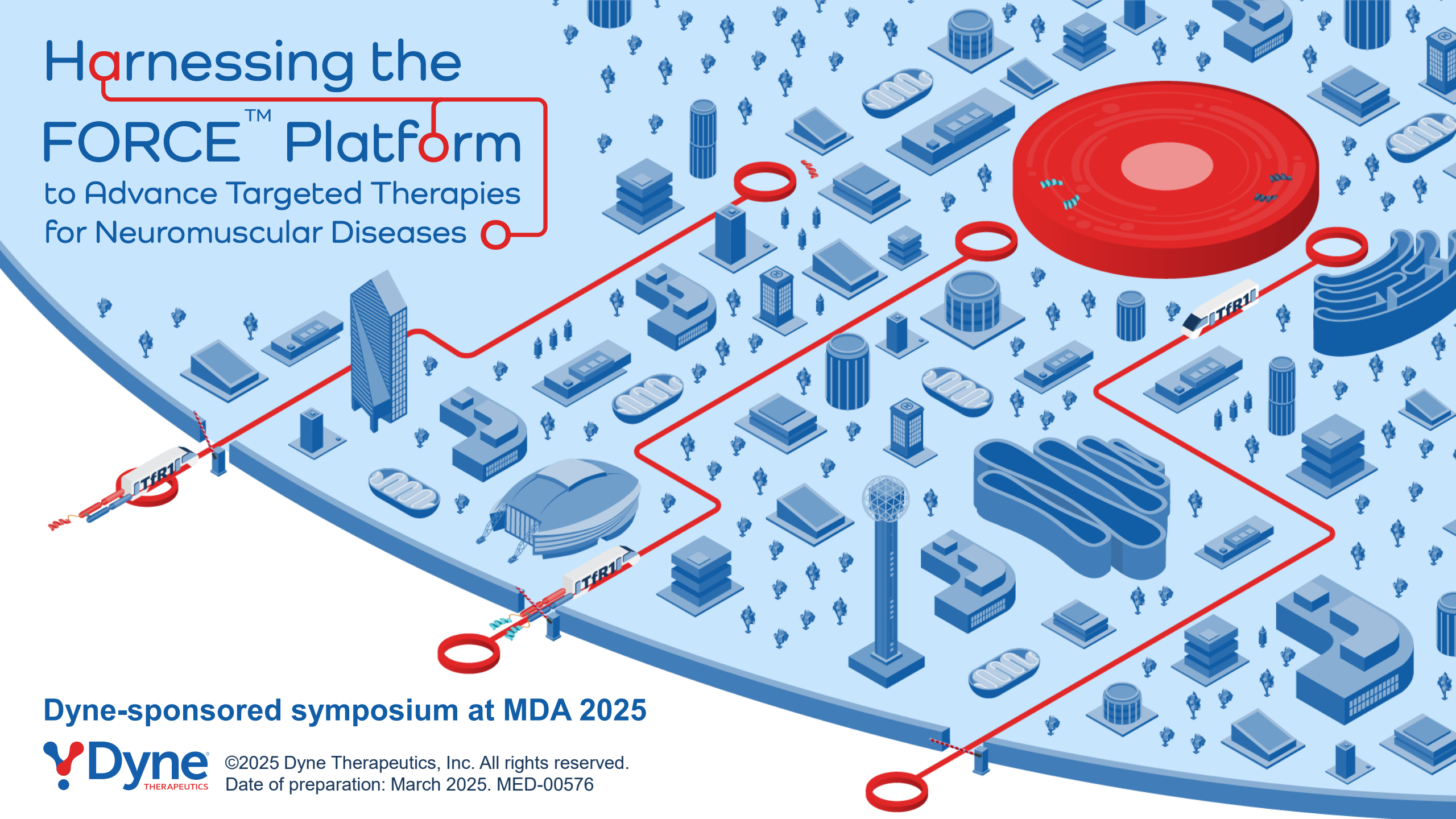
Harnessing the FORCE™ Platform to Advance Targeted Therapies for Neuromuscular Diseases



Dyne-sponsored symposium at MDA 2025

Dyne THERAPEUTICS

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Date of preparation: March 2025. MED-00576

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Dyne-sponsored symposium: Harnessing the FORCE platform to advance targeted therapies for neuromuscular diseases

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- The clinical impact of the FORCE platform: myotonic dystrophy type 1 (DM1), including data on the use of splicing correction as a prognostic biomarker of functional outcomes in DM1
- Advancing the FORCE platform into additional neuromuscular diseases

Forward-looking statements and disclaimer

- This symposium is organized and funded by Dyne Therapeutics
- The FORCE™ platform, DYNE-251, DYNE-101, DYNE-302, and DYNE-401 are investigational or otherwise in development and have not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority
- 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 Dyne's strategy, future operations, prospects and plans, objectives of management, the potential of the FORCE platform, the therapeutic potential of DYNE-101 DYNE-251, DYNE-302, and DYNE-401, the anticipated timelines for reporting additional data from the ACHIEVE and DELIVER clinical trials, enrolling registrational cohorts and initiating additional clinical trials, and plans to provide future updates on pipeline programs, 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. Dyne 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 initiation and completion of preclinical studies and clinical trials; uncertainties as to the availability and timing of results from preclinical studies and clinical trials; the timing of and Dyne's ability to enroll patients in clinical trials; whether results from preclinical studies and data from clinical trials will be predictive of the final results of the clinical trials or other trials; whether data from clinical trials will support submission for regulatory approvals; uncertainties as to the FDA's and other regulatory authorities' interpretation of the data from Dyne's clinical trials and acceptance of Dyne's clinical programs and as to the regulatory approval process for Dyne's product candidates; whether Dyne's cash resources will be sufficient to fund its foreseeable and unforeseeable operating expenses and capital expenditure requirements; as well as the risks and uncertainties identified in Dyne's filings with the Securities and Exchange Commission (SEC), including the Company's most recent Form 10-K and in subsequent filings Dyne may make with the SEC. In addition, the forward-looking statements included in this presentation represent Dyne's views as of the date of this presentation. Dyne anticipates that subsequent events and developments will cause its views to change. However, while Dyne 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 Dyne's views as of any date subsequent to the date of this presentation.

Today’s faculty

Chamindra Laverty, MD

Clinical Professor of Neurosciences and Neuromuscular Specialist, University of California, San Diego, USA

James Lilleker, MD

Consultant Neurologist and Honorary Senior Lecturer, Manchester Centre for Clinical Neurosciences, University of Manchester and Northern Care Alliance NHS Foundation Trust, UK

Kevin Flanigan, MD

Director of the Center for Gene Therapy, Nationwide Children’s Hospital, USA

Douglas Kerr, MD, PhD

Chief Medical Officer, Dyne Therapeutics, USA

Disclosures

Chamindra Laverty

- Consultant for Avidity Biosciences, Sarepta, Dyne Therapeutics, Italfarmaco, Novartis, Catalyst, Biogen, PTC, and Solid Biosciences

James Lilleker

- Participation in advisory boards and/or conference support/presentations for Dyne Therapeutics, Roche Holding, and Sanofi

Kevin Flanigan

- Clinical trial support from Dyne Therapeutics, Avidity Biosciences, and Ultragenyx
- Advisor compensation from Apic Bio, Encoded Therapeutics, BioMarin Pharmaceutical, Locanobio, and Sanofi
- Scientific advisory board for Armatus Bio

Douglas Kerr

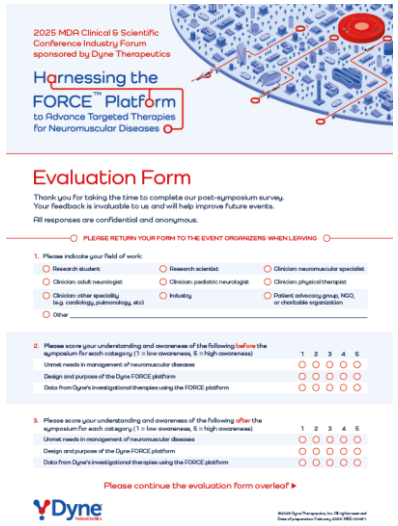
- Employment and stock ownership in Dyne Therapeutics

Submit your questions and complete the evaluation form

Virtual attendees

Please submit your questions using the **chat box** on the app and virtual platform

Please complete the virtual evaluation form using the **link available** in the **chat box** or scan the **QR code** below



Live attendees

Please **raise your hand** to signal your question, and a hostess will pass you a microphone

Please complete the evaluation form **available on your table**

Alternatively, please scan the **QR code** on the tent card at your table to complete the online form

