Corporate Presentation

August 2023

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ENTRADA'S MISSION

Treating Devastating Diseases With Intracellular Therapeutics

ENTRADA AT A GLANCE

Entrada is leveraging its Endosomal Escape Vehicle platform (EEV™) to create a diverse and expanding development portfolio of RNA-, antibody- and enzyme-based therapeutics

- **Advancing new therapeutic options for people living with Duchenne muscular dystrophy (DMD)**
  - Lead DMD program (ENTR-601-44): First participant expected to be dosed in September 2023
  - Additional programs focus on clinical candidate, ENTR-601-45, with discovery efforts underway in exons 50 and 51
- **Transformative Vertex partnership for the development of myotonic dystrophy, type 1 (DM1)**
  - $224M upfront payment and $26M equity investment; Up to $485M for the achievement of certain milestones, plus royalties; Four-year global research collaboration
  - Entrada is responsible for preclinical development; Vertex is responsible for global development, regulatory, manufacturing and commercialization
- **Expanding our commitment to non-neuromuscular disease programs**
  - EEV's unique mechanism of action is designed to enable delivery of various moieties into organs and tissues
- Strong financial position with **cash runway through 2025***
- Experienced leadership team and Board of Directors, supported by leading biotech investors

*Assumes existing cash, cash equivalents, marketable securities, together with Vertex collaboration ongoing research support and achievement of certain milestones.

LEADERSHIP TEAM AND BOARD OF DIRECTORS

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President and CEO

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Chief Scientific Officer

Nerissa Kreher, MD
Chief Medical Officer

Nathan Dowden
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Industry Leader and Independent
Board Member

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Industry Leader and Independent
Board Member

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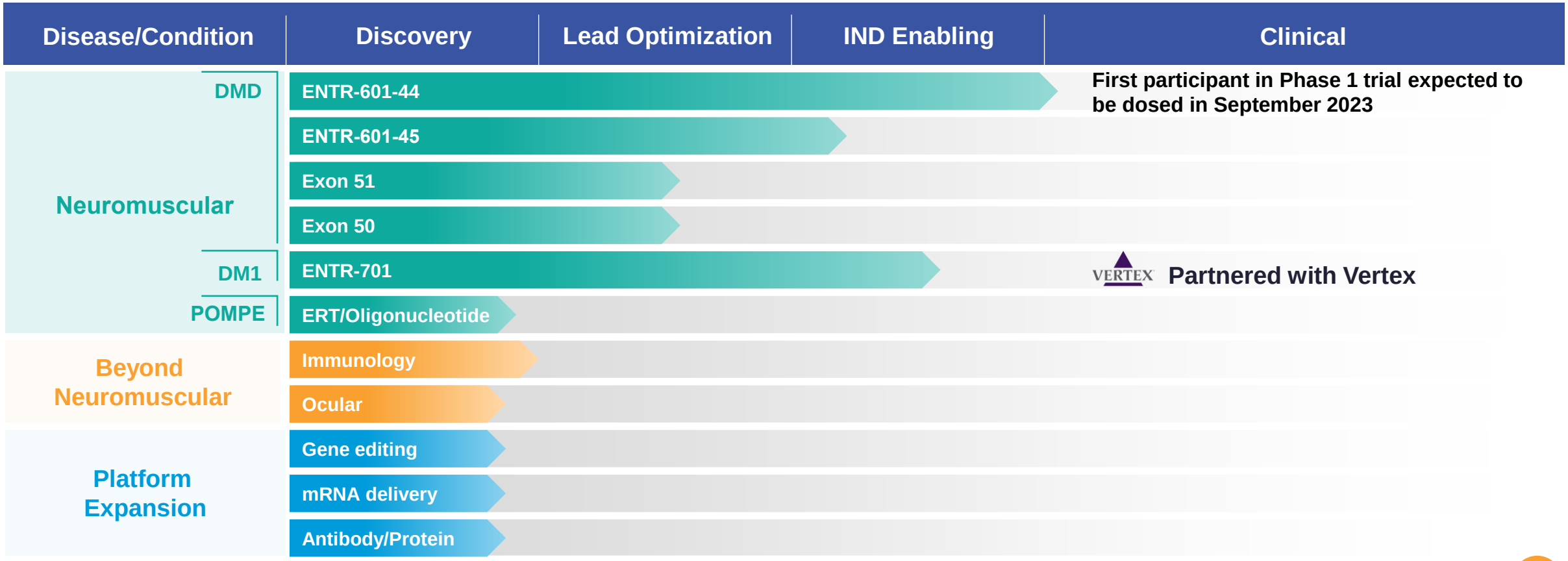
Executive Chairman
Amicus Therapeutics

Dipal Doshi
President and CEO

OUR DIFFERENTIATED AND EXPANDING PIPELINE

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

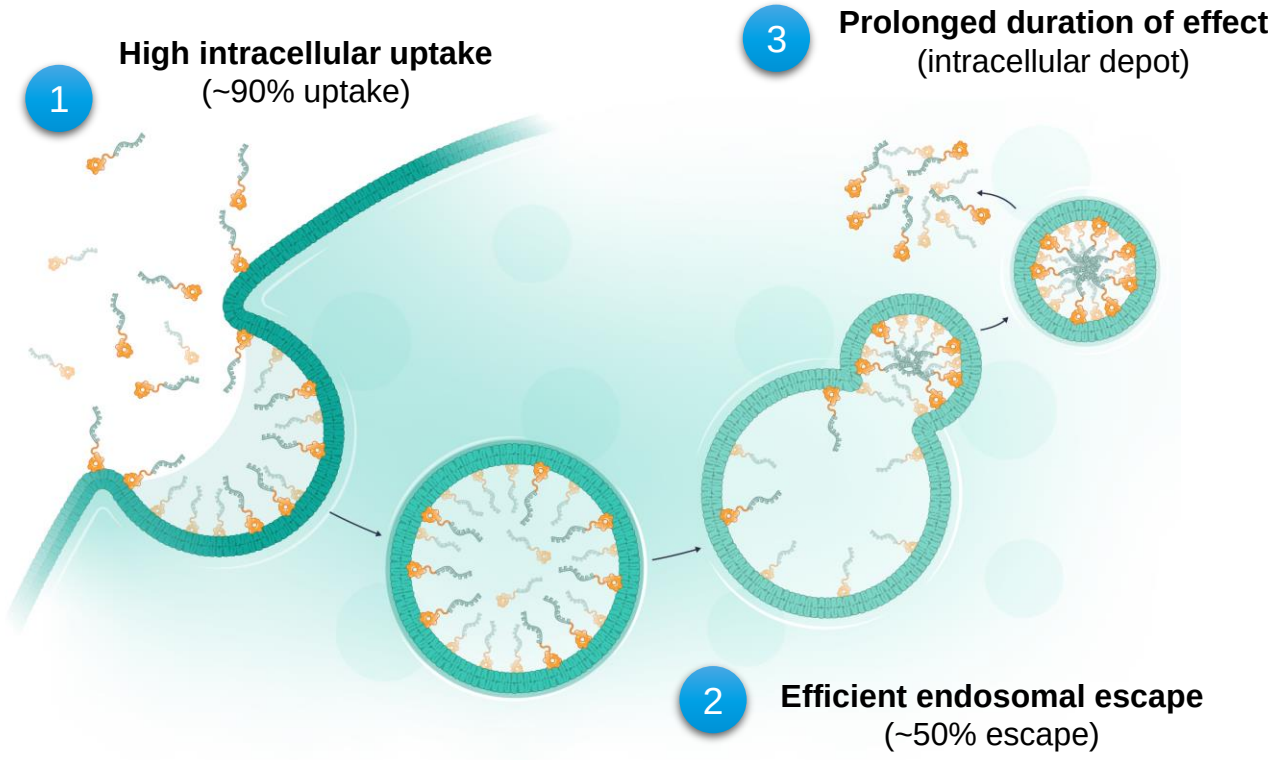


EEV PLATFORM

ENDOSOMAL ESCAPE VEHICLE (EEV™) PLATFORM

Entrada seeks to solve a fundamental problem: lack of efficient cellular uptake and escape from the endosome; Both are critical to intracellular target engagement and therapeutic benefit

- Unique chemistry results in **improved uptake and endosomal escape**
- Cyclic structure designed to **extend half life and increase stability**
- Phospholipid binding potentially **enables broad biodistribution to all cells**
- Mechanism of **internalization conserved across species**

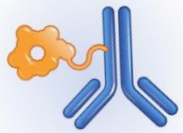


Qian, Z. et al. *ACS Chem. Biol.* 2013; Qian, Z. et al. *Biochemistry* 2014; Qian, Z. et al. *Biochemistry* 2016; Sahni, A. et al. *ACS Chem. Biol.* 2020; Pei, D. *Acc. Chem. Res.* 2022.

