients, expectations regarding the importance of endosomal escape to therapeutic index optimization, the translatability of the data from the Phase 1 clinical study for ENTR-601-44 to future clinical studies for ENTR-601-44, expectations regarding the ability of the Company’s preclinical studies and clinical studies to demonstrate safety and efficacy of its therapeutic candidates, and other positive results, expectations regarding the approvals and specific protocols for the Company’s planned Phase 1/2 clinical studies for ENTR-601-44 and ENTR-601-45, the timing of regulatory filings for the planned Phase 1/2 clinical studies for ENTR-601-50 in 2025 and ENTR-601-51 in 2026, the ability to recruit for and complete a global Phase 1/2 study for ENTR-601-44, ENTR-601-45, ENTR-601-50 and ENTR-601-51, the potential of its EEV product candidates and EEV platform, including the potential for ENTR-601-44 to be a transformative treatment option, the continued development and advancement of ENTR-601-44, ENTR-601-45, ENTR-601-50 and ENTR-601-51 for the treatment of Duchenne and the partnered product VX-670 for the treatment of myotonic dystrophy type 1, and the sufficiency of the Company’s cash resources extending into 2027, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. The words “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “might,” “objective,” “ongoing,” “plan,” “predict,” “project,” “potential,” “should,” or “would,” or the negative of these terms, or other comparable terminology are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. The Company may not actually achieve the plans, intentions or expectations disclosed in these forward-looking statements, and you should not place undue reliance on these forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in these forward-looking statements as a result of various important factors, including: uncertainties inherent in the identification and development of product candidates, including the conduct of research activities and the initiation and completion of preclinical studies and clinical studies; uncertainties as to the availability and timing of results from preclinical and clinical studies; timing of and expectations regarding the Company’s ability to submit and obtain regulatory clearance and initiate clinical studies; whether results from preclinical studies will be predictive of the results of later preclinical studies and clinical studies; whether earlier clinical data will be predictive of later clinical data; our ability to establish and maintain collaborations or strategic relationships; whether the Company's cash resources will be sufficient to fund the Company's foreseeable and unforeseeable operating expenses and capital expenditure requirements; as well as the risks and uncertainties identified in the Company's filings with the SEC, including the Company's most recent Form 10-K and in subsequent filings the Company may make with the SEC. In addition, the forward-looking statements included in this presentation represent the Company's views as of the date of this presentation. The Company anticipates that subsequent events and developments will cause its views to change. However, while the Company may elect to update these forward-looking statements at some point in the future, it specifically disclaims any obligation to do so. These forward-looking statements should not be relied upon as representing the Company's views as of any date subsequent to the date of this presentation.

Entrada enters 2025 with significant momentum

Entrada expects to have four Phase 1/2 MAD patient studies in DMD and DM1 by the end of 2025*

Rapidly expanding DMD franchise

Actively planning the initiation of two global Phase 1/2 MAD studies in H1 2025 and one in H2 2025

Ex-US clinical strategy designed to efficiently advance franchise

Vertex accelerating DM1 program

Initiated MAD portion of VX-670 global Phase 1/2 to evaluate safety and efficacy

Partnership terms include milestone payments, plus royalties

Advancing preclinical pipeline

Generating preclinical data from programs outside of neuromuscular

Includes new moieties

Bolstered financial position**

Ended 2024 with ~$420M cash balance

Cash runway extended into Q2 2027

*All references in this presentation regarding planned regulatory filings and clinical study designs are subject to ongoing discussion with US and international regulatory authorities;
**Based on current operating plans and ~$420M in preliminary unaudited cash, cash equivalents and marketable securities as of December 31, 2024; MAD: Multiple ascending dose; DMD: Duchenne muscular dystrophy; DM1: myotonic dystrophy type 1.

OUR MISSION:

To Treat Devastating Diseases With Intracellular Therapeutics

Breakthrough approach to intracellular therapeutics

75% of disease-causing targets are located inside cells[1]

These targets are largely considered to be inaccessible and undruggable as only 2% of biological material will escape the endosome to reach an intracellular target[2]

Increasing cellular uptake and improving endosomal escape

We are leveraging our Endosomal Escape Vehicles (EEV™) and other technologies to optimize intracellular target engagement and therapeutic benefit

Potential for best-in-class therapeutics

Initial focus on DMD and DM1, where we are working to develop safe and effective therapies that meet the significant needs of patients

[1]Verdine GL, Walensky LD. The challenge of drugging undruggable targets in cancer: lessons learned from targeting BCL-2 family members. Clin Cancer Res. 2007;13(24):7264-70;
[2]Kilchrist KV, et al. Gal8 visualization of endosome disruption predicts carrier-mediated biologic drug intracellular bioavailability. ACS Nano. 2019;13(2):1136-52.

Endosomal Escape Vehicle (EEV™)-based therapies

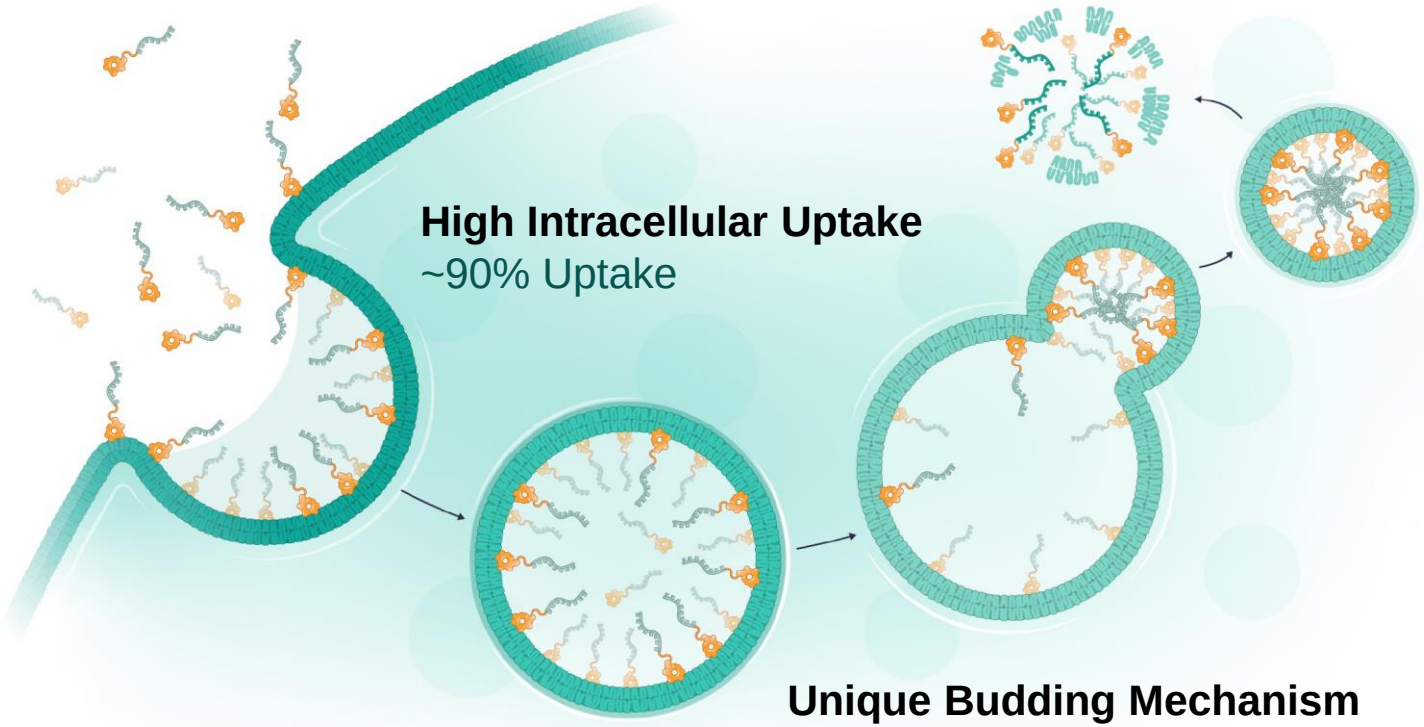
Unique chemistry
Improved uptake and endosomal escape