Key scientific highlights

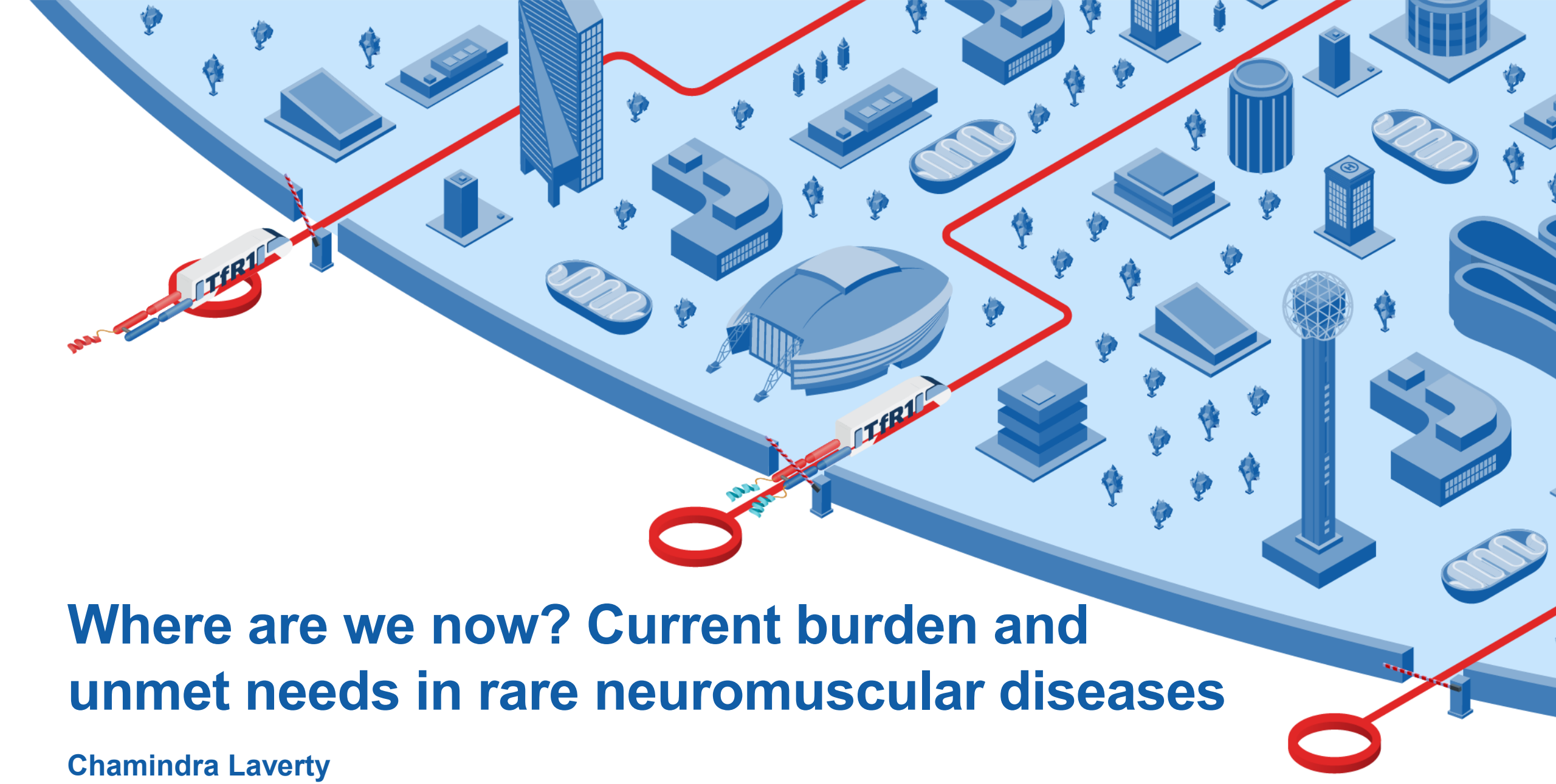
The FORCE platform leverages the natural expression of TfR1 to enable targeted delivery of rationally selected disease-modifying therapies to correct the underlying cause of neuromuscular diseases and achieve broad distribution to tissues relevant to disease pathology	**Payload and distribution matter**
DYNE-251 has a favorable safety profile, with some participants on therapy for 2.5 years[a], and has shown long-term improvement in clinical and real-world functional outcomes in individuals with DMD	**Long-term, sustained efficacy and favorable safety with DYNE-251**
DYNE-101 addresses the underlying pathobiology (dysregulated splicing) of DM1 and has demonstrated a favorable safety profile[b] and clinically meaningful improvements on measures of strength, mobility and QoL, including CNS manifestations – Improvements in areas that patients find most impactful: muscle weakness and CNS-related manifestations[1]	**Splicing correction with DYNE-101 predicts clinically meaningful functional outcomes**
The FORCE platform has the potential to transform the lives of individuals living with neuromuscular disorders by addressing the totality of symptoms experienced by these individuals, including CNS manifestations	**Transformational potential of the FORCE platform**

The FORCE platform, DYNE-251 and DYNE-101 are investigational or otherwise in development and have not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.

a. Data as of February 7, 2025; b. Data as of December 6, 2024.

CNS, central nervous system; DM1, myotonic dystrophy type 1, DMD, Duchenne muscular dystrophy; HCP, healthcare provider; PRO, patient-reported outcome; QoL, quality of life; TfR1, transferrin receptor 1.

1. Hagerman KA, et al. *Muscle Nerve* 2019;59:457–464.



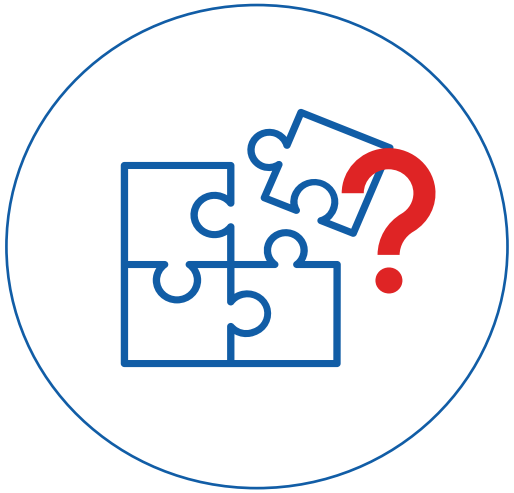
Where are we now? Current burden and unmet needs in rare neuromuscular diseases

Chamindra Laverty

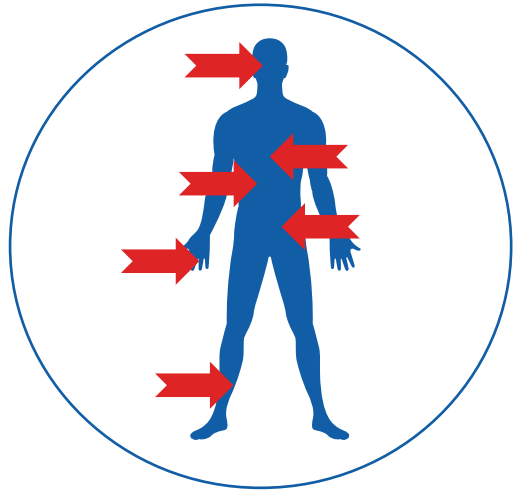
NMD management is a multifaceted challenge

Complexities in NMD management relate to:

Identifying affected patients[1,2]



Disease knowledge and awareness[1,2]

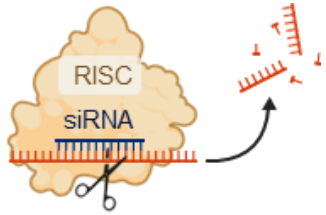
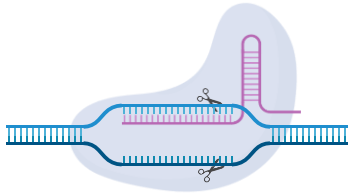
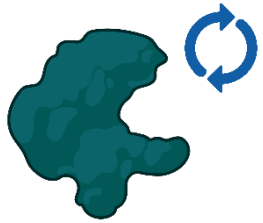
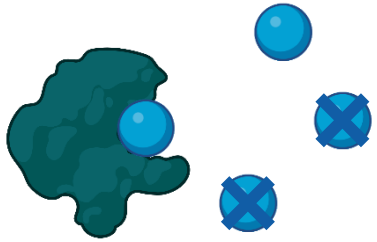


Addressing the totality of symptoms[3,4]

NMD, neuromuscular disease.

1. Ricci G, et al. *Acta Myol*. 2022;41(1):24–29; 2. Pini J, et al. *J Neuromuscul Dis*. 2021;8(4):743–754;
3. Gökirmak T, et al. *Trends Pharmacol Sci*. 2021;42(7):588–604; 4. Roberts TC, et al. *Nat Rev Drug Discov*. 2020;19(10):673–694.

However, the developmental landscape of therapies for NMDs has continued to evolve

Antisense oligonucleotides (ASOs)[1]	RNA interference[2,3]	Gene therapies[2,4]	Enzyme replacement therapy[4,5]	Substrate reduction therapy[4,5]
				
Modulate gene expression through activation of RNases, steric hindrance and splicing modulation	Suppress pathogenic variants that cause toxic gain of function via double stranded small interfering RNA oligonucleotides	Rectify genetic anomalies at the DNA level, including gene replacement, gene editing, and gene addition	Target the functional loss of the enzyme by infusion of a recombinant one ± enzyme stabilizers	Decrease the production of harmful substrates in cells using small molecules or ASOs

Slide presents main current and future therapeutic approaches for Duchenne muscular dystrophy (DMD), myotonic dystrophy type 1 (DM1), facioscapulohumeral muscular dystrophy (FSHD) and Pompe disease. Figures created by BioRender.com.

ASO, antisense oligonucleotide; NMD, neuromuscular disease; Rnase, ribonuclease.

1. Collotta D, et al. *Front Pharmacol.* 2023;14:1304342; 2. Andrea ZA, et al. *Cell Mol Life Sci.* 2024;81(1):198; 3. Roberts TC, et al. *Nat Rev Drug Discov.* 2020;19(10):673–694;
4. Labella B, et al. *Biomolecules.* 2023;13(9):1279; 5. Stevens D, et al. *Curr Treat Options Neurol.* 2022;24(11):573–588.

However, the developmental landscape of therapies for NMDs has continued to evolve

Antisense oligonucleotides (ASOs)[1]	RNA interference[2,3]	Gene therapies[2,4]	Enzyme replacement therapy[4,5]	Substrate reduction therapy[4,5]
activation of RNases, steric hindrance and splicing modulation	toxic gain of function via double stranded small interfering RNA oligonucleotides	at the DNA level, including gene replacement, gene editing, and gene addition	loss of the enzyme by infusion of a recombinant one ± enzyme stabilizers	production of harmful substrates in cells using small molecules or ASOs

… but how can we improve the delivery of novel therapies to tissues that are relevant to disease pathology, such as muscle and CNS?