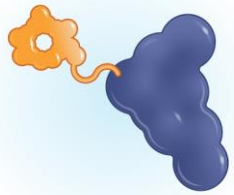
A BROADLY APPLICABLE PLATFORM

Entrada has demonstrated intracellular uptake of unique moieties ranging from 1 kDa to 600 kDa

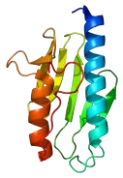
Antibodies



Enzymes

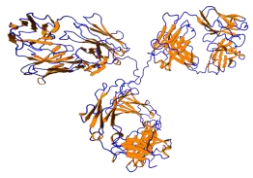


Oligonucleotides



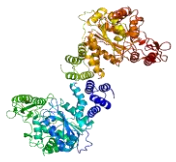
550-600 KDa

Hybrid frataxin



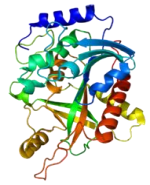
150 KDa

Antibody



98 KDa

Thymidine phosphorylase

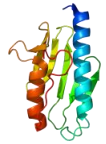


96 KDa

Purine nucleoside phosphorylase

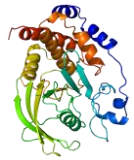
86 KDa

Alanine-glyoxylate aminotransferase



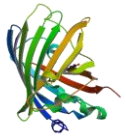
46 KDa

Human frataxin



37 KDa

PTP1B catalytic domain



32 KDa

EGFP

16 KDa

Nanobody

6 KDa

Oligonucleotide

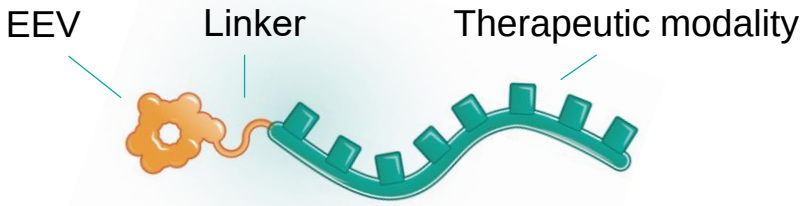
1-3 KDa

Various peptide cargos

FUNCTIONAL DELIVERY FOR TARGET TISSUES

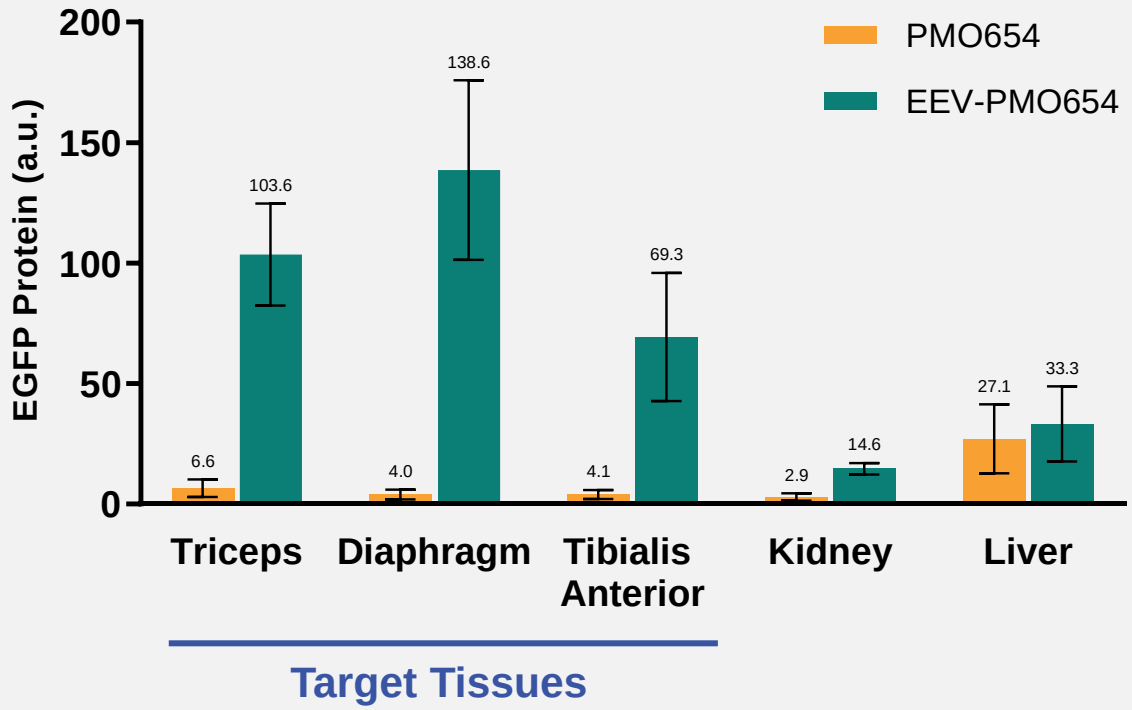
EEV-therapeutic candidates can be designed to enhance functional delivery to target tissues

Discovery Engine for Intracellular Therapeutics



- High-throughput **EEV library screening** *in vitro*
- Functional validation of lead EEVs with **PMO therapeutic modality** *in vitro* and *in vivo*
- **EEV** and **linker** optimized for the functional delivery to target tissues *in vivo*

Functional Delivery in the EGFP-654 Transgenic Mice



PMO, phosphorodiamidate morpholino oligomer; EGFP-654 transgenic mouse model contains an EGFP gene interrupted by human beta-globin intron 2 with mutated nt654 (Sazani, P. et al. *Nature Biotech.* 2002); PMO654, splicing switching PMO targeting nt654; shown as mean ± standard deviation.

TRANSLATION FROM UPTAKE TO OUTCOMES
Murine Example

EEV-therapeutic candidates have demonstrated favorable pharmacological properties: efficient intracellular delivery, significant uptake in target tissues and potent pharmacodynamic outcomes

Tissue Uptake in Muscle

- ✓ Skeletal muscle
- ✓ Cardiac muscle

+

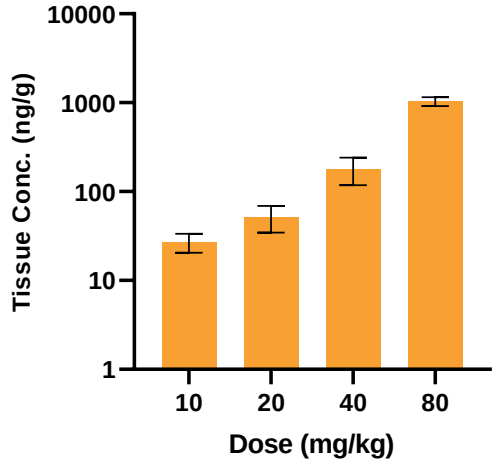
Intracellular Delivery

- ✓ Endosomal escape
- ✓ Nuclear localization

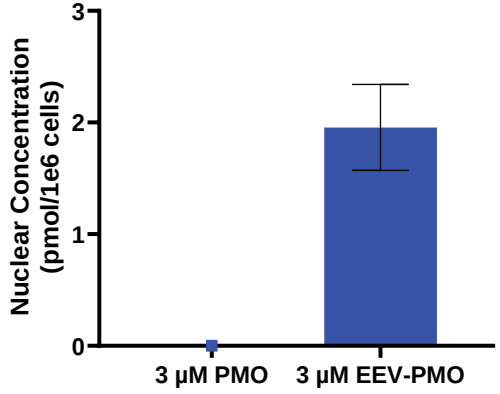
=

Pharmacodynamic Outcome

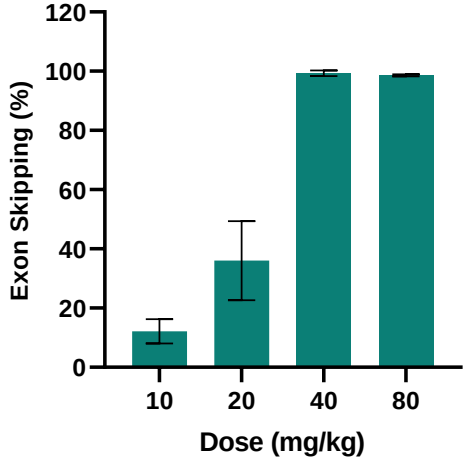
- ✓ Rapid, dose-dependent response
- ✓ Duration of at least 12 weeks



IV, hDMD mice, 5-day post injection



24-hour incubation



IV, hDMD mice, 5-day post injection

hDMD mice express full-length human dystrophin gene.