Cyclic structure
Extended half-life and increased stability

Phospholipid binding
Broad biodistribution to all cells

Consistent and predictable pharmacokinetics
Same EEV used across initial programs

Efficient Endosomal Escape
~50% Escape vs. ~2% Standard

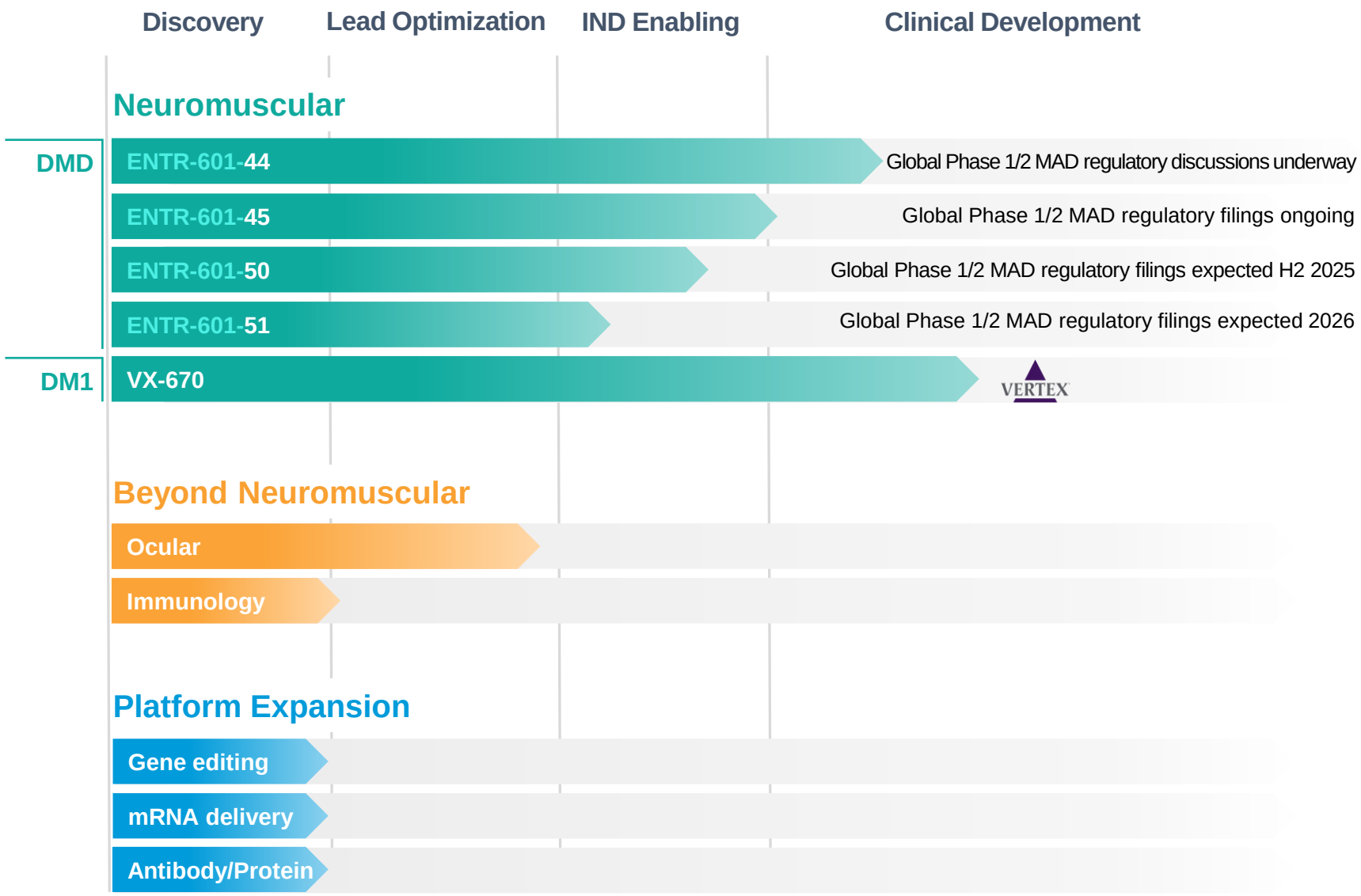


Qian, Z. et al. ACS Chem. Biol. 2013; Qian, Z. et al. Biochemistry 2014; Qian, Z. et al. Biochemistry 2016; Sahni, A. et al. ACS Chem. Biol. 2020; Pei, D. Acc. Chem. Res. 2022.

An Expanding Pipeline of Intracellular Therapeutics

Entrada's pipeline includes a diverse array of high potential and high value assets

Each target disease has a substantial patient population with a significant unmet medical need



EEV therapies have the potential for a best-in-class approach in neuromuscular diseases

Entrada expects to have four Phase 1/2 MAD patient studies in DMD and DM1 by the end of 2025

Delivered positive Phase 1 data in DMD (ENTR-601-44)

- Robust clinical validation in healthy volunteers
- No treatment-related AEs
- Potential best-in-class target exposure and target engagement
- Potential for minimum of 6-week dosing intervals

Strong, translational DMD data support franchise expansion

- Leverages ENTR-601-44's positive Phase 1 results
- Best-in-class potential for ENTR-601-45, ENTR-601-50 and ENTR-601-51
- Pursuing efficient, direct-to-patient clinical strategy

Vertex partnership further validates EEV potential (VX-670)

- Vertex completed SAD portion of VX-670 global Phase 1/2 clinical study
- Vertex initiated MAD portion of VX-670 global Phase 1/2 to evaluate safety and efficacy in patients with DM1

Positive ENTR-601-44 Phase 1 data support the initiation of a Phase 1/2 MAD clinical study in patients

ENTR-601-44-101: Placebo-controlled single ascending dose (SAD) study in healthy volunteers*