Slide presents main current and future therapeutic approaches for Duchenne muscular dystrophy (DMD), myotonic dystrophy type 1 (DM1), facioscapulohumeral muscular dystrophy (FSHD) and Pompe disease. Figures created by BioRender.com.
ASO, antisense oligonucleotide; NMD, neuromuscular disease; Rnase, ribonuclease.
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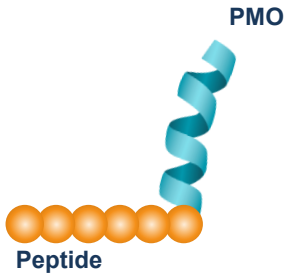
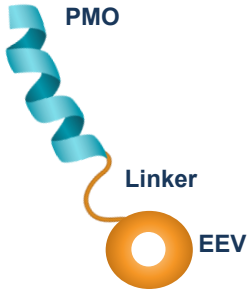
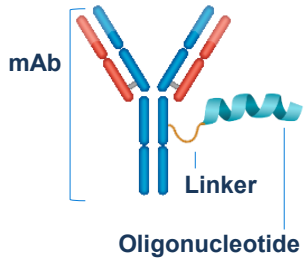
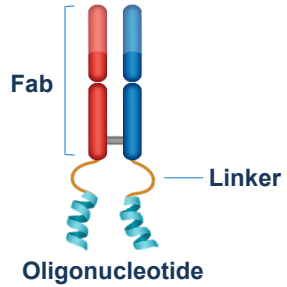
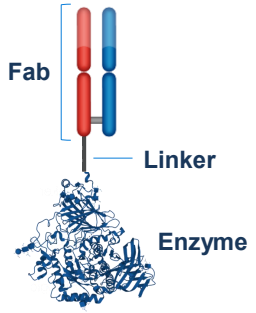
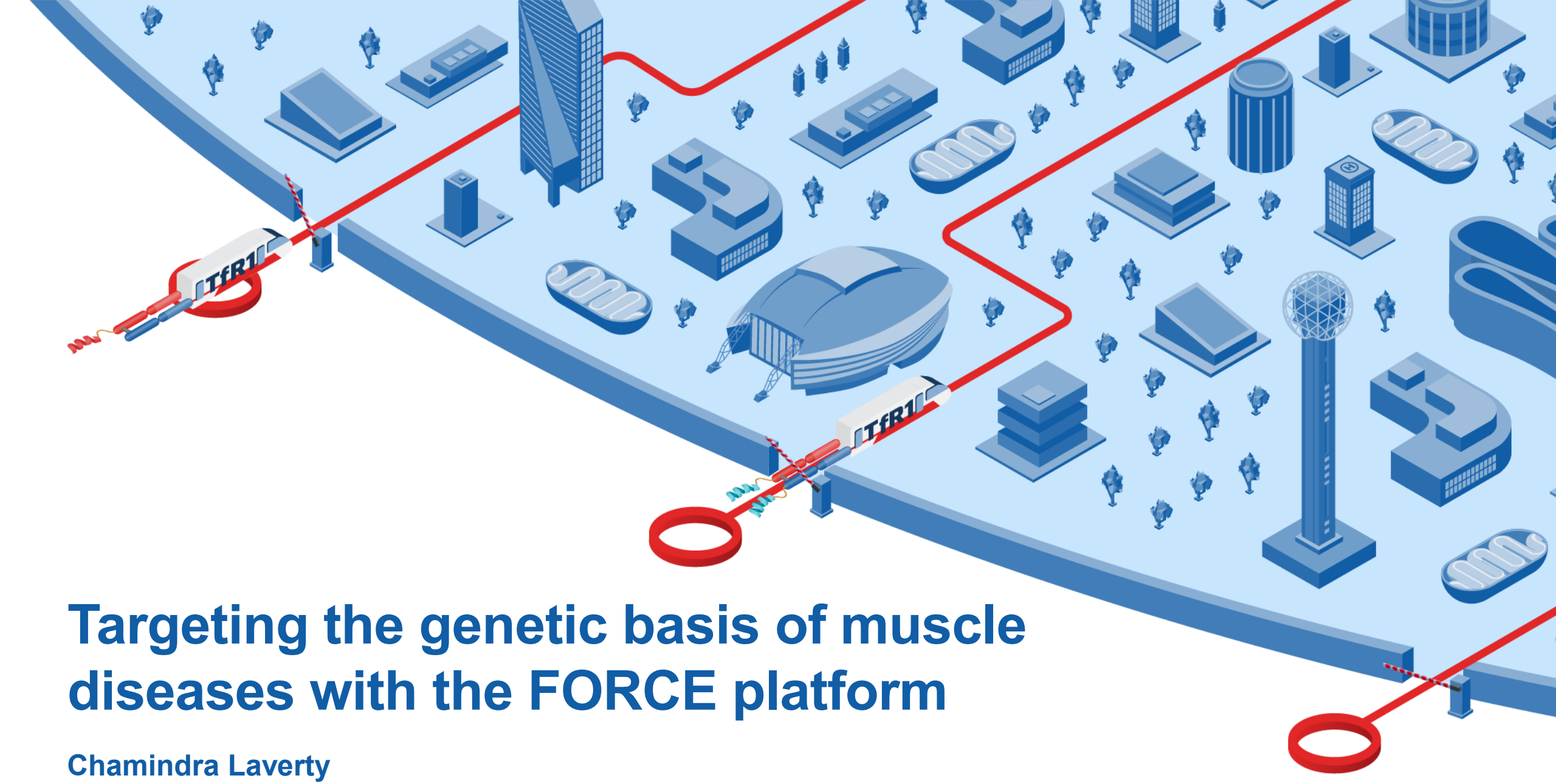
4. Labella B, et al. *Biomolecules.* 2023;13(9):1279; 5. Stevens D, et al. *Curr Treat Options Neurol.* 2022;24(11):573–588.

Different approaches are in development to enhance delivery of therapeutics

Delivery systems in development					
Cell-penetrating peptides (CPP)			Antibody–oligonucleotide conjugates/fusion proteins		
Peptide-conjugated PMO (PPMO)[1,3]	Enhanced delivery oligonucleotide (EDO)[2,3]	Endosomal escape vehicle (EEV)[4,5]	Monoclonal antibody (mAb)–oligonucleotide conjugates[6,7]	Fab–oligonucleotide conjugates[8]	Fab–biologic fusion protein[9]
					
Conjugation of PMOs to internalization peptides (with or without linkers) to enhance cell penetration		Oligonucleotides conjugated to cyclic cell-penetrating peptides that harness the inherent endocytic mechanism of cells	Monoclonal antibody–oligonucleotide conjugates	Fab antibody–oligonucleotide conjugates	Fab antibody–enzyme fusion protein

Fab, antigen-binding fragment; PMO, phosphorodiamidate morpholino oligomer.

1. Tsoumpra MK, et al. *EBioMedicine.* 2019;45:630–645; 2. Klein AF, et al. *J Clin Invest.* 2019;129(11):4739–4744; 3. McClorey G, Banerjee S. *Biomedicines.* 2018;6(2):51. 4. Li X, et al. *Mol Ther Nucleic Acids.* 2023;33:273–285; 5. Qian Z, et al. *Biochemistry.* 2016;55(18):2601–2612; 6. Gagliardi M, Ashizawa AT. *Biomedicines.* 2021;9(4):433; 7. Dugal-Tessier J, Thirumalairajan S, Jain N. *J Clin Med.* 2021;10(4):838; 8. Desjardins CA, et al. *Nucleic Acids Res.* 2022;50(20):11401–11414; 9. Picariello T, et al. Poster presentation at the World Muscle Society Annual Congress, Prague, Czechia, October 8–12, 2024. Poster 669.



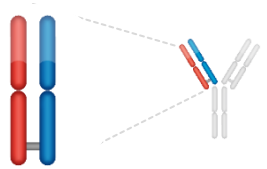
Targeting the genetic basis of muscle diseases with the FORCE platform

Chamindra Laverty

Dyne FORCE platform modularity enables delivery of therapeutics that target the genetic cause of rare neuromuscular diseases

ANTIBODY[1,2]

Proprietary Fab against TfR1 to enable targeted delivery to muscle and CNS

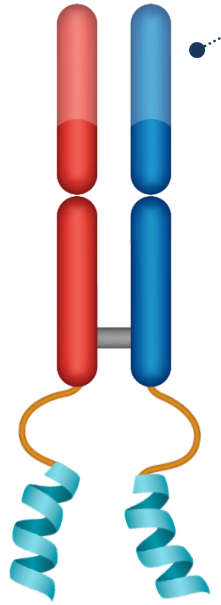


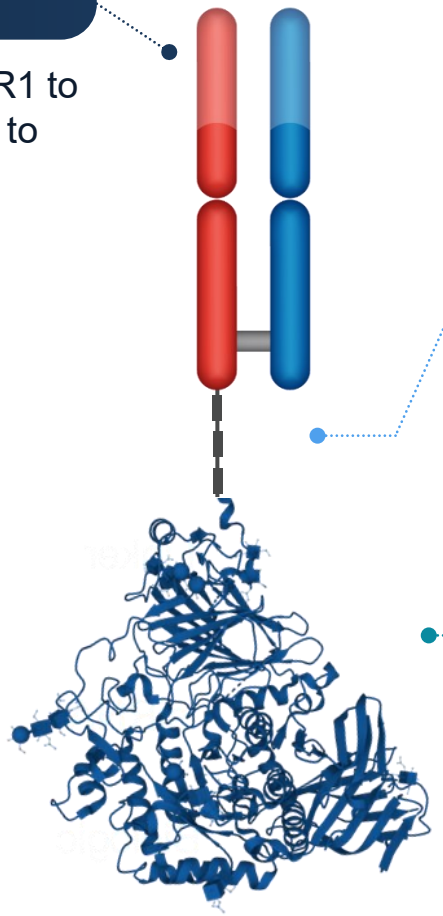
LINKER[1,2]

Connects Fab and payload

OLIGO PAYLOAD[1,2]

Modularity enables rational selection of payload to target the genetic basis of disease





LINKER[3]

Connects Fab and payload

BIOLOGIC PAYLOAD[3]

Modularity enables rational selection of payload to target the genetic basis of disease

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CNS, central nervous system; Fab, antigen-binding fragment; TfR1, transferrin receptor 1.

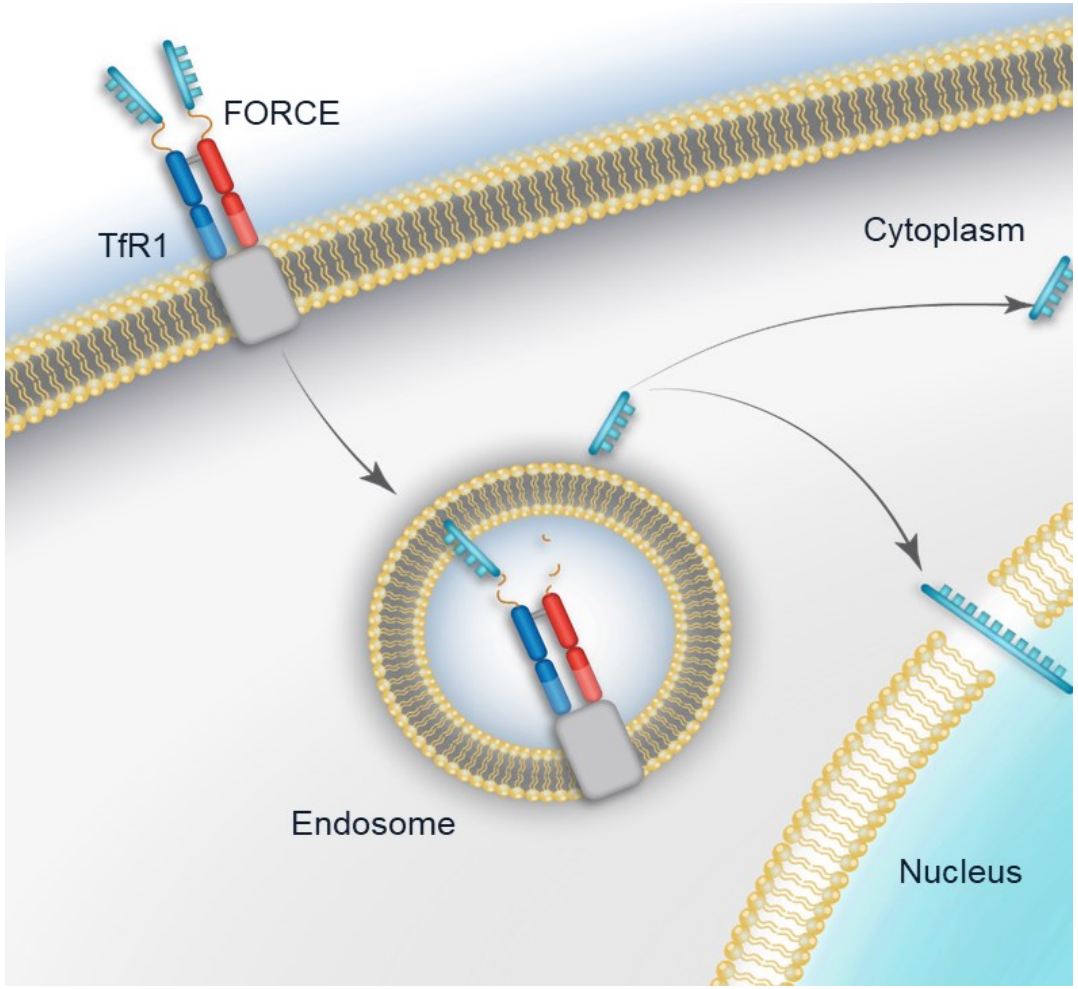
1. Desjardins CA, et al. *Nucleic Acids Res.* 2022;50(20):11401–11414; 2. Ohrt T, et al. *Nucleic Acids Res* 2006;34(5):1369;
3. Picariello T, et al. Poster presentation at the World Muscle Society Annual Congress, Prague, Czechia, October 8–12, 2024. Poster 669.