DUCHENNE MUSCULAR DYSTROPHY

SIGNIFICANT THERAPEUTIC NEED EXISTS WITHIN A VALIDATED DUCHENNE MARKET

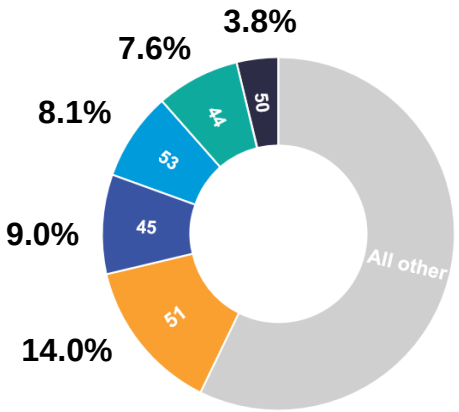
Duchenne is caused by **mutations in the *DMD* gene, which lead to a lack of functional dystrophin**, causing progressive loss of muscle function throughout the body

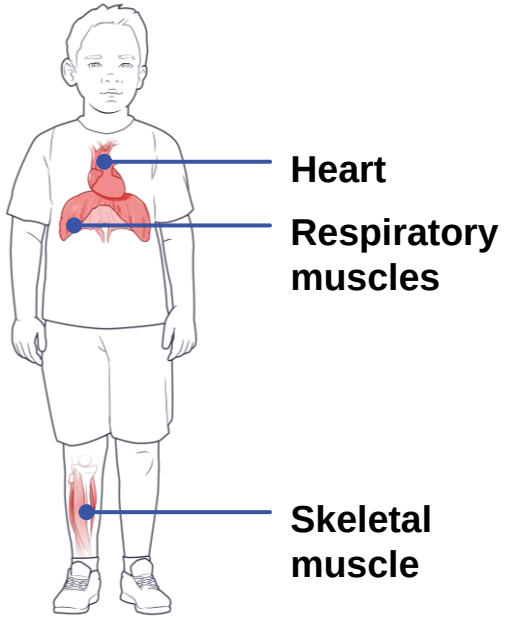
~30,000

people in the **U.S. and Europe** have Duchenne[1]

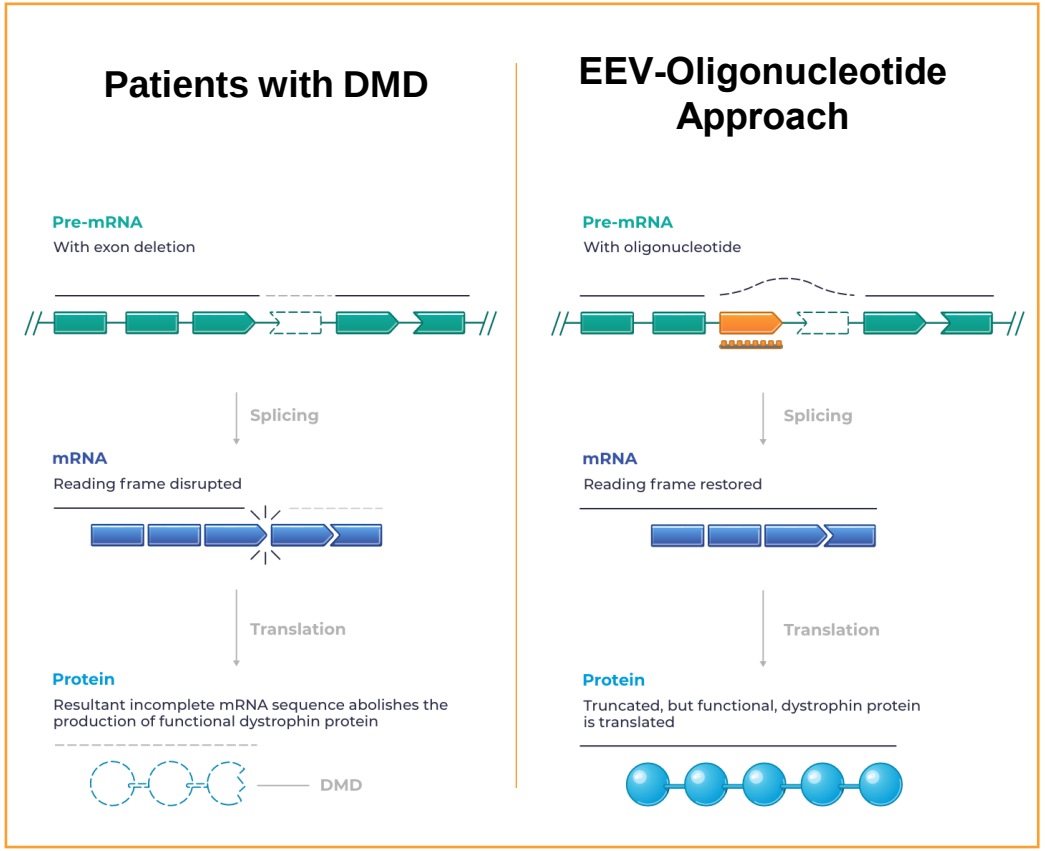
>40% of patients with Duchenne

have mutations amenable to exon skipping of exons 44, 45, 50, 51 and 53





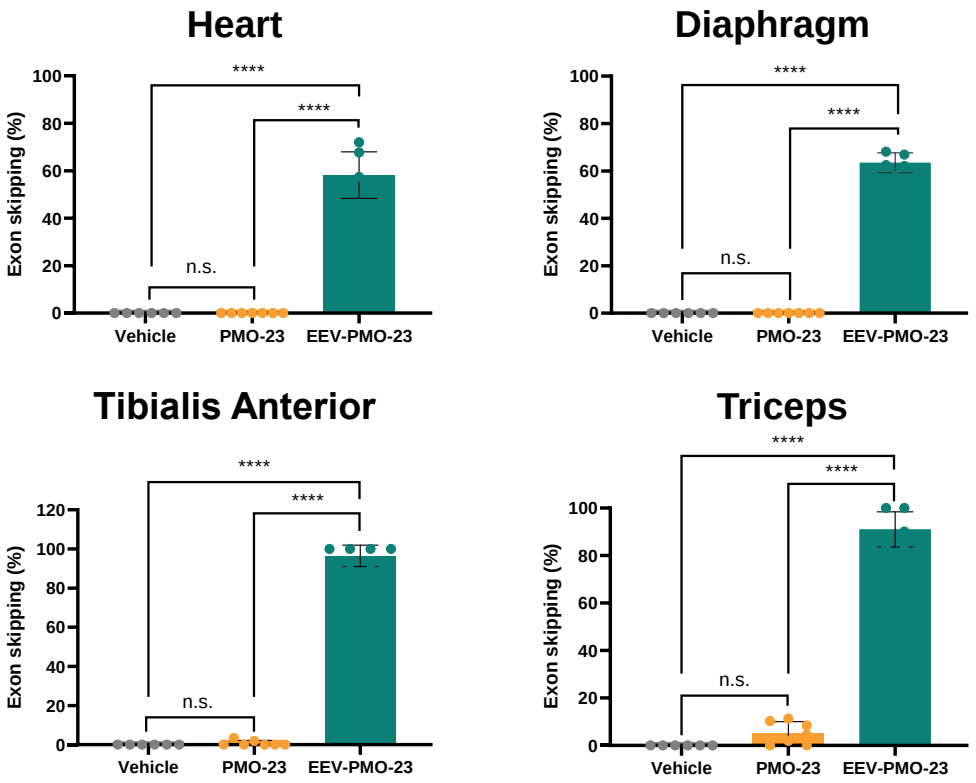
Exon skipping therapeutics have been approved based on **modest improvement in dystrophin levels ranging from ~1 to 6%**



[1]Crispi V, Matsakas A. Duchenne muscular dystrophy: genome editing gives new hope for treatment. Postgraduate Medical Journal. 2018;94(1111):296-304. doi: 10.1136/postgradmedj-2017-135377.