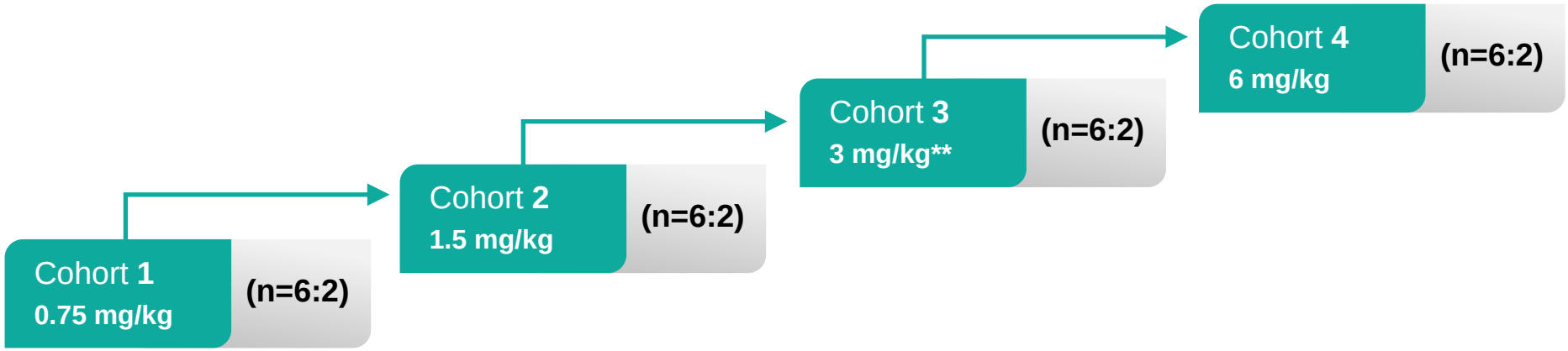
32 Adult Subjects

6:2 randomization
Single IV dose

Total Active: Placebo = 24:8

Outcome Measures

- Safety and tolerability
- Evaluation of PK and PD
- Target engagement as measured via exon skipping



Key findings: Strong clinical safety up to 6 mg/kg, with the potential for best-in-class pharmacokinetics and pharmacodynamics in patients

*Data presented at 2024 World Muscle Society conference; **One participant enrolled and randomized into Cohort 3 was removed prior to dosing.

ENTR-601-44-101: Safety

ENTR-601-44-101: No treatment-related adverse events were reported in the ENTR-601-44-101 study up to the highest dose of 6 mg/kg

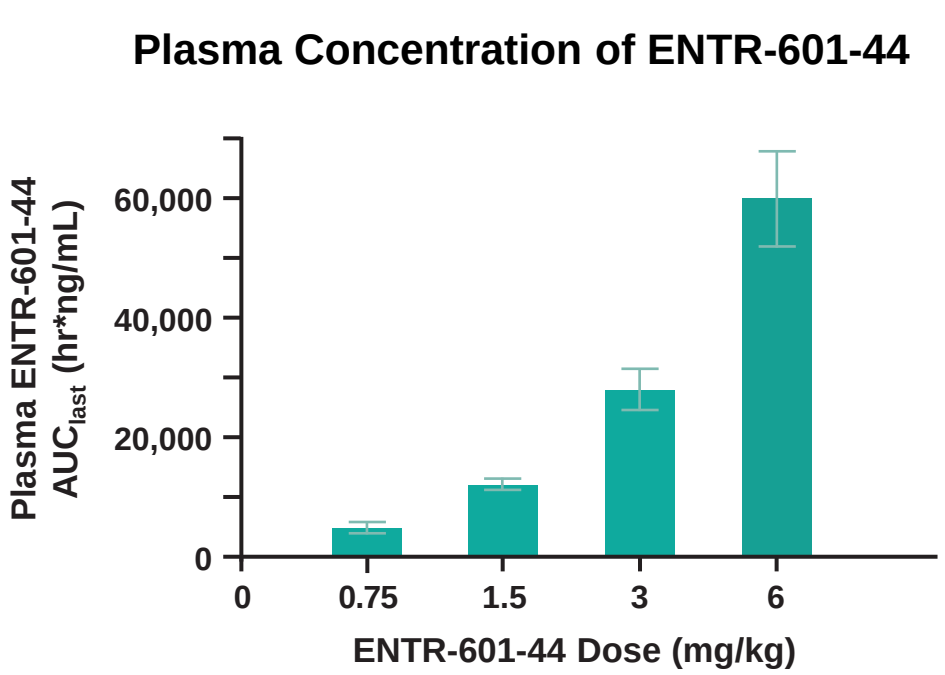
- No AEs related to study drug
- Most common AE was headache (n=7; 5 mild and 2 moderate)
- No clinically significant findings with lab values, ECG or vital signs
- No adverse findings or clinically relevant changes to biomarkers of renal toxicity at highest dose of 6 mg/kg

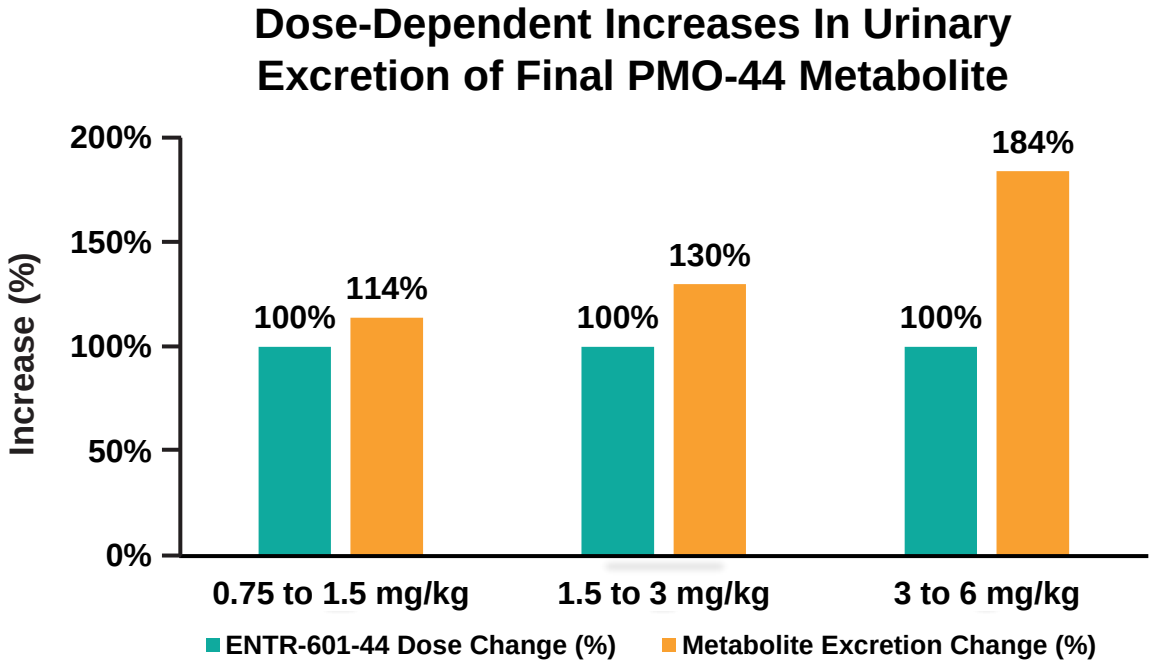
		ENTR-601-44				
n (%)	**Pooled placebo (N=8)**	0.75 mg/kg (n=6)	1.5 mg/kg (n=6)	3.0 mg/kg (n=7)	6.0 mg/kg (n=6)	Total (N=25)
Dosed	8	6	6	6	6	24
Completed Study	8	6	6	6	6	24
Any TEAE	1	5	2	3	3	13
Treatment-related TEAE	**0**	**0**	**0**	**0**	**0**	**0**

Safety and tolerability were assessed at each study visit following a single IV dose of ENTR-601-44 or placebo. One participant enrolled and randomized into Cohort 3 was removed prior to dosing. Renal biomarkers assessed using FNIH and the C-Path. Kidney Safety CM Biomarker User's Guide v1.1, 2019; AE: adverse event; SAE: serious adverse event; TEAE: treatment-emergent adverse event.