The FORCE platform was designed to harness the natural expression and function of TfR1 on muscle cells

TfR1 facilitates iron transport
at the cell surface[1]

TfR1 is expressed on the surface
of skeletal, smooth, and cardiac muscle cells, and is critical for iron uptake in these tissues[2–5]

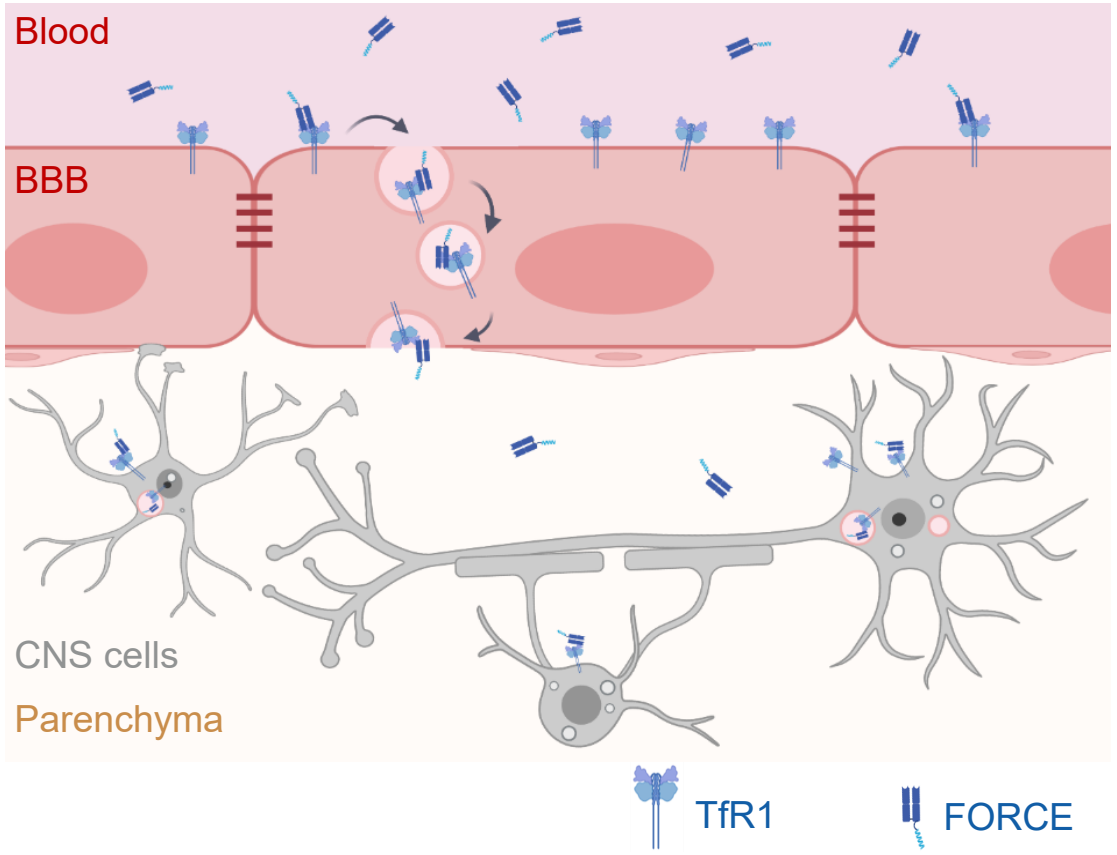
The choice of targeting TfR1
to enable muscle tissue uptake is justified by its expression in muscle tissue, and by its internalization kinetics[2,3,6]



The FORCE platform is investigational or otherwise in development and has not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.
Adapted from Desjardins CA, et al. *Nucleic Acids Res.* 2022;50(20):11401–11414.
siRNA, small interfering ribonucleic acid; TfR1, transferrin receptor 1.
1. Wang S, et al. *Haematologica.* 2020;105(8):2071–2082; 2. TFRC. The Human Protein Atlas. Accessed March 13, 2025. https://www.proteinatlas.org/ENSG00000072274-TFRC/tissue;
3. Barrientos T, et al. *EBioMedicine.* 2015;2(11):1705–1717; 4. Naito Y, et al. *Am J Hypertens.* 2016;29(6):713–718; 5. Xu W, et al. *Cell Rep.* 2015;13(3):533–545; 6. Ciechanover A, et al. *J Biol Chem.* 1983;258(16):9681–9689.

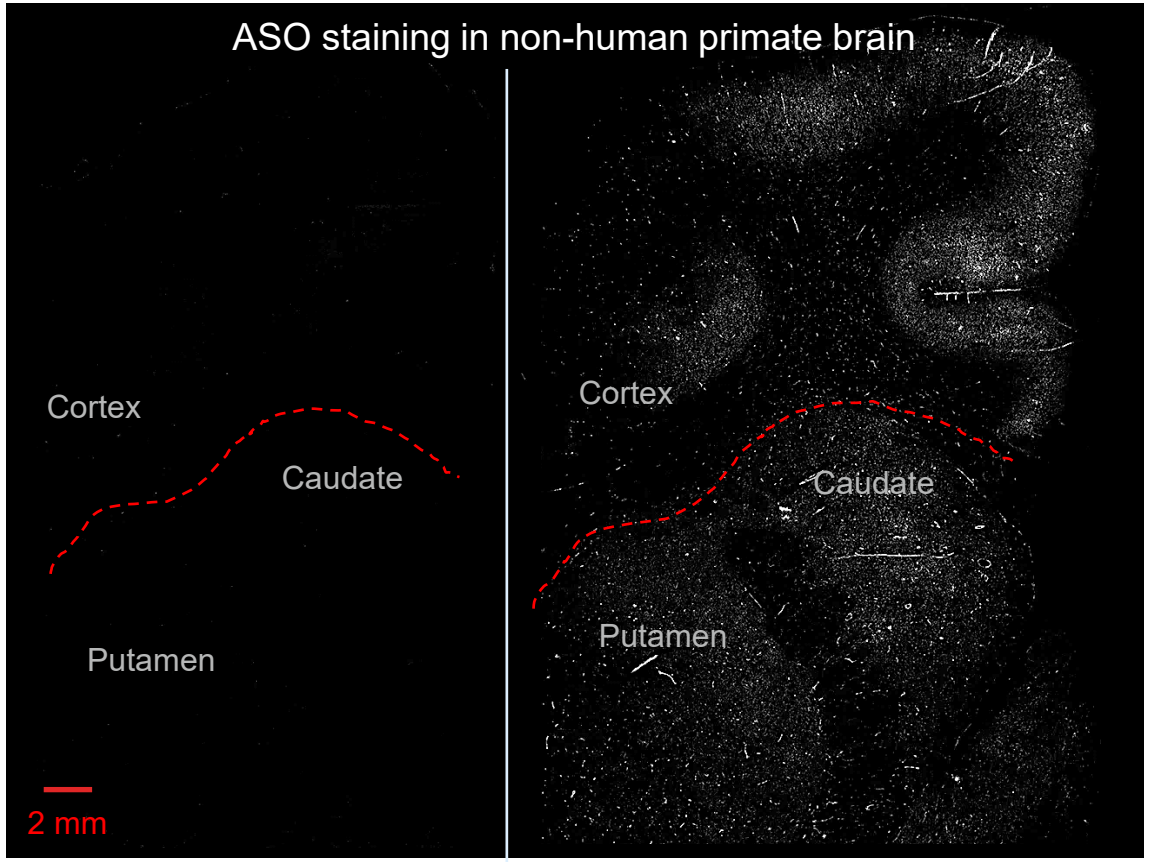
The FORCE platform can cross the blood–brain barrier and achieve widespread brain delivery

TfR1-mediated transcytosis: potential for crossing the BBB



Naked ASO, IV
No ASO delivery

FORCE, IV
Widespread ASO delivery



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Adapted from Pulgar VM. *Front Neurosci.* 2019;12:1019 and Liu K, et al. *Sci Rep.* 2016;6:21019. Schematic created by BioRender.com.

ASO, antisense oligonucleotide; BBB, blood–brain barrier; CNS, central nervous system; IV, intravenous; TfR1, transferrin receptor 1.

Zanotti S. Presentation at the 26th American Society of Gene and Cell Therapy Annual Meeting. May 17, 2023. Los Angeles, USA. Abstract 82.