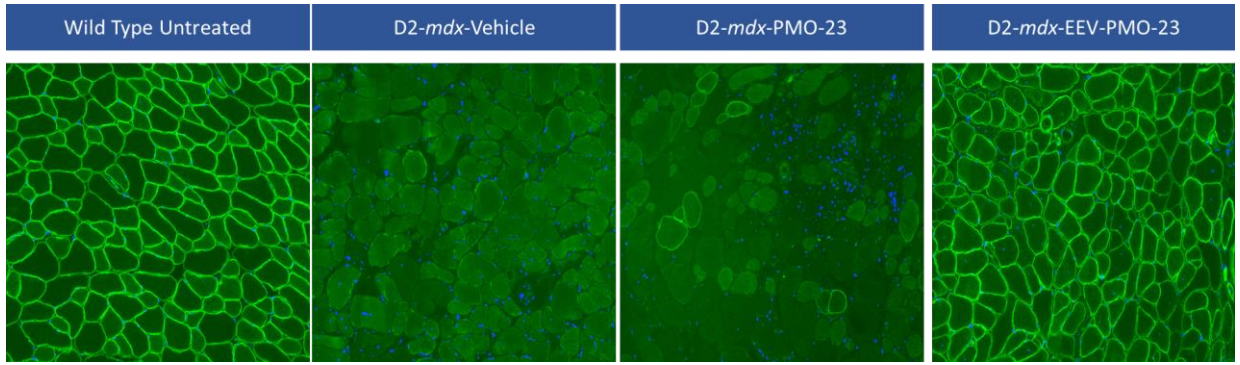
REPEAT EEV-PMO TREATMENT RESTORES MUSCLE INTEGRITY IN D2-*mdx* MICE

Robust exon 23 skipping after four monthly IV doses of EEV-PMO-23 in D2-*mdx* mice

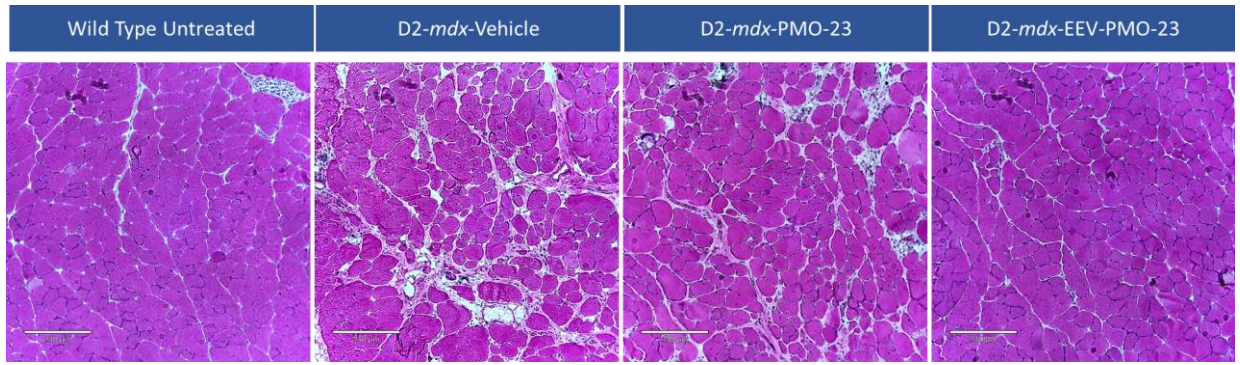


Broad dystrophin expression and restoration of muscle integrity after four monthly IV doses of EEV-PMO-23 in D2-*mdx* mice

Representative Immunofluorescence of Gastrocnemius Muscle (Dystrophin Staining in Green)



Representative Histopathology of Gastrocnemius Muscle (H&E Staining)

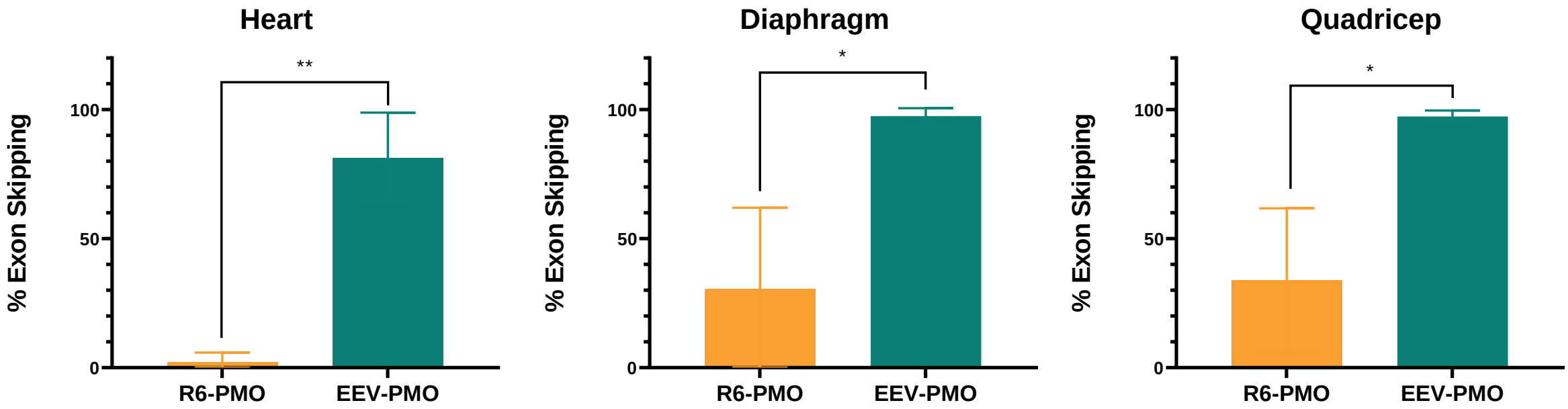


- D2-*mdx* mice (male, n=6-7) were treated with 4 monthly doses of either vehicle, 20 mg/kg PMO-23 or 20 mg/kg PMO-23 equivalent of EEV-PMO-23, and the data were collected ~4 weeks after the last dose

EEV, Endosomal Escape Vehicle; PMO-23, mouse *Dmd* exon 23 skipping phosphorodiamidate morpholino oligomer; D2-*mdx* is a DMD mouse model with a nonsense mutation in DMD exon 23 (Coley et al. *Hum. Mol. Genet.* 2016); ****p<0.0001; n.s., not significant; shown as mean ± standard deviation.

COMPARISON TO ALTERNATIVE R6-PMO

EEV-PMO significantly improved exon 23 skipping after 3 days in *mdx* mice as compared to competitive R6-PMO



*p<0.05, **p<0.01

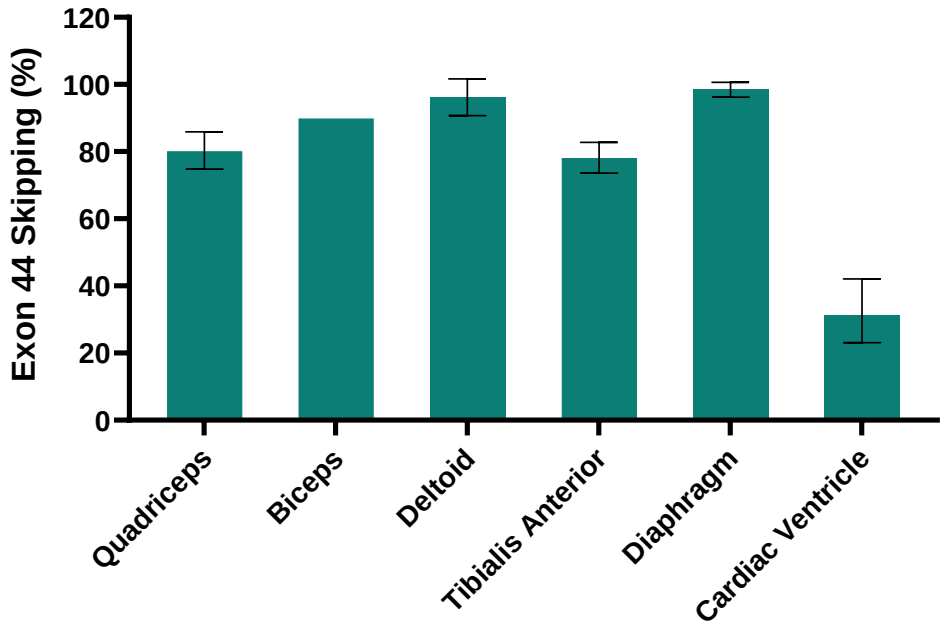
- EEV-PMO-23 demonstrates significantly improved PD effects after single 40 mg/kg IV dose in *mdx* mice

ENTR-601-44

ENTR-601-44 IN NHP

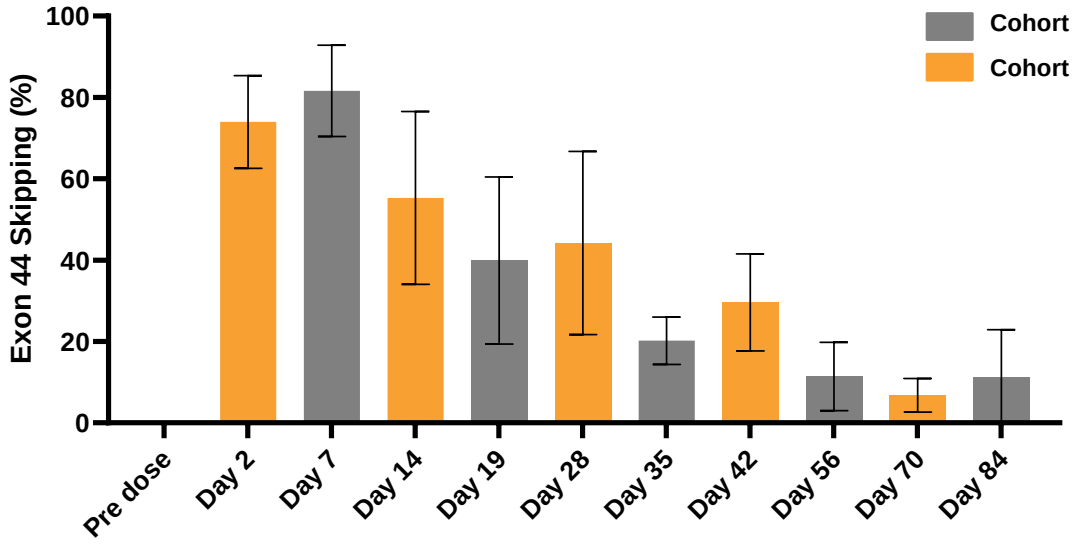
A single IV dose of ENTR-601-44 resulted in robust exon skipping in both skeletal and cardiac muscles in NHP, as well as prolonged duration of effect for at least 12 weeks

Exon Skipping in NHP Muscles at Day 7



- At 7 days post IV infusion of 30 mg/kg (PMO equivalent), robust exon 44 skipping across different muscle groups isolated from the ENTR-601-44 treated NHP

Duration of Effect in NHP Biceps for at Least 12 Weeks



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

NHP, non-human primates; shown as mean ± standard deviation.