ENTR-601-44-101: Pharmacokinetics

ENTR-601-44-101: Potential best-in-class dose-dependent pharmacokinetics





High drug concentration supports potential for efficacy at relatively low doses

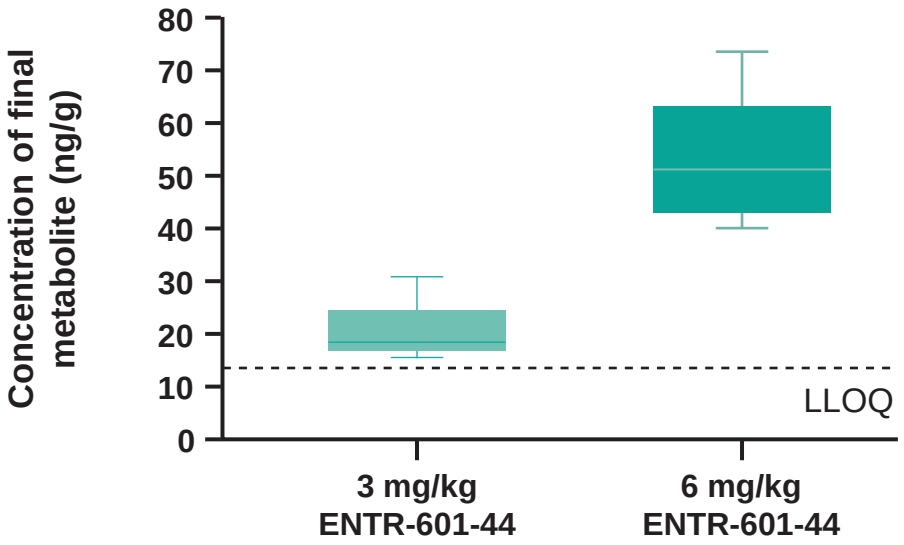
For every doubling of dose, there is a more than doubling of metabolite excretion, implying the potential for increasing efficacy without a proportional risk of increasing toxicity

(Left) Blood samples for PK assessment were collected at 2 hours pre-dose and post-end of infusion: 5 minutes, 1 hour, 4 hours, 8 hours, 16 hours, 24 hours, and every 24 hours after. Additional samples were taken at follow-up study visits; (Right) 24-hour urine samples for PK assessment were collected the day prior to dosing and every 24 hours after. Additional samples were taken at follow-up study visits. Data shown as mean ± standard deviation; AUC_{last}: area under the plasma concentration-time curve to the last measurable plasma concentration; PMO: phosphorodiamidate morpholino oligomer.

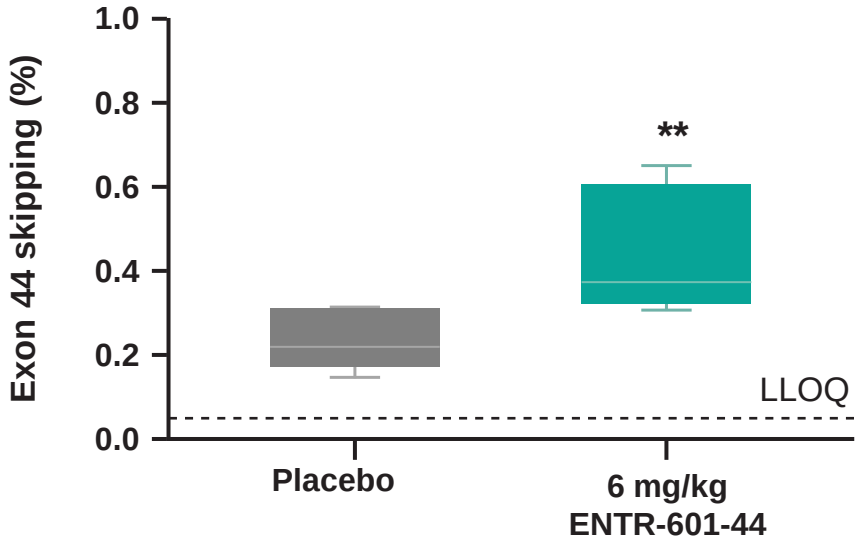
ENTR-601-44-101: Target Exposure and Engagement

ENTR-601-44-101: Favorable target exposure and engagement at 6 mg/kg

Skeletal Muscle Concentration



DMD Exon 44 Skipping



Dose-dependent skeletal muscle concentration was observed

Robust target engagement with statistically significant exon skipping observed versus placebo

Muscle concentrations and exon skipping were assessed using a needle muscle biopsy taken from biceps brachii 72 hours (±4 hours) post-dose of ENTR-601-44. Box and whisker plot illustration: the boxes represent the IQR and median. Whiskers show the smallest and largest values within 1.5 times the IQR; $^{**}p<0.005$ vs. placebo using Mann-Whitney U test; IQR: interquartile range; LLOQ: lower level of quantification.

Rapidly expanding DMD clinical programs

ENTR-601-44's Phase 1 results unlock DMD portfolio investment across multiple populations

Regulatory Filings Under Review

ENTR-601-44

- Discussions underway with several regulatory agencies
- Global Phase 1/2 MAD preparedness ongoing

ENTR-601-45

Ex-US clinical strategy designed to efficiently advance franchise

- Regulatory filings in additional geographies underway
- Global Phase 1/2 MAD preparedness ongoing

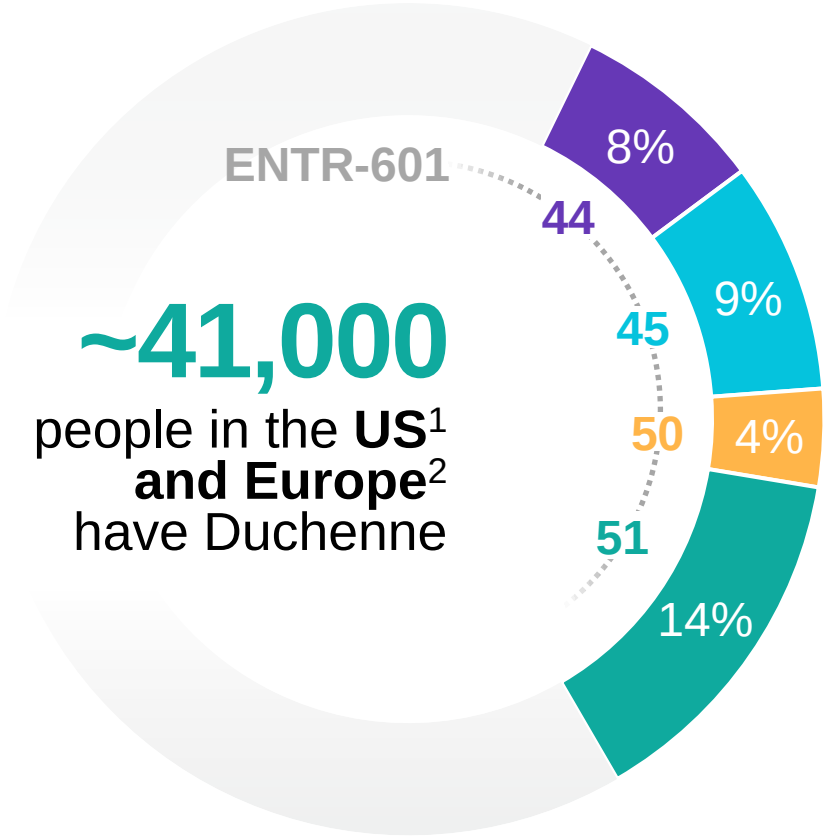
Accelerated Program Timelines

ENTR-601-50
IND Enabling

- On track to submit regulatory filings in H2 2025
- Global Phase 1/2 MAD initiation expected in Q4 2025