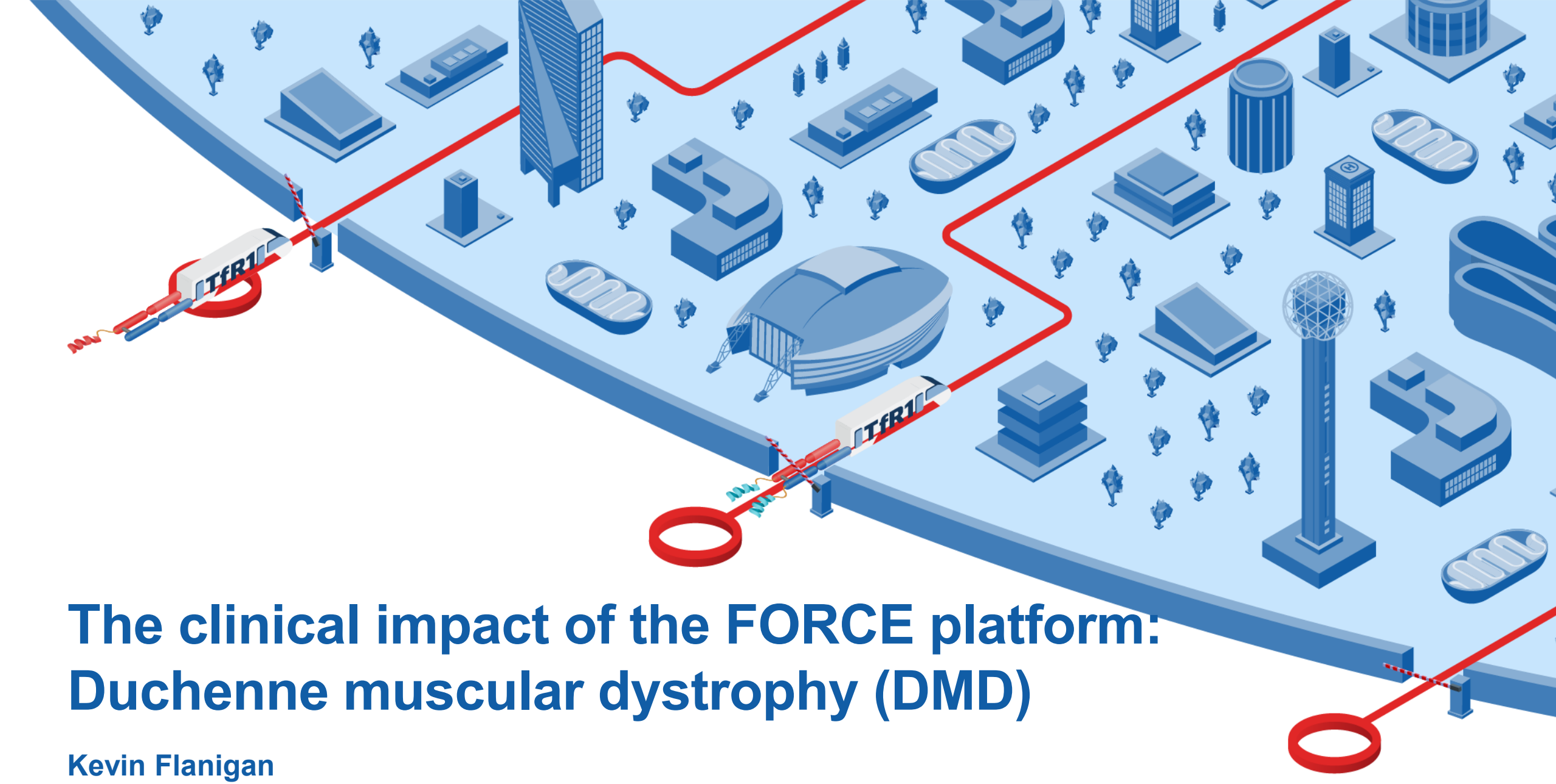
Summary

- The **FORCE** platform was developed to **overcome limitations** of therapeutic oligonucleotide delivery to muscle in rare neuromuscular disorders[1]
- The platform harnesses the natural expression of **TfR1** in muscle and CNS for **targeted delivery of a rationally selected payload** with the goal of addressing the **underlying cause of disease**[1–3]
- Preclinical data demonstrate that by leveraging TfR1, the **FORCE** platform achieves **broad distribution** to tissues relevant to disease pathology, including **skeletal, respiratory, cardiac, and smooth muscles**, as well as **CNS**[1,3]

The FORCE platform is investigational or otherwise in development and has not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.

CNS, central nervous system; TfR1, transferrin receptor 1.

1. Desjardins CA, et al. *Nucleic Acids Res.* 2022;50(20):11401–11414; 2. Shieh P, et al. Poster presentation the American Academy of Neurology Annual Meeting. April 15–18, 2024. Denver, USA. Poster 004;
3. Zanotti S. Presentation at the 26th American Society of Gene and Cell Therapy Annual Meeting Annual Meeting. May 17, 2023. Los Angeles, USA. Abstract 82.



The clinical impact of the FORCE platform: Duchenne muscular dystrophy (DMD)

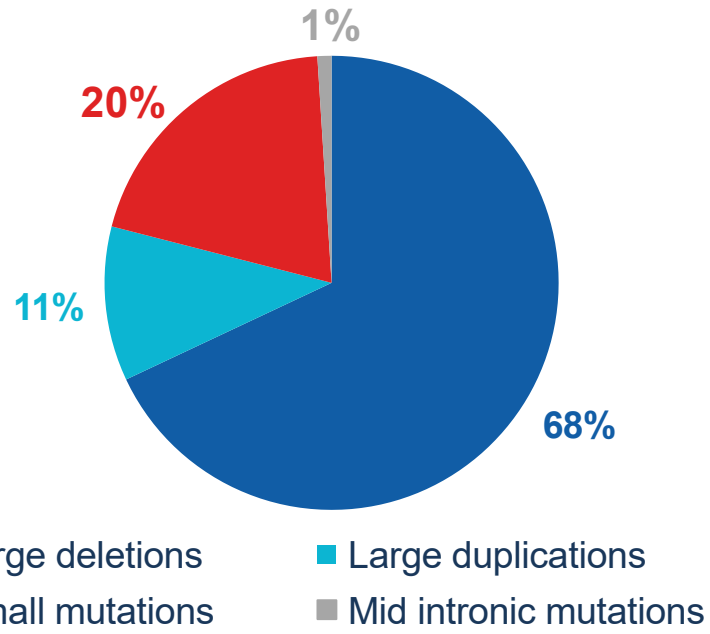
Kevin Flanigan

DMD is caused by mutations in the *DMD* gene

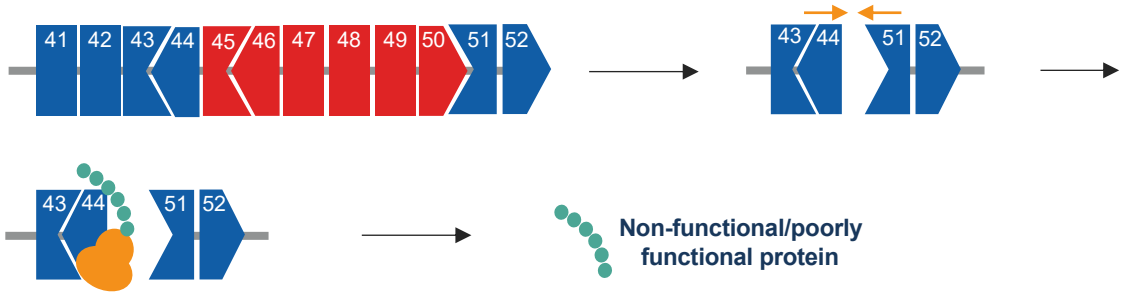
- DMD is caused by mutations in the *DMD* gene, which result in greatly reduced production of dystrophin protein, essential for muscle structure, function, and preservation[1–5]

- PMO-induced exon skipping restores the *DMD* mRNA reading frame, leading to the production of internally shortened, near full-length, functional dystrophin protein[7,8]

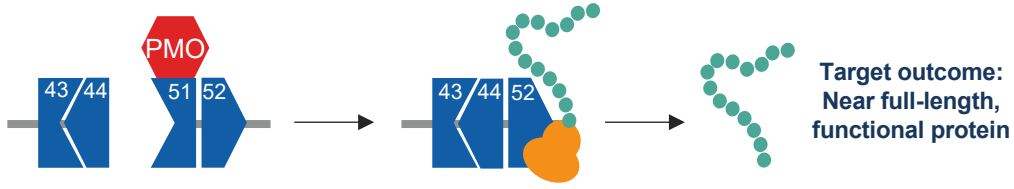
Deletions account for more than two-thirds of DMD cases[6]



Exon 45–50 deletion disrupts reading frame



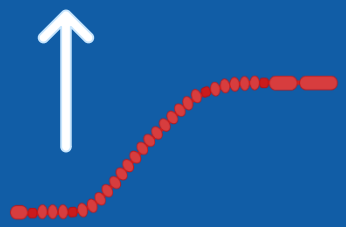
Skipping exon 51 with PMO restores reading frame



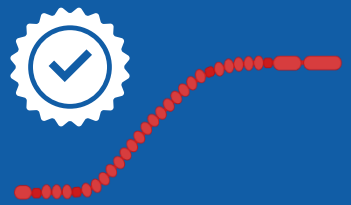
DMD, Duchenne muscular dystrophy; mRNA, messenger ribonucleic acid; PMO, phosphorodiamidate morpholino oligomer.

1. Claflin DR, Brooks SV. *Am J Physiol Cell Physiol.* 2008;294(2):C651–58; 2. Ervasti JM, Campbell KP. *J Cell Biol.* 1993;122(4):809–23;
3. Hoffman EP, Brown RH, Jr, Kunkel LM. *Cell.* 1987;51(6):919–28; 4. de Feraudy Y, et al. *Ann Neurol.* 2021;89(2):280–92; 5. Ohlendieck K, et al. *Neurology.* 1993;43(4):795–800;
6. Bladen CL, et al. *Hum Mutat.* 2015;36(4):395–402; 7. Niks EH, Aartsma-Rus A. *Expert Opin Biol Ther.* 2017;17(2):225–36; 8. Nakamura A. et al. *J Hum Genet.* 2017;62(10):871–76.

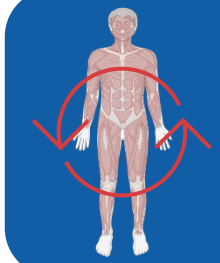
Improving clinical outcomes in DMD requires therapeutic approaches that improve the quantity, quality, and distribution of dystrophin



Increased dystrophin production



Production of high-quality dystrophin



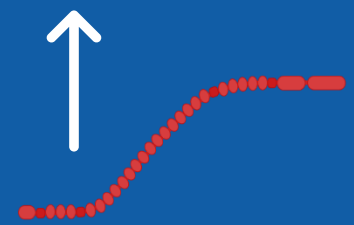
Broad and effective distribution of dystrophin restorative treatments to key muscles (skeletal, smooth, and cardiac) and the CNS

Mean % normal dystrophin level of 0.3%

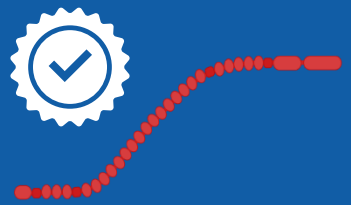
with currently approved[a] exon 51 skip therapy after 24 weeks[1]

a. Eteplirsen is not approved in most countries, including all EU countries.
CNS, central nervous system; DMD, Duchenne muscular dystrophy.
1. McDonald CM, et al. *J Neuromuscul Dis.* 2021;8(6):989–1001.