ENTR-601-44 CURRENT CLINICAL STRATEGY

First-in-Human Trial

Single Ascending Dose Study
in Healthy Volunteers

- **First participant expected to be dosed Sept 2023**
- **Data expected 2H 2024**
- **~40 participants**

OUTCOME MEASURES

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

Multiple Ascending Dose/Phase 2b

Multiple Ascending Dose Study*
in Exon 44 Skipping Amenable Patients

Phase 2b Study*
in Exon 44 Skipping Amenable Patients

Target Product Profile:

- ***Double digit dystrophin improvement from baseline***
- ***Dosing interval ≥ every 6 weeks***

Dose Selection

File for Accelerated Approval

Phase 2b | **Open-label Extension**

OUTCOME MEASURES

- Safety and tolerability
- Evaluation of PK and PD
- Evaluation of exon skipping and dystrophin production (skeletal muscle)

PRIMARY EFFICACY MEASURES

- Change in dystrophin level (skeletal muscle)

SECONDARY/EXPLORATORY EFFICACY MEASURES

- NSAA (North Star Ambulatory Assessment)
- Other timed function tests
- Other parameters may include cardiac MRI, FVC, QoL

*Multiple Ascending Dose/Phase 2b trial is subject to regulatory feedback and the outcome of the single ascending dose trial.

ENTR-601-44 DATA SUMMARY

Entrada has generated a robust set of translational data in mice and non-human primates; Phase 1 Clinical Trial authorized with data anticipated in 2H 2024

- High levels of exon skipping across *mdx*, D2-*mdx,* human dystrophin mouse and NHP studies
- Exon skipping translates to promising dystrophin production in heart and skeletal muscles
- Dystrophin production observed to result in functional improvement
- Extended circulating half-life and durable dystrophin production over 12+ weeks from a single injection of ENTR-601-44 was observed in the NHP

Phase 1 Clinical Trial of ENTR-601-44

- Received authorization in the U.K. to initiate a Phase 1 clinical trial in healthy volunteers
- First participant is expected to be dosed in September 2023 with data anticipated in the 2H 2024
- Clinical data from the Phase 1 trial to support program's next steps, including a global MAD trial in patients*
- Update on IND hold in the U.S. expected in Q4 2023

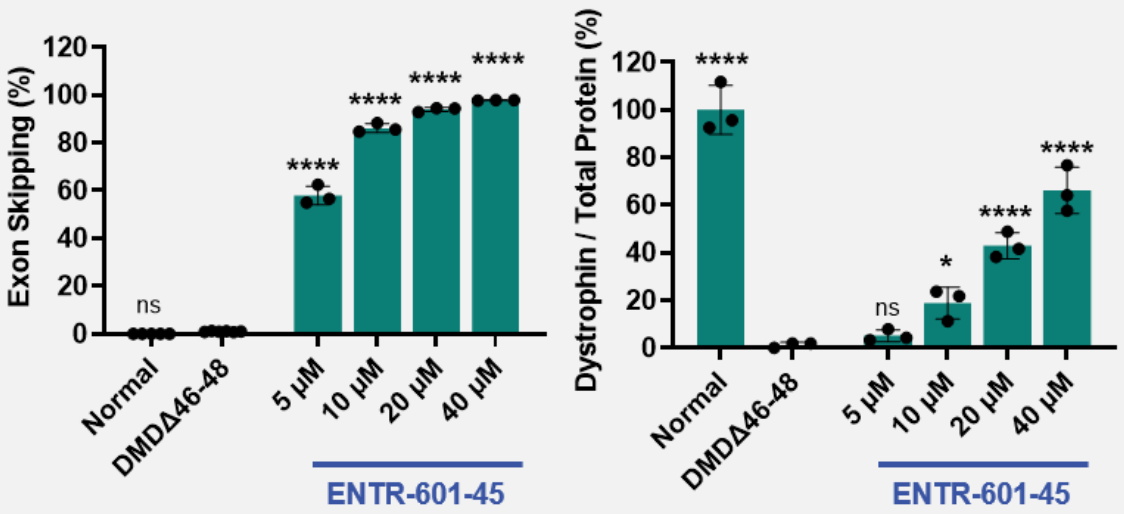
*Multiple Ascending Dose/Phase 2b trial is subject to regulatory feedback and the outcome of the single ascending dose trial.

ENTR-601-45

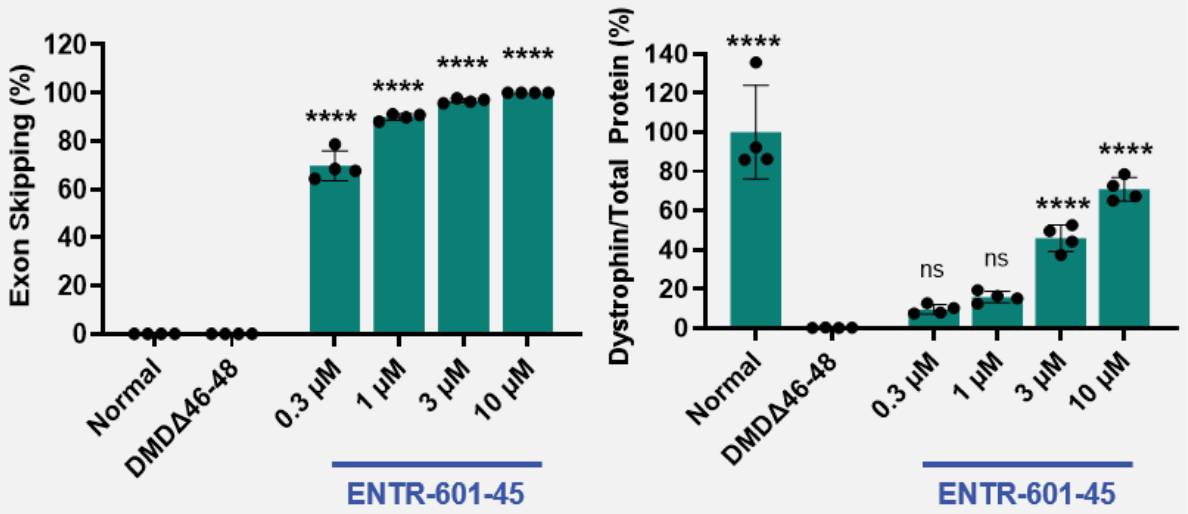
ENTR-601-45 *IN VITRO* EFFICACY

ENTR-601-45 showed robust exon skipping and dystrophin production in patient-derived skeletal and cardiac muscle cells