ENTR-601-51
IND Enabling

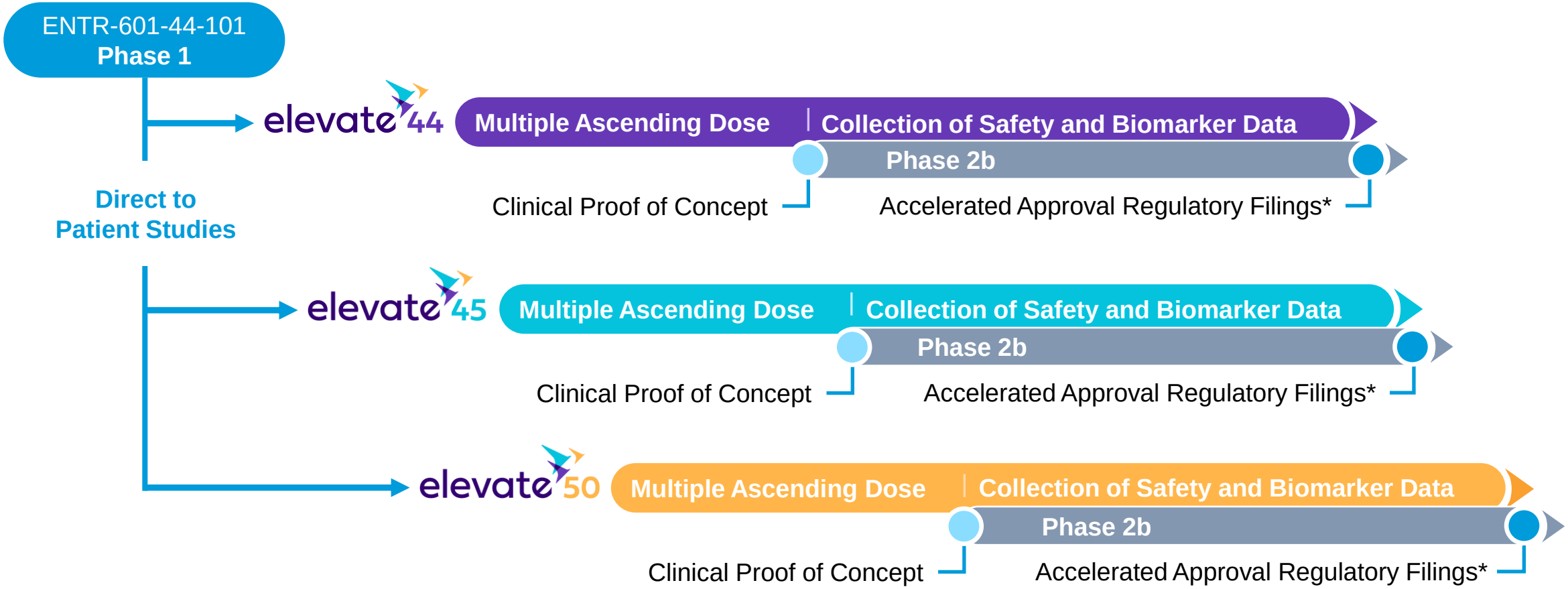
- Candidate selected in December 2024
- Global Phase 1/2 MAD regulatory filings expected 2026



[1]Parent Project Muscular Dystrophy; [2]European Medicines Agency: orphan designation for treatment of Duchenne muscular dystrophy (EU/3/20/2375).

Clinical strategy is designed for efficient regulatory path

All ENTR-601-series programs will follow a similar clinical and regulatory approach



Protocols pending regulatory feedback; *Accelerated Approval in the US, followed by confirmatory Phase 3 studies to obtain Full Approval in the US and ex-US countries.

Robust preclinical data support global direct-to-patient Phase 1/2 MAD clinical studies across DMD franchise

ENTR-601-45

- Robust dystrophin restoration in del44hDMD.*mdx* mouse model after just 3 doses, 6 weeks apart
- Complete functional correction and maintenance of correction 6 weeks post-washout

Global Phase 1/2 MAD Study

Regulatory filings ongoing

ENTR-601-50

- Robust dose-dependent response and saturation of exon 50 skipping in hDMD mouse model after just 3 doses, 6 weeks apart
- Preclinical data support potential for high and persistent dystrophin restoration in patients

Global Phase 1/2 MAD Study

Regulatory filings expected H2 2025

ENTR-601-51

- Robust dose-dependent exon 51 pharmacodynamics in both del52hDMD.*mdx* and hDMD mouse models
- Preclinical data support potential for high and persistent dystrophin restoration in patients

Global Phase 1/2 MAD Study

Regulatory filings expected 2026

Ongoing exploration of pipeline expansion opportunities

Entrada's flexible approach to intracellular therapeutics enables pipeline expansion by leveraging new moieties and by targeting additional therapeutic areas

	DNA	RNA			PROTEINS		
TARGET							
APPROACH	**Gene Editing**	**RNA Editing**	**RNA Splicing**	**RNA Blocking**	**RNA Silencing**	**Protein Replacement**	**Protein Inhibition**	**Protein Degradation**
GOAL	Deliver CRISPR enzyme and repair gene function with guide RNA	Deliver oligonucleotide therapeutics for RNA editing	Modify RNA via exon/intron splicing to activate protein expression	Block trinucleotide repeats in RNA to inhibit adverse binding	Silence or knockdown RNA to prevent protein expression	Replace proteins and enzymes	Inhibit protein signaling pathways	Degrade disease-causing proteins

Multiple near and long-term value drivers

Four clinical programs expected in 2025

- **ENTR-601-44:** Discussions underway with several regulatory agencies
- **ENTR-601-45:** Global Phase 1/2 MAD regulatory filings ongoing
- **ENTR-601-50:** Global Phase 1/2 MAD regulatory filings expected in H2 2025
- **ENTR-601-51:** IND enabling studies ongoing
- **VX-670:** MAD portion of global Phase 1/2 ongoing

Moving beyond neuromuscular

- EEV platform is broadly applicable to intracellular targets and a wide range of diseases
- Efficient development framework in place for advancing new therapeutic candidates
- Preclinical data support potential for broad therapeutic index across multiple modalities
- Initial focus on ocular and metabolic diseases