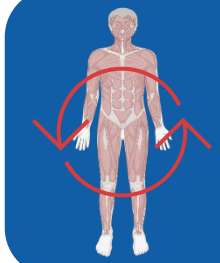
Improving clinical outcomes in DMD requires therapeutic approaches that improve the quantity, quality, and distribution of dystrophin



Increased dystrophin production



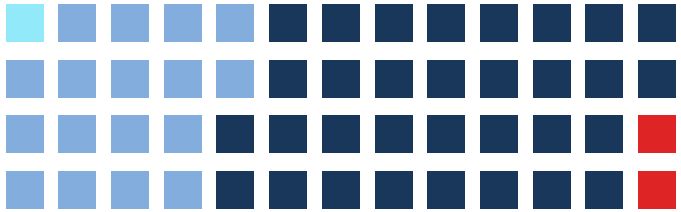
Production of high-quality dystrophin



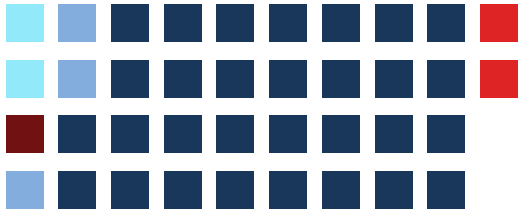
Broad and effective distribution of dystrophin restorative treatments to key muscles (skeletal, smooth, and cardiac) and the CNS

Phenotypic features of patients with exon 51 'skip-equivalent' deletions[1]

Exon 45 to 51 (n=52)



Exon 48 to 51 (n=38)



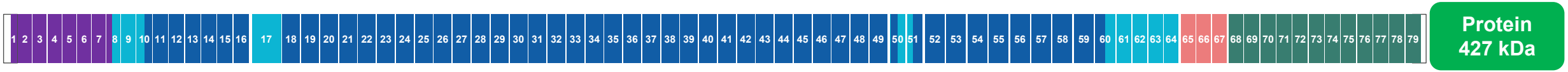
- Asymptomatic
- XLDCM
- HyperCKemia
- BMD
- DMD

BMD, Becker muscular dystrophy; CNS, central nervous system; DMD, Duchenne muscular dystrophy; XLDCM, X-linked dilated cardiomyopathy.

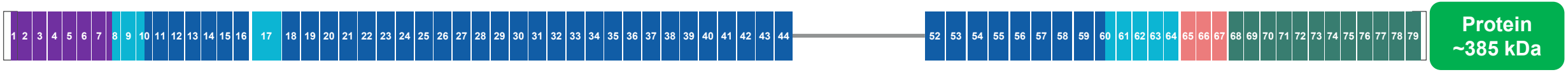
1. Waldrop MA, et al. *J Neuromuscul Dis.* 2020;7(3):217–229.

Compared with mini/microdystrophin, exon skip-produced dystrophin is closer in size to full-length dystrophin

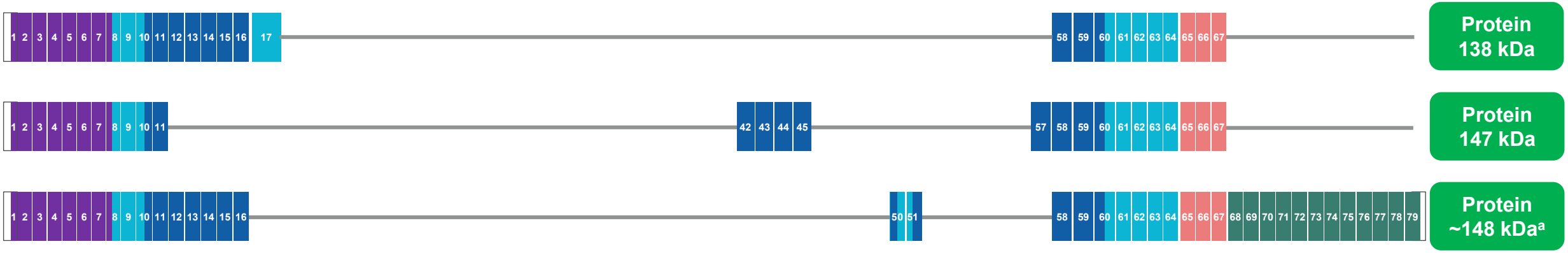
DMD transcript[1,2]



DMD transcript produced by exon 51 skipping of Δ exons 45–50[1,3,4]



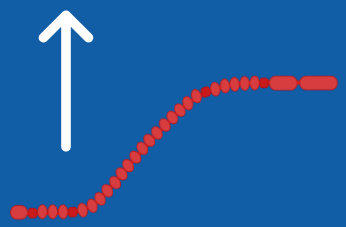
Constructs encoding gene therapy-produced microdystrophin[1,2,5–8]



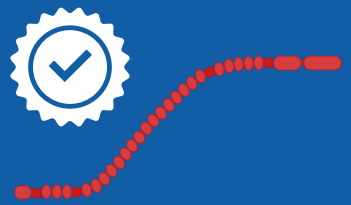
a. Approximate molecular weight based on cDNA size of 4.0 kb.[7] Calculated using the University of Pittsburgh DNA Size (kb) Protein Size (kDa) Conversion Tool.
Figures adapted from Asher DR, et al. *Expert Opin Biol Ther.* 2020;20:263–74.
DMD, Duchenne muscular dystrophy; kb, kilobase; kDa, kilodalton.

1. Roberts RG, et al. *Genomics.* 1993;16(2):536–538; 2. Elangkovan N, Dickson G. *J Neuromuscul Dis.* 2021;8(S2):S303–S316; 3. Nakamura A. et al. *J Hum Genet.* 2017;62(10):871–76;
4. Nicolas A, et al. *Hum Mol Genet.* 2015;24(5):1267–79; 5. FDA. News release. Accessed March 13, 2025. https://www.fda.gov/news-events/press-announcements/fda-expands-approval-gene-therapy-patients-duchenne-muscular-dystrophy;
6. Chamberlain JS, et al. *Hum Gene Ther* 2023;34(9–10):404–15; 7. Dastgir J, et al. Oral presentation at the American Society of Gene & Cell Therapy 27th annual meeting, May 7–11, 2024, Baltimore, USA. Oral 407;
8. Gonzalez P, et al. Oral presentation at the American Society of Gene & Cell Therapy 23rd Annual Meeting, Boston, MA, USA, May 12–15, 2020. Oral 500.

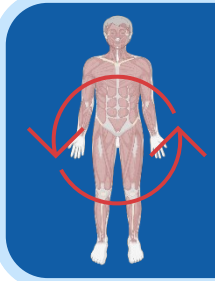
Improving clinical outcomes in DMD requires therapeutic approaches that improve the quantity, quality, and distribution of dystrophin



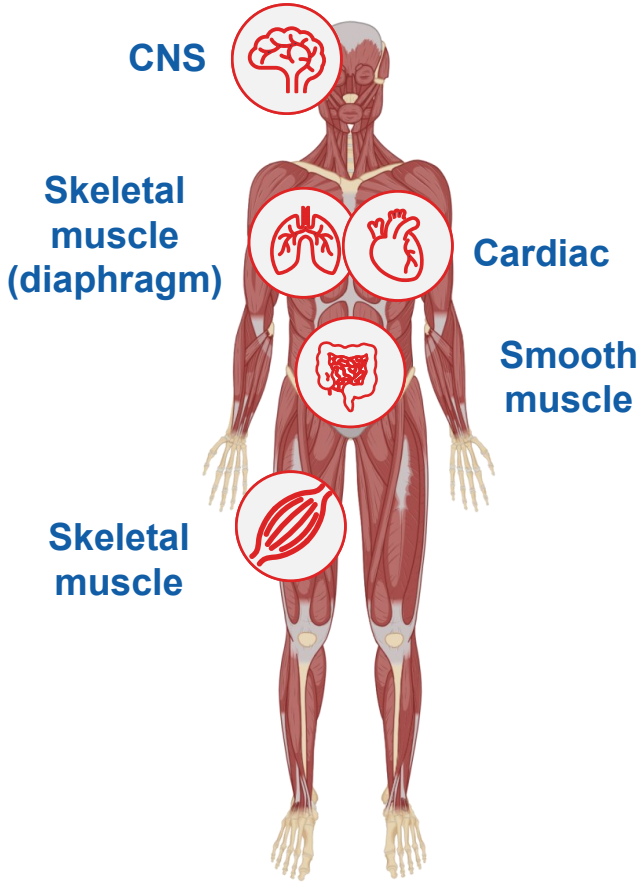
Increased dystrophin production



Production of high-quality dystrophin



Broad and effective distribution of dystrophin restorative treatments to key muscles (skeletal, smooth, and cardiac) and the CNS



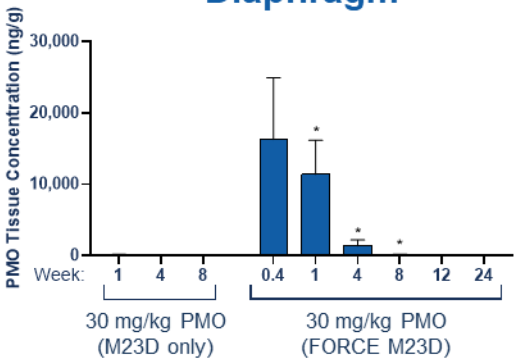
CNS, central nervous system; DMD, Duchenne muscular dystrophy.

Elangkovan N, Dickson G. *J Neuromuscul Dis.* 2021;8(s2):S303–S316; Ohlendieck K, Swandulla D. *Pflügers Arch.* 2021;473(12):1813–39.

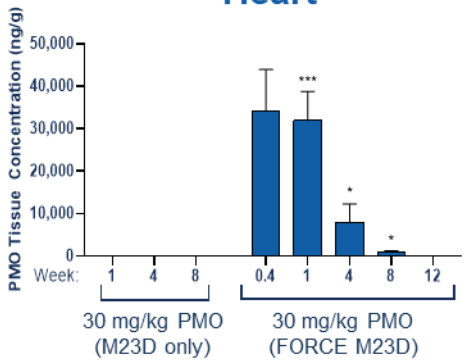
The FORCE platform drives broad PMO delivery and distribution in a *mdx* mouse model

PMO tissue concentration

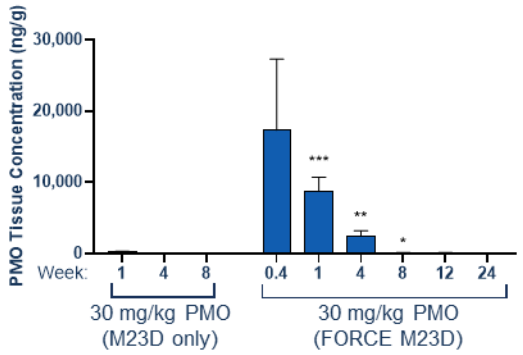
Diaphragm[1]



Heart[1]

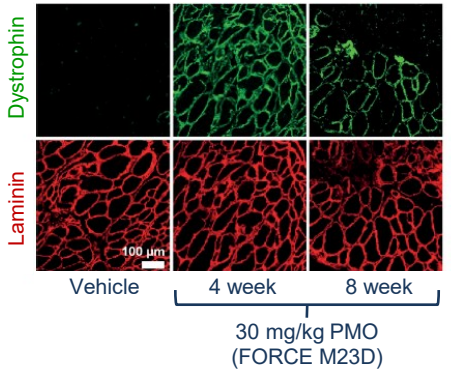


Quadriceps[1]