ENTR-601-45 in Skeletal Muscle Cells



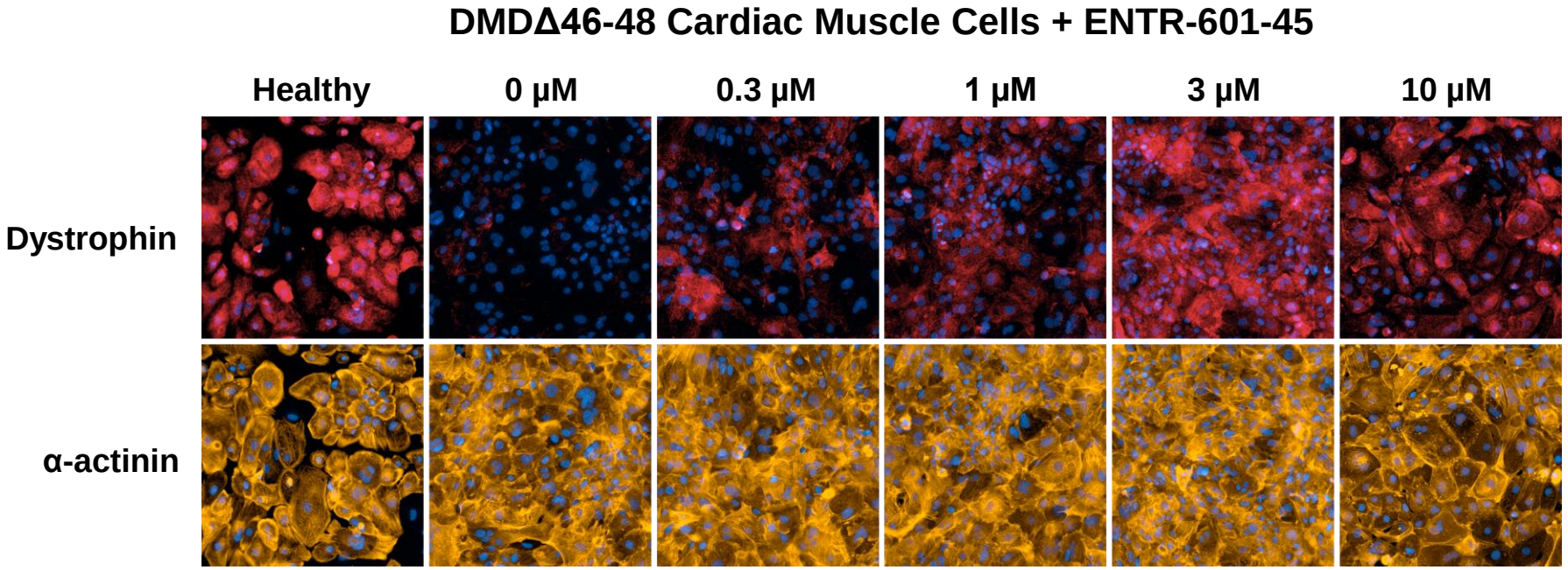
ENTR-601-45 in Cardiac Muscle Cells

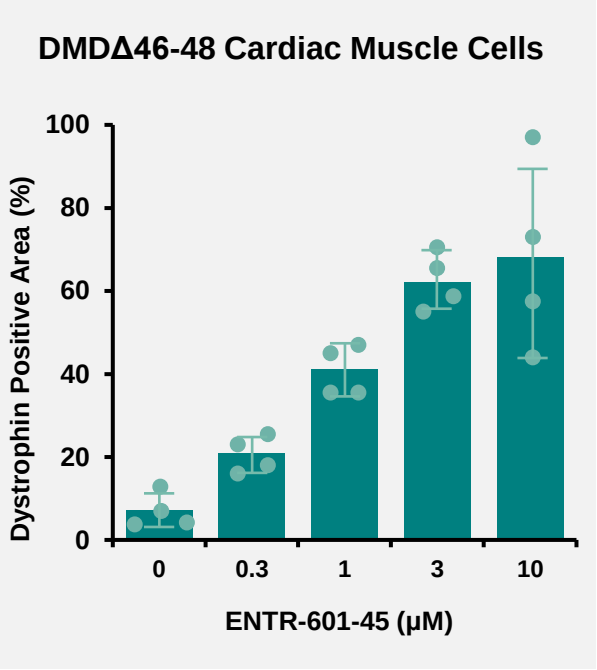


Data are shown as mean ± SD (n = 3 skeletal muscle; n = 4 cardiac muscle); one-way ANOVA; *p<0.05, ****p<0.0001; relative to untreated DMDΔ46-48.
Concentrations provided are PMO equivalent.

ENTR-601-45 IN CARDIAC MUSCLE CELLS

ENTR-601-45 produced dose-dependent dystrophin restoration in patient-derived cardiac muscle cells





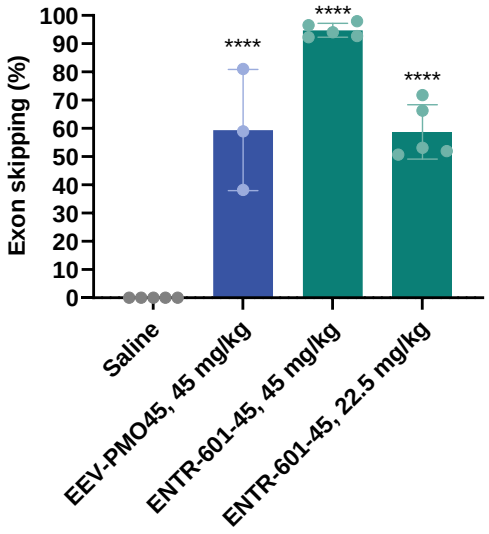
- DMD patient-derived cardiac muscle cells (DMDΔ46-48, n=4) were treated with ENTR-601-45 for 24 hours and analyzed 48 hours later

DMDΔ46-48 iPSC-derived cardiac muscle cells from an exon 45 skip amenable DMD patient harboring an exon 46-48 deletion mutation were treated for 24 hours and analyzed 48 hours later. Data are shown as mean ± SD.

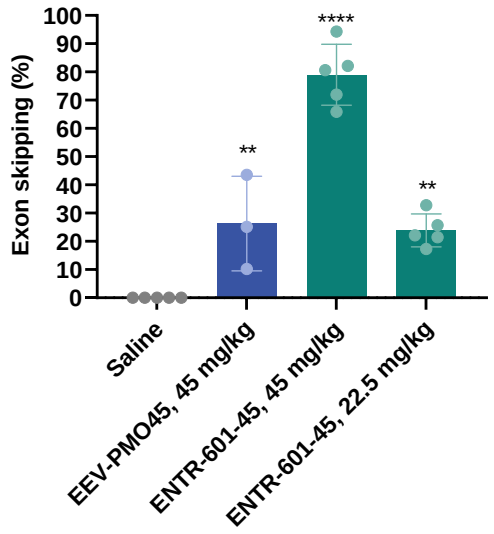
ENTR-601-45 TARGET ENGAGEMENT IN HUMAN DMD MICE

ENTR-601-45 delivered up to a two-fold improvement in exon skipping when compared to an equivalent dose of the same EEV conjugated to a casimersen sequence

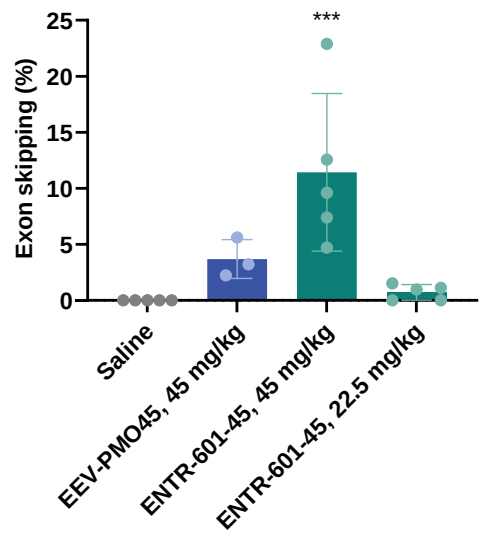
Tibialis Anterior



Diaphragm



Heart



- A single IV dose of ENTR-601-45 resulted in high levels of exon skipping in hDMD in the mouse skeletal muscle and heart after 1 week
- Both EEV-PMO45 (casimersen sequence) and ENTR-601-45 utilize the same EEV
- EEV-PMO45 uses the same oligonucleotide sequence as casimersen

Data are shown as mean ± SD (n = 3-5); one-way ANOVA; **p<0.01, ***p<0.001, ****p<0.0001; relative to saline; Concentrations provided are PMO equivalent.