Cash runway extended into Q2 2027

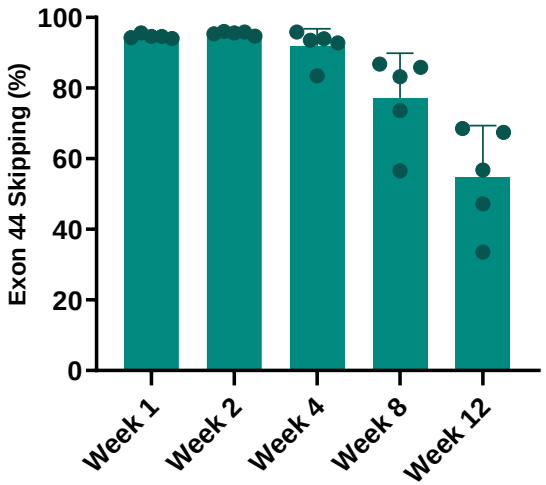
Appendix

Consistent and durable efficacy across species

ENTR-601-44

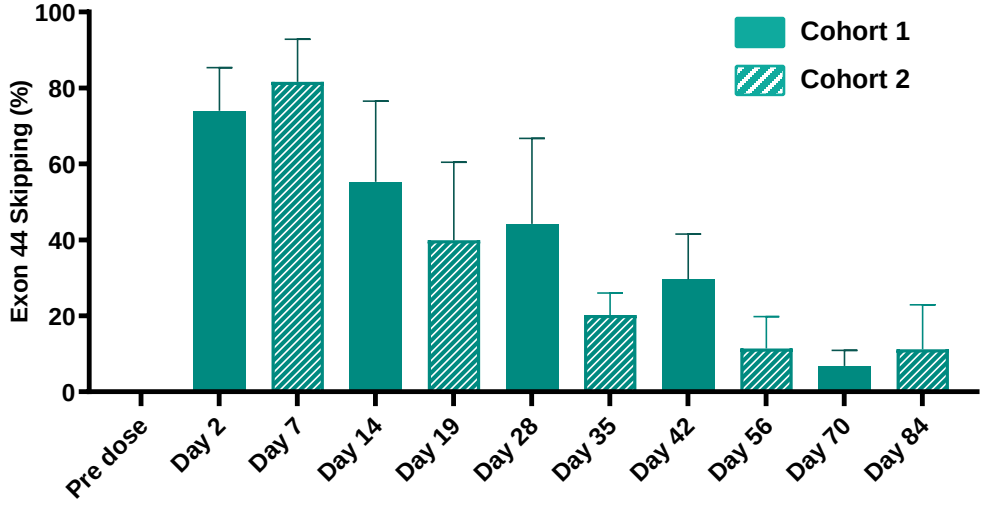
Significant potential for patient benefit is supported by ENTR-601-44 data in the mouse and the NHP at clinically relevant levels; *in vitro* data suggest much higher target engagement in patient cells

Exon 44 Skipping in hDMD Mouse



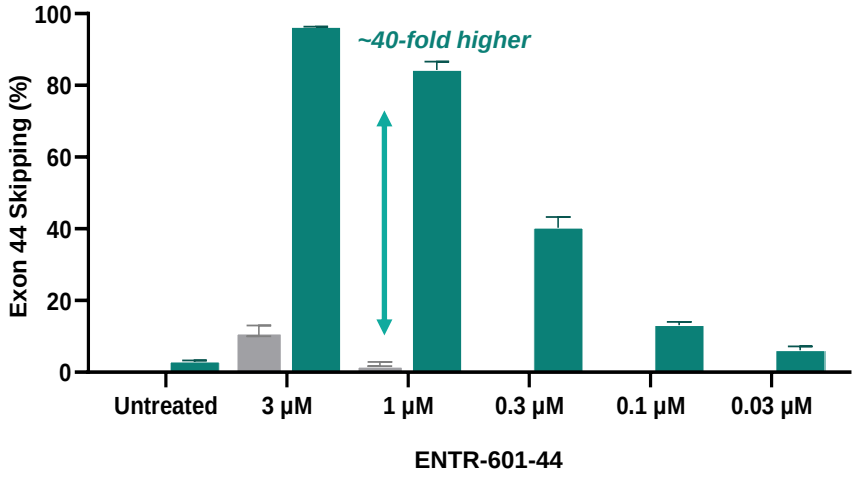
- Single 60 mg/kg (PMO equivalent) dose
- Tibialis anterior

Exon 44 Skipping in NHP



- Post-IV infusion of single 35 mg/kg (PMO equivalent) dose, robust exon 44 skipping observed in biceps in the ENTR-601-44 treated NHPs (n=3 per cohort) for at least 12 weeks

Exon 44 Skipping in Healthy and Patient Myoblasts



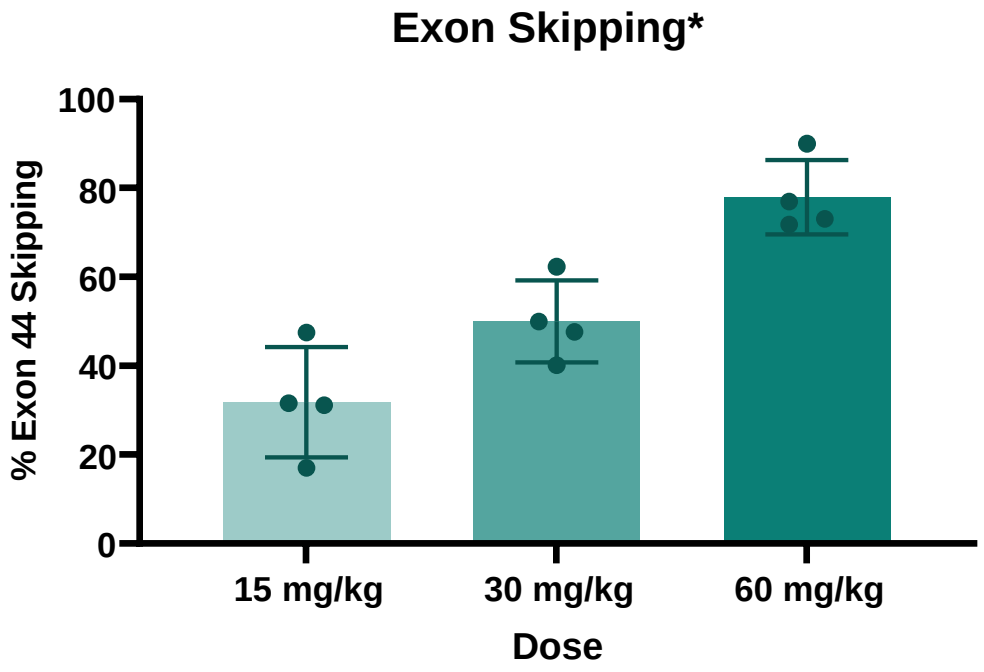
- Patient Cells (DMDD45); n=4 cells/dose
- Healthy Cells; n=4 cells/dose