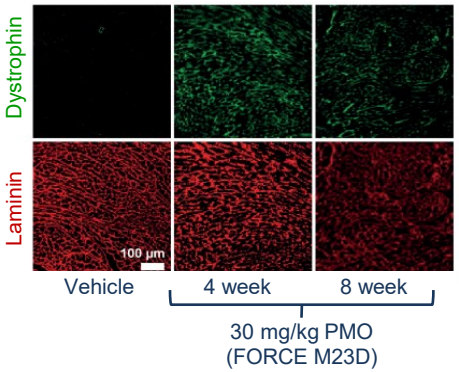


Dystrophin-positive myofibers

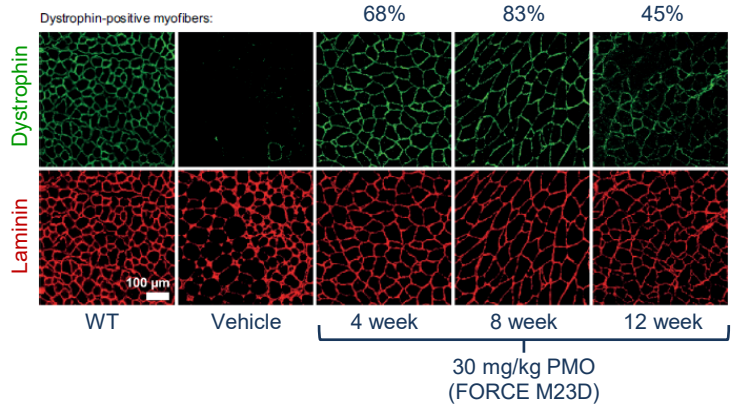
Diaphragm[1]



Heart[1]



Quadriceps[1]



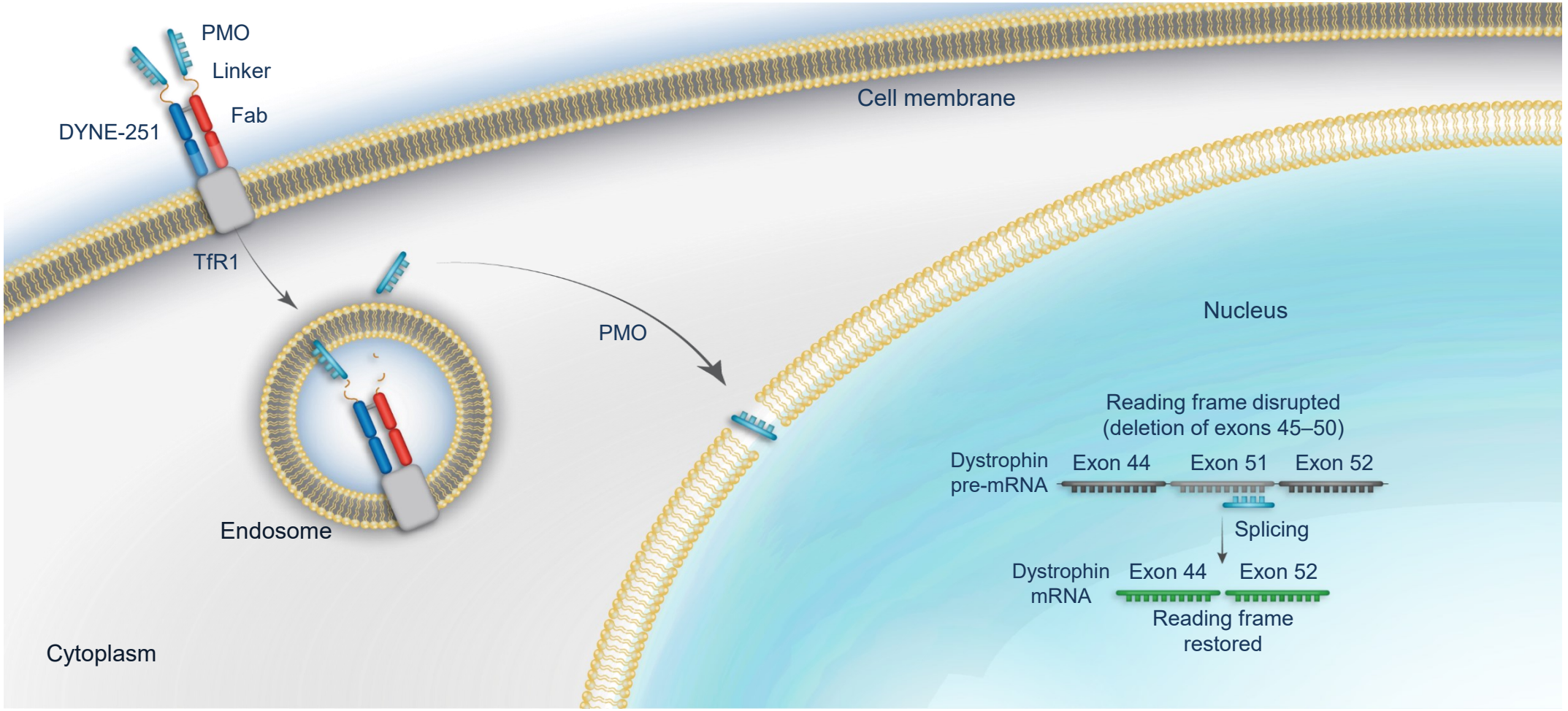
The FORCE platform is investigational or otherwise in development and has not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.

Note for the PMO data: 5-week-old *mdx* mice injected via tail vein. PMO exposure determined by hELISA. Data represent mean ± SD. *p<0.05, **p<0.01, ***p<0.0001.

hELISA, hybridization enzyme-linked immunosorbent assay; PMO, phosphorodiamidate morpholino oligomer; WT, wild type.

1. Desjardins CA, et al. *Nucleic Acids Res.* 2022;50(20):11401–11414.

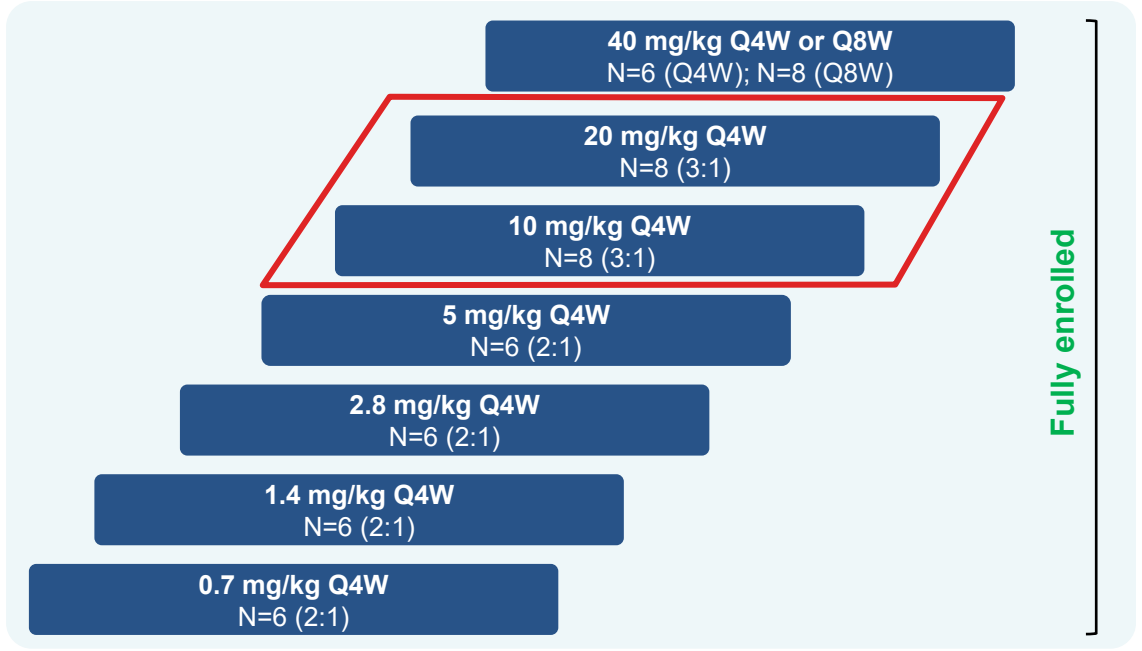
DYNE-251 is designed to leverage TfR1 to deliver exon 51-skipping PMO to affected muscle in DMD



DYNE-251 is investigational or otherwise in development and has not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.
Image depicts intended mechanism of action of DYNE-251. Applicable to all DMD mutations amenable to skipping of exon 51.
DMD, Duchenne muscular dystrophy; Fab, antigen-binding fragment; PMO, phosphorodiamidate morpholino oligomer; TfR1, transferrin receptor 1.
Adapted from Desjardins CA, et al. *Nucleic Acids Res.* 2022;50(20):11401–11414.

DELIVER trial of DYNE-251 in males with *DMD* mutations amenable to exon 51 skipping

Placebo-controlled period (MAD cohorts)



Muscle biopsies at baseline and 24 weeks (except for 0.7 mg/kg and 1.4 mg/kg cohorts)

Transition to 20 mg/kg[a,b]

Open-label extension (OLE)

Long-term extension (LTE)

Population

- Ages 4–16 years
- Ambulant and non-ambulant

Primary endpoints

- Safety and tolerability
- Change from baseline in dystrophin levels by western blot

Select additional endpoints

- Pharmacokinetics
- Change from baseline of:
  - Exon 51 skipping levels
  - Muscle tissue PDPF
  - Multiple assessments of muscle function, including NSAA score, SV95C, and certain timed functional tests