ENTR-601-45 DATA SUMMARY

ENTR-601-45 consistently demonstrated robust *in vitro* and *in vivo* data;
Regulatory submission planned in Q4 2024

- **Patient-derived Cells**
  - ENTR-601-45 showed robust exon skipping and dystrophin protein production in patient-derived cardiac and skeletal muscle cells
- **DMD Mouse Models**
  - High levels of exon skipping were measured in hDMD mouse heart and skeletal muscle tissue
  - Exon 44 deletion mouse amenable to exon 45 skipping has been generated and population is being expanded externally
- **Process Development**
  - Process development completed
  - Non-GMP ENTR-601-45 generated in house to support non-GLP toxicology studies

Next Steps

- Finalize clinical strategy pending input from regulatory authorities
- Planning for a direct to MAD trial in Duchenne patients for ENTR-601-45
- Current toxicology plan includes subchronic studies to support MAD

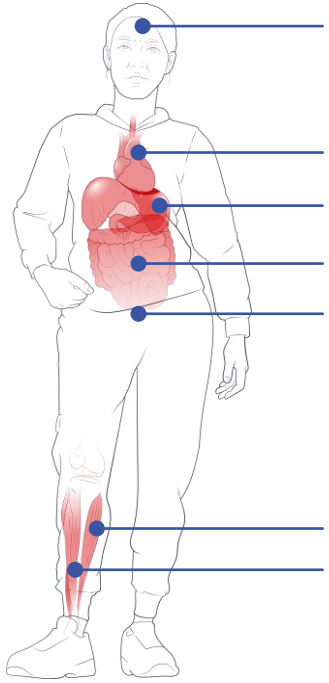
MYOTONIC DYSTROPHY TYPE 1 (DM1)

DM1 IS A DEBILITATING, MULTISYSTEMIC DISEASE WITH NO AVAILABLE TREATMENTS

40,000+
people in the **U.S.** have DM1[1]

50,000+
people in **Europe** have DM1[1]

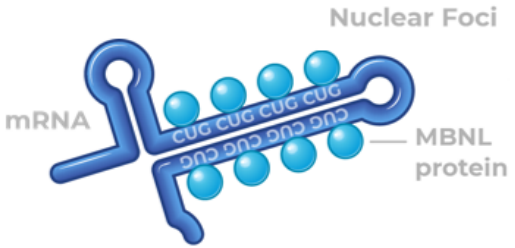
Symptoms include:



- Fatigue and excessive daytime sleepiness
- Cardiac conduction irregularities
- Respiratory muscle impairment
- Gastrointestinal complications
- Incontinence
- Generalized limb weakness
- Myotonia (delayed relaxation of skeletal muscle)

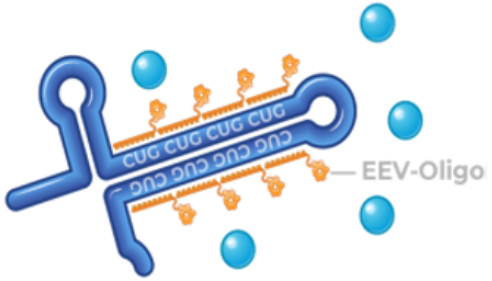
DM1 is caused by a mutation in the *dystrophia myotonica protein kinase (DMPK)* gene

Mutant *DMPK* mRNA



- Nuclear foci formation
- mRNA accumulation
- Reduced MBNL function
- Aberrant splicing

EEV-Oligonucleotide Approach



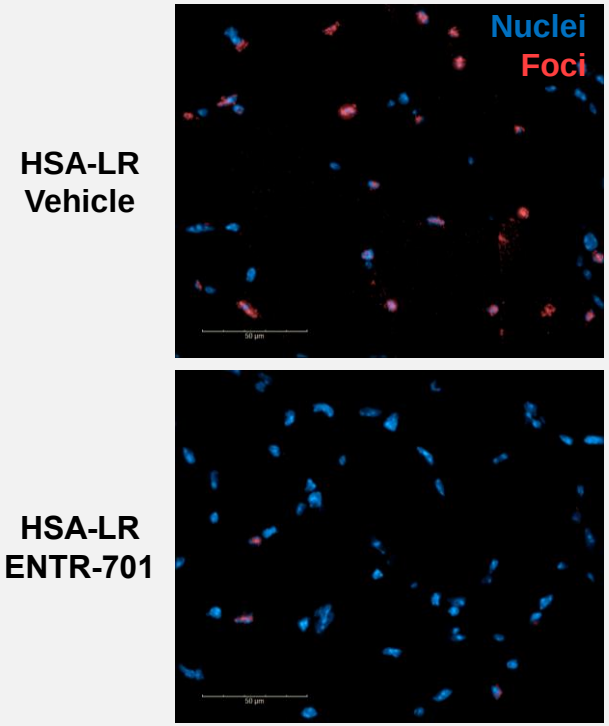
- Reduced nuclear foci
- Selective mRNA reduction
- Normal MBNL function
- Corrected spliceopathy

[1]Pascual-Gilabert M, López-Castel A, Artero R. Myotonic dystrophy type 1 drug development: a pipeline toward the market. *Drug Discovery Today*. 2021;26(7):1765-72. doi: 10.1016/j.drudis.2021.03.024.

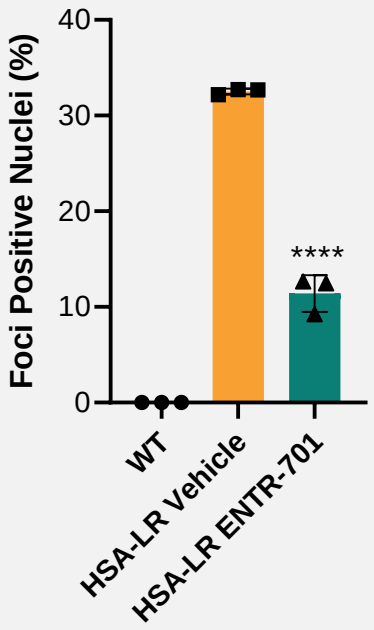
ENTR-701 EFFICACY IN HSA-LR MICE

ENTR-701 treatment reduced nuclear foci and CUG-repeat expansion transcript level and corrected aberrant splicing in HSA-LR mice, in a dose dependent manner