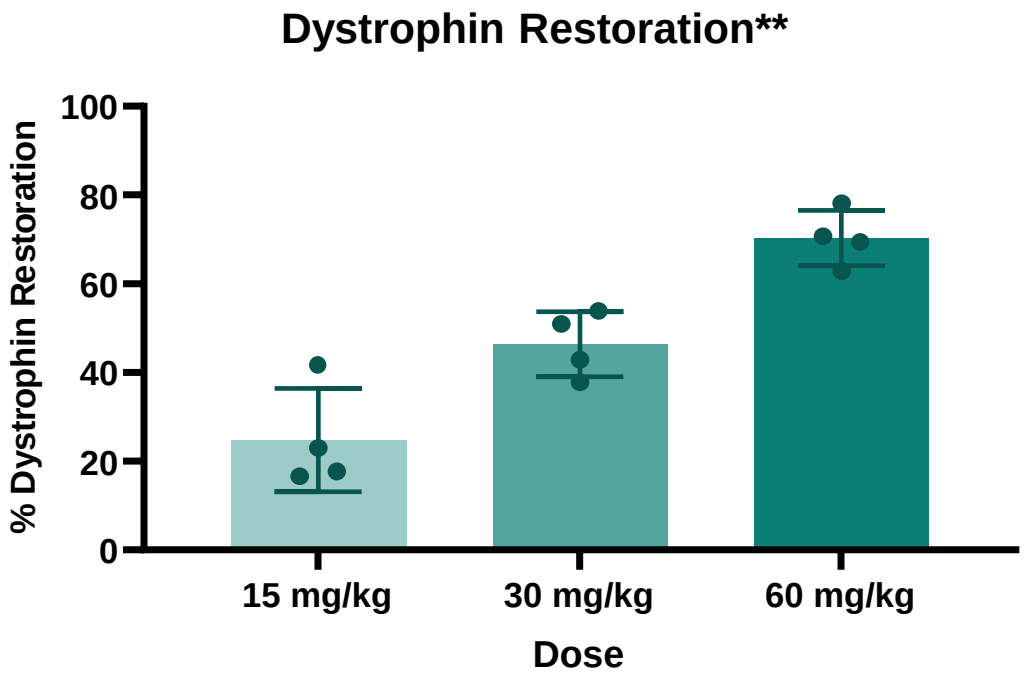
Data presented at the 2022 MDA Clinical and Scientific Conference, TIDES 2022 and OPT 2024.

Dose-dependent exon skipping and dystrophin

ENTR-601-44

Dose-dependent response at a minimally effective dose of 15 mg/kg is observed, with near saturation at a clinically relevant dose of 60 mg/kg implying a wide therapeutic index





- Del45hDMD.mdx mice dosed with EEV-PMO-44***
- n=4, gastrocnemius sample collection 2 weeks post-injection

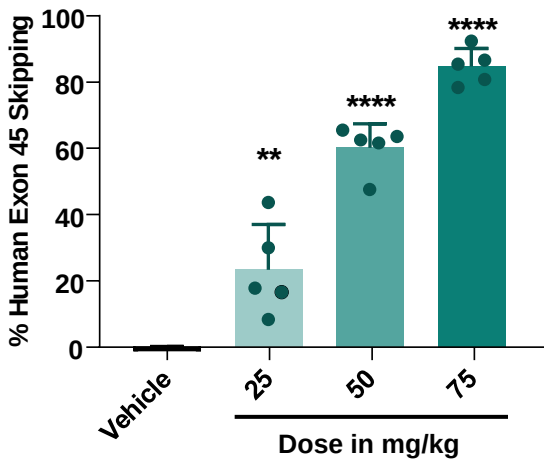
*ddPCR: double drop PCR; **JESS: automated western blot system; ***EEV conjugated to an exon 44 skipping PMO; Data on file.

Preclinical data support potential for best-in-class clinical profile

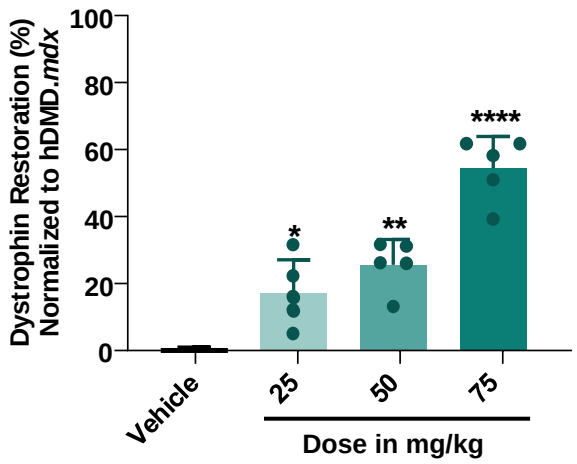
ENTR-601-45

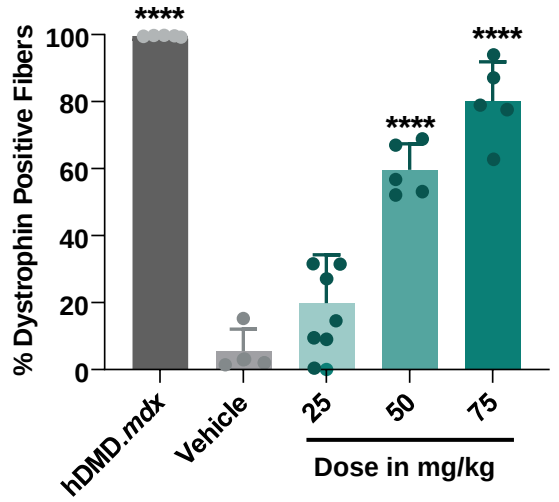
Dose-dependent increase in exon skipping and dystrophin expression correlates to functional correction to wild type

Exon Skipping

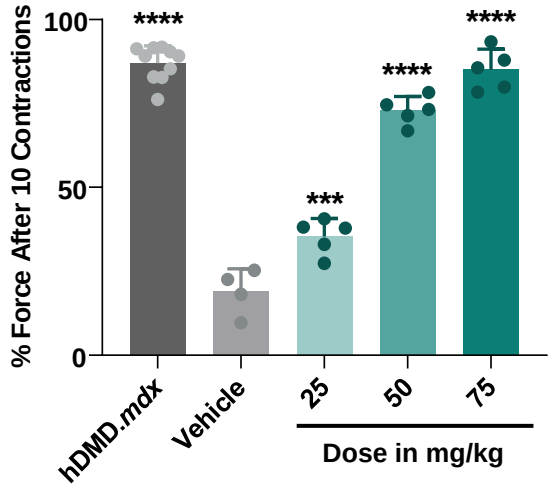


Dystrophin Restoration





Functional Correction



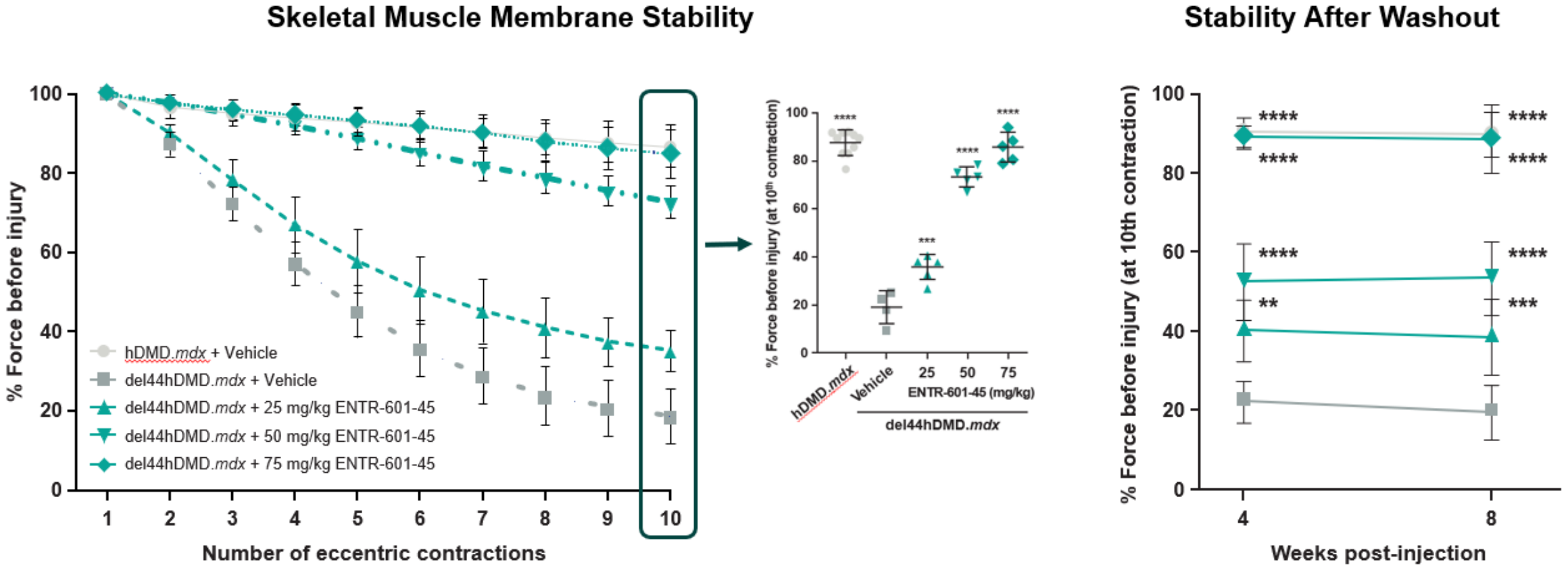
- Active and vehicle del44hDMD.*mdx* mice, n=5 per cohort, EEV-PMO-45 (Q6W x 3 doses); Control saline treated hDMD.*mdx* mice, n=10 (Q6W x 3 doses)
- Skipping (ddPCR) and dystrophin production (JESS) is significantly increased 6 weeks after the third dose of ENTR-601-45 (gastrocnemius muscle shown)

Data are shown as mean ± SD; *p ≤ 0.05, **p ≤ 0.01, ***p ≤ 0.001, ****p ≤ 0.0001; 25 mg/kg correlates to ~5 mg/kg human equivalent dose (HED), 50 mg/kg correlates to ~10 mg/kg HED, 75 mg/kg correlates to ~15 mg/kg HED; JESS: automated western blot system; ddPCR: droplet digital PCR; Data presented at the 2024 World Muscle Society conference.

Dose-dependent and durable improvements in muscle function observed in del44hDMD.*mdx* mice

ENTR-601-45

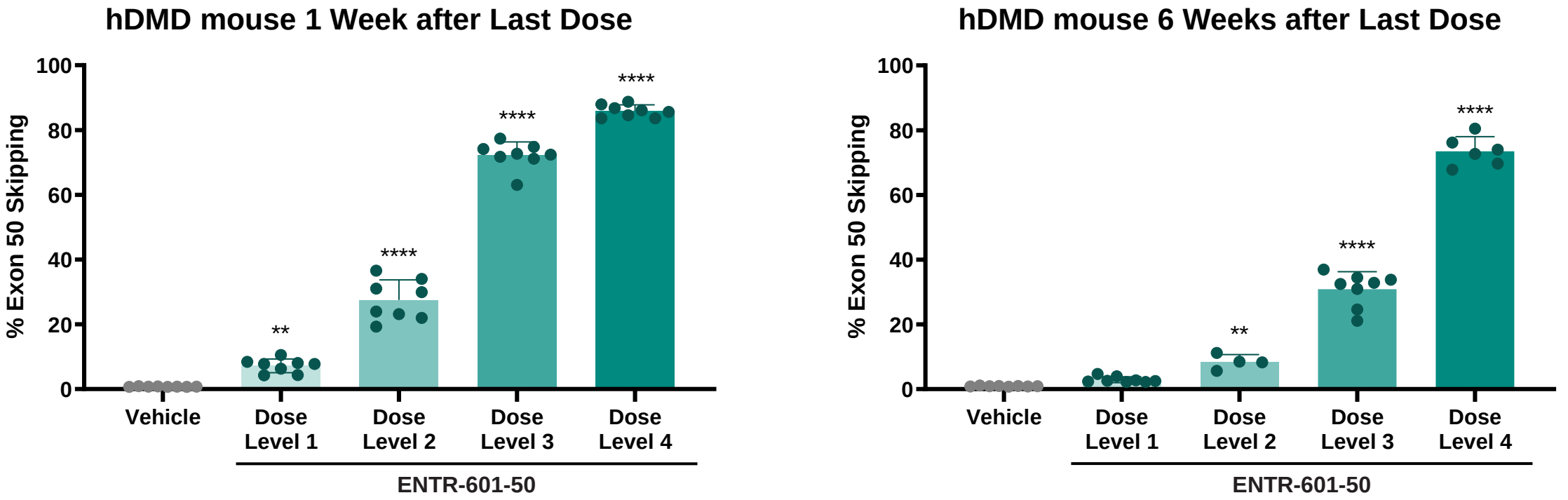
Dose-dependent increase in resistance to membrane damage was observed following the tenth contraction, which was maintained until at least 8 weeks after the third Q6W dose of ENTR-601-45



del44hDMD.*mdx* mice were treated with three Q6W IV injections of ENTR-601-45 or vehicle. ECC-induced muscle force loss generated by repeated eccentric force (ECC) contraction of the gastrocnemius muscle was assessed 5 weeks (left/center) or 4 and 8 weeks (right) after the third dose. Data (mean ± standard deviation) shown across 10 ECC contractions normalized into a percentage of the initial force before any ECC contractions and as the percentage of force retained after the 10th contraction. Vehicle-treated hDMD.*mdx* mice were used as a control group for normal muscle function. One-way ANOVA was used for statistical comparison to vehicle-treated del44hDMD.*mdx* mice; Q6W: every 6 weeks. **p < 0.01, ***p < 0.001, ****p < 0.0001 vs. vehicle; Data presented at the 2024 World Muscle Society conference.

ENTR-601-50 in hDMD show high levels of durable exon skipping

Repeated doses of ENTR-601-50 in hDMD mice leads to robust dose-responsive levels of exon 50 skipping that largely persists to 6 weeks, supporting the potential for persistent dystrophin production



- Repeated doses administered via IV injection (Q6W x 3 doses) with 1 or 6-week washout; Exon skipping assessed by ddPCR (tibialis anterior muscle shown)

Data are shown as mean ± SD; **p ≤ 0.01, ****p ≤ 0.0001 vs vehicle. ddPCR, droplet digital PCR; Data on file.


Learn more at
EntradaTx.com
entrada
THERAPEUTICS