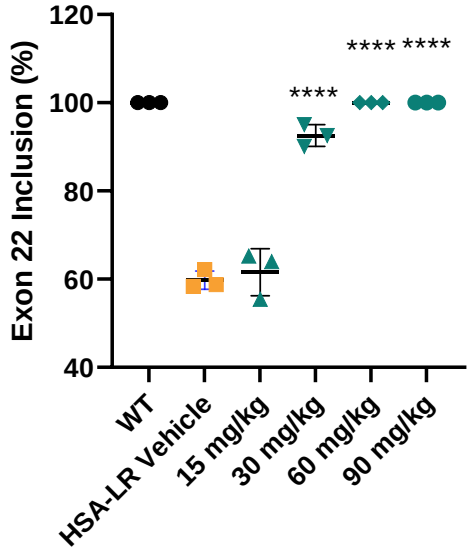
Nuclear Foci Reduction



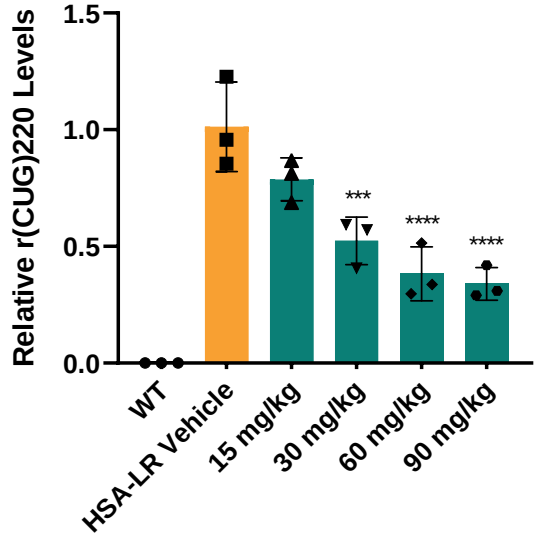
Tibialis anterior section



Atp2a1 Splicing Correction



HSA-r(CUG)220 Reduction

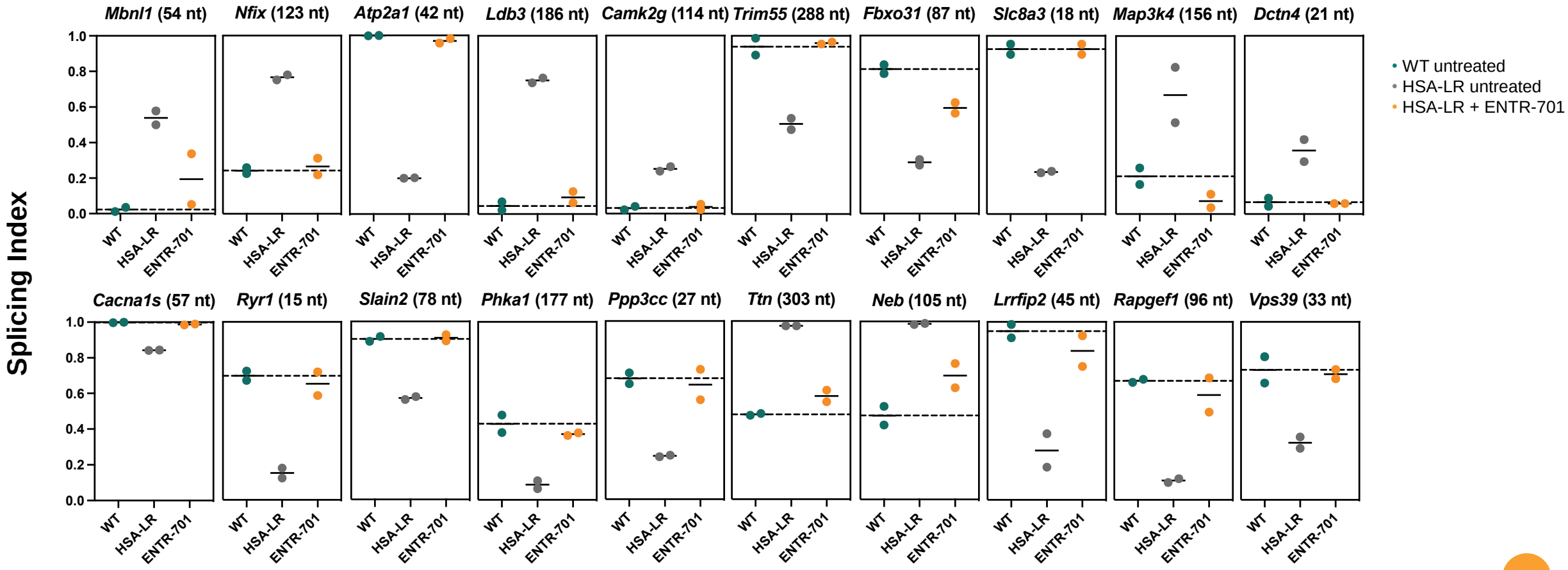


- **HSA-LR** model carries a transgene resulting in CUG repeat expansion and recapitulates DM1 phenotype and molecular pathology
- HSA-LR mice were dosed with vehicle or ENTR-701 and taken down 1-week post injection; tibialis anterior samples analyzed as a representative skeletal group

ENTR-701 is the clinical candidate selected for DM1, composed of CUG-repeat blocking PMO conjugated to EEV; ***p<0.001, ****p<0.0001, shown as mean ± standard deviation.

ENTR-701 CORRECTED SPLICEOPATHY IN HSA-LR MICE

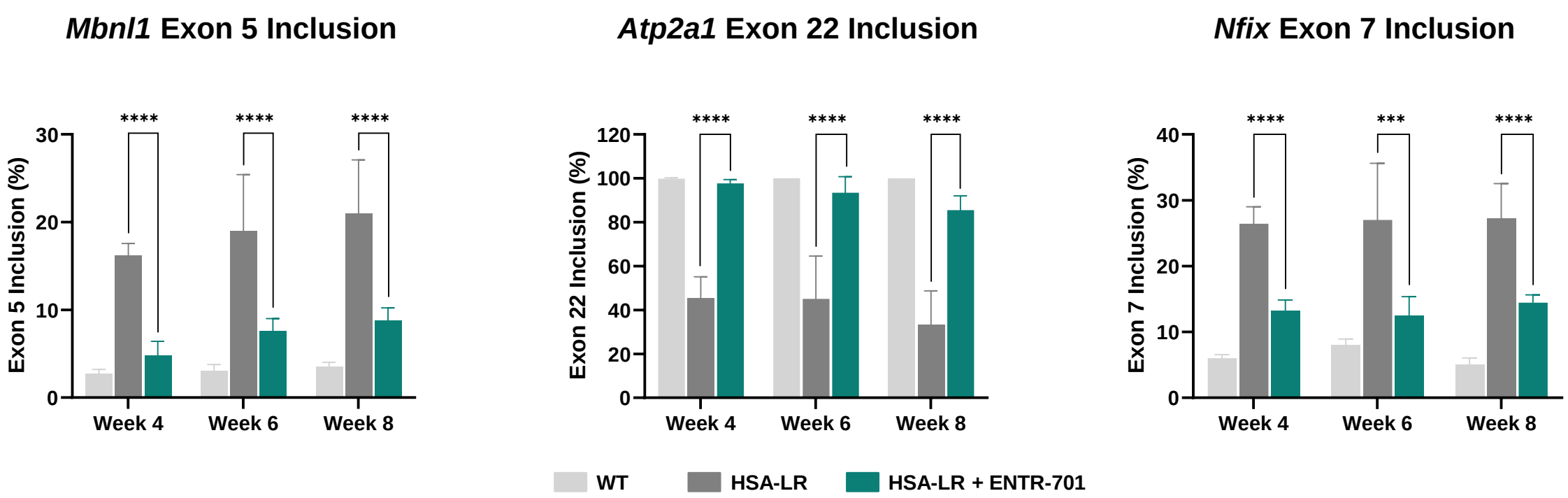
A single dose of ENTR-701 demonstrated substantial and robust splice correction across a panel of 20 different genes



DM1-affected splicing events analyzed by RNA-seq; ENTR-701 is the clinical candidate selected for DM1, composed of CUG-repeat blocking PMO conjugated to EEV.

ENTR-701 DURABILITY IN HSA-LR MICE

A single dose of ENTR-701 resulted in splicing correction in HSA-LR mice for at least 8 weeks



- Post single IV dosage of 60 mg/kg (PMO equivalent), robust splicing correction in the ENTR-701 treated HSA-LR mice 4, 6 or 8 weeks post injection

ENTR-701 is the clinical candidate selected for DM1, composed of CUG-repeat blocking PMO conjugated to EEV; *Mbnl1*, muscleblind like splicing regulator 1; *Atp2a1*, sarcoplasmic/endoplasmic reticulum calcium ATPase; *Nfix*, nuclear factor I X; ***p<0.001, ****p<0.0001, shown as mean ± standard deviation.

DM1 DATA SUMMARY

ENTR-701 demonstrated potential to treat DM1 via a CUG-repeat steric blocking approach both *in vitro* and *in vivo*

- Robust *in vitro* and *in vivo* data set demonstrating:
  - Highly specific reduction of pathogenic CUG-repeat containing mRNA
  - Reduction of nuclear foci
  - Correction of *Mbnl1* and downstream aberrant splicing
  - Correction of global transcriptome
- Single dose of ENTR-701 demonstrated durable splicing correction and amelioration of myotonia for at least 8 weeks post-dose in HSA-LR model

Established transformational collaboration with Vertex for the discovery and development of EEV-therapeutics for the potential treatment of DM1

PLATFORM EXPANSION

ADDITIONAL PLATFORM OPPORTUNITIES

Entrada continues to invest in and build upon our EEV platform to extend our efforts in developing novel EEV-therapeutic candidates

Target	Platform Approach	Goal
DNA	Gene editing	Deliver CRISPR enzyme and repair gene function with guide RNA
RNA	RNA editing	Deliver oligonucleotide therapeutics for RNA editing
	RNA splicing	Modify RNA via exon/intron splicing to activate protein expression
	RNA blocking	Block trinucleotide repeats in RNA to inhibit adverse binding
	RNA silencing	Silence or knockdown RNA to prevent protein expression
Protein	Protein replacement	Replace proteins and enzymes
	Protein inhibition	Inhibit protein signaling pathways
	Protein degradation	Degrade disease-causing proteins

CORPORATE HIGHLIGHTS AND MILESTONES

KEY CORPORATE HIGHLIGHTS

With ~$377M cash, cash equivalents and marketable securities as of June 30, 2023, Entrada is capitalized to deliver ENTR-601-44 Phase 1 clinical data and progress the broader pipeline

Strong Financial Position

- Cash, cash equivalents and marketable securities: ~$377M
- Cash runway: Through 2025*
- Common shares outstanding at June 30, 2023: 33,239,813

52 Distinct Patent Families on File

- Including exclusive EEV platform rights
- 11 families with one or more granted patents related to our technology

~130 Employees

- Seasoned leadership team across functions
- Recognized as a Top Place to Work by *The Boston Globe* and *BioSpace*
- ~75% have advanced degrees and ~50% have PhDs

*Assumes existing cash, cash equivalents, marketable securities, together with Vertex collaboration ongoing research support and achievement of certain milestones.

ENTRADA AT A GLANCE

Entrada is leveraging its Endosomal Escape Vehicle platform (EEV™) to create a diverse and expanding development portfolio of RNA-, antibody- and enzyme-based therapeutics

- **Advancing new therapeutic options for people living with Duchenne muscular dystrophy (DMD)**
  - Lead DMD program (ENTR-601-44): First participant expected to be dosed in September 2023
  - Additional programs focus on clinical candidate, ENTR-601-45, with discovery efforts underway in exons 50 and 51
- **Transformative Vertex partnership for the development of myotonic dystrophy, type 1 (DM1)**
  - $224M upfront payment and $26M equity investment; Up to $485M for the achievement of certain milestones, plus royalties; Four-year global research collaboration
  - Entrada is responsible for preclinical development; Vertex is responsible for global development, regulatory, manufacturing and commercialization
- **Expanding our commitment to non-neuromuscular disease programs**
  - EEV's unique mechanism of action is designed to enable delivery of various moieties into organs and tissues
- Strong financial position with **cash runway through 2025***
- Experienced leadership team and Board of Directors, supported by leading biotech investors

*Assumes existing cash, cash equivalents, marketable securities, together with Vertex collaboration ongoing research support and achievement of certain milestones.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