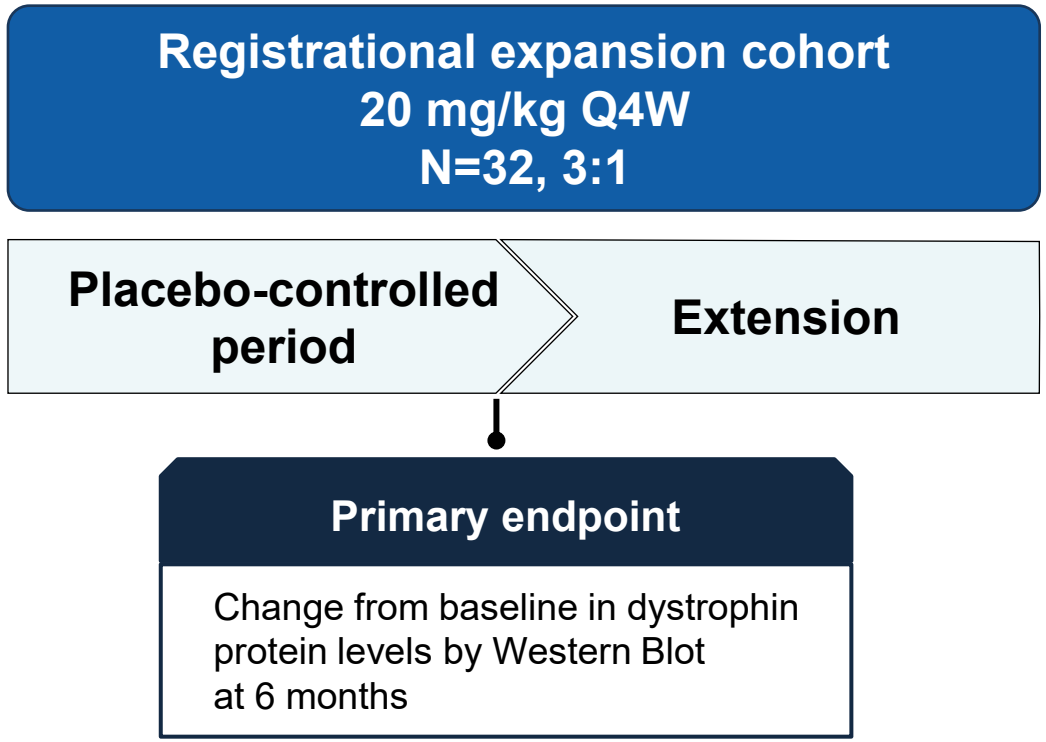
Registrational dose and dose regimen selected at 20 mg/kg Q4W; registrational expansion cohort fully enrolled (N=32, 3:1 randomization)

DYNE-251 is investigational or otherwise in development and has not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.

Doses provided refer to PMO component of DYNE-251. Cohorts randomized to active arm or placebo. a. Transition to 20 mg/kg dose started either in the placebo-controlled period or OLE for participants initiated at 40 mg/kg; b. Transition to 20 mg/kg dose occurred at non-uniform times during OLE or LTE. DMD, Duchenne muscular dystrophy; MAD, multiple ascending dose; NSAA, North Star Ambulatory Assessment; PDPF, percent dystrophin-positive fibers; PMO, phosphorodiamidate morpholino oligomer; Q4W, every 4 weeks; Q8W, every 8 weeks; SV95C, stride velocity 95th centile.

De Waele L, et al. Poster presentation at the World Muscle Society Annual Congress, Prague, Czechia, October 8–12, 2024. Poster 225P;
Phan H, et al. Oral presentation at the MDA Clinical and Scientific Conference, Dallas, TX, USA, March 16–19, 2025. Oral O83.

DELIVER trial: Registrational expansion cohort



Additional endpoints

- Change from baseline of:
  - Exon 51 skipping levels
  - Muscle tissue PDPF
- NSAA
- SV95C
- Time to rise

Registrational expansion cohort fully enrolled; data expected in late 2025

DYNE-251 is investigational or otherwise in development and has not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.
Dose provided refers to PMO component of DYNE-251. Cohort randomized to active arm or placebo.
NSAA, North Star Ambulatory Assessment; PDPF, percent dystrophin-positive fibers; Q4W, every 4 weeks; SV95C, stride velocity 95th centile.
Phan H, et al. Oral presentation at the MDA Clinical and Scientific Conference, Dallas, TX, USA, March 16–19, 2025. Oral O83.

DELIVER baseline participant characteristics: 10 mg/kg and 20 mg/kg cohorts

Mean (SD) or n (%)	10 mg/kg (N=8)	20 mg/kg (N=8)
Age (years)	6.6 (2.2)	8.1 (2.4)
BMI (kg/m^2)	18.3 (3.2)	18.6 (5.1)
Age of symptom onset (years)	2.8 (1.6)	2.9 (2.0)
Most recent corticosteroid dosing regimen, n (%)[a] Daily Other	 8 (100) 0 (0.0)	 8 (100) 0 (0.0)
Duration of corticosteroid treatment (years)[b]	1.6 (1.8)	2.0 (2.1)
Prior DMD therapy Eteplirsen Other	 1 (12.5) 1 (12.5)	 0 (0.0) 2 (25.0)
NSAA total score[c]	25.3 (6.40)	15.6 (5.09)
Time to rise from floor (sec)[c]	6.3 (5.60)	5.1 (2.28)
Timed 10-meter walk/run (sec)[c]	4.6 (1.86)	7.7 (3.84)
SV95C (m/sec)[c]	1.9 (0.45)	1.4 (0.47)

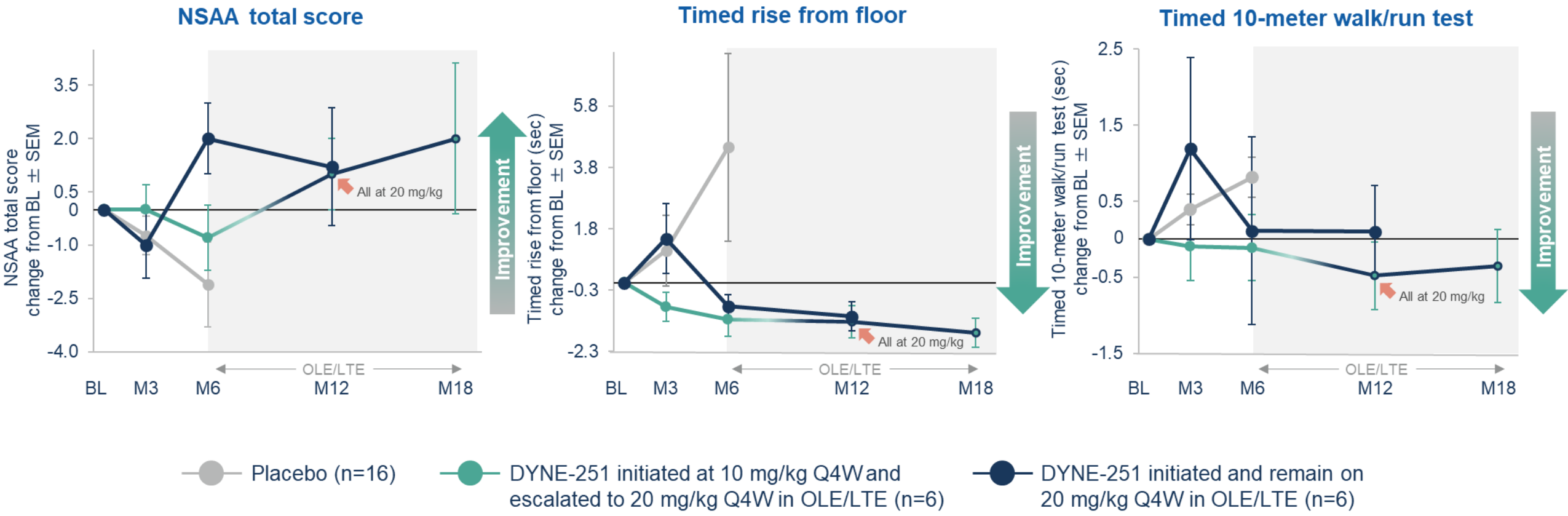
DYNE-251 is an investigational medicine being evaluated in the ongoing DELIVER trial and has not received approval by FDA, EMA, or any other regulatory authorities.

Note: DYNE-251 and placebo participants are reported together for baseline characteristics; a. Most recent corticosteroid regimen refers to corticosteroid at baseline at time of randomization; b. Cumulative duration of previous and most recent corticosteroid treatment at the time of randomization; c. Ambulatory participants only.

BMI, body mass index; DMD, Duchenne muscular dystrophy; m, meter; NSAA, North Star Ambulatory Assessment; SD, standard deviation; SV95C, stride velocity 95th centile.

Phan H, et al. Oral presentation at the MDA Clinical and Scientific Conference, Dallas, TX, USA, March 16–19, 2025. Oral O83.

Long-term improvements observed versus baseline across multiple functional endpoints through 18 months



DYNE-251 is an investigational medicine being evaluated in the ongoing DELIVER trial and has not received approval by FDA, EMA, or any other regulatory authorities.

3 months = 85 days; 6 months = 169 days; 12 months = 337 days; 18 months = 505 days.

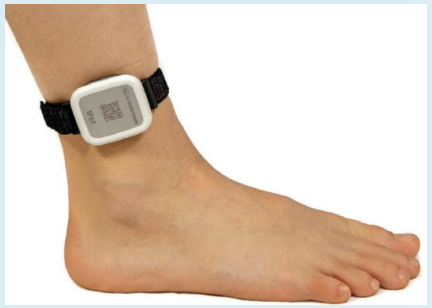
BL, baseline; LTE, long-term extension; m, meter; M, month; NSAA, North Star Ambulatory Assessment; OLE, open-label extension; Q4W, every 4 weeks; sec, seconds; SEM, standard error of mean.

Phan H, et al. Oral presentation at the MDA Clinical and Scientific Conference, Dallas, TX, USA, March 16–19, 2025. Oral O83.

Stride velocity 95th centile (SV95C) is qualified as a digital primary endpoint by EMA in studies in boys with DMD ≥4 years old[1]

SV95C | A digital objective endpoint of ambulatory performance in patients' normal daily environment[1,2]

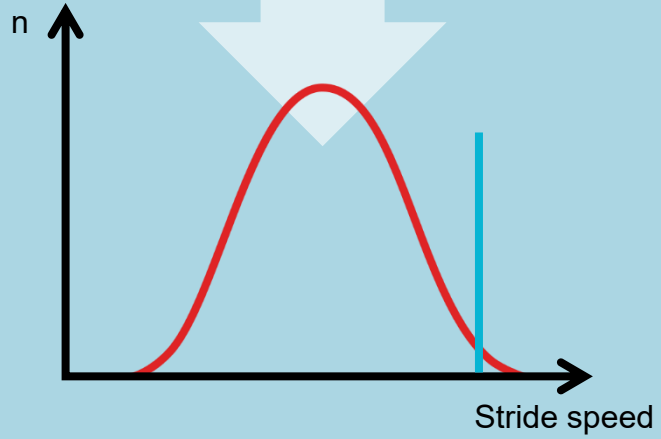
- Correlated with traditional hospital-based clinical outcomes (6MWT, NSAA, 4SC)[1,2]
- Demonstrated sensitivity to detect change over time in natural history, steroid-treated patients, and in clinical trials[1]
  - SV95C has greater sensitivity vs other function tests, i.e. can detect change earlier[1,3]
- Proposed SV95C MCID = 0.1 m/s (36 m in 6 min) corresponds to 6MWT MCID = 30 m[1,4,5]
- Continuously collects data over a period of time; minimally impacted by social, familial, or environmental factors[1,5]



Each stride identified[1]

Each stride quantified:
Stride speed, stride length[1]

Distribution of stride speed computed[1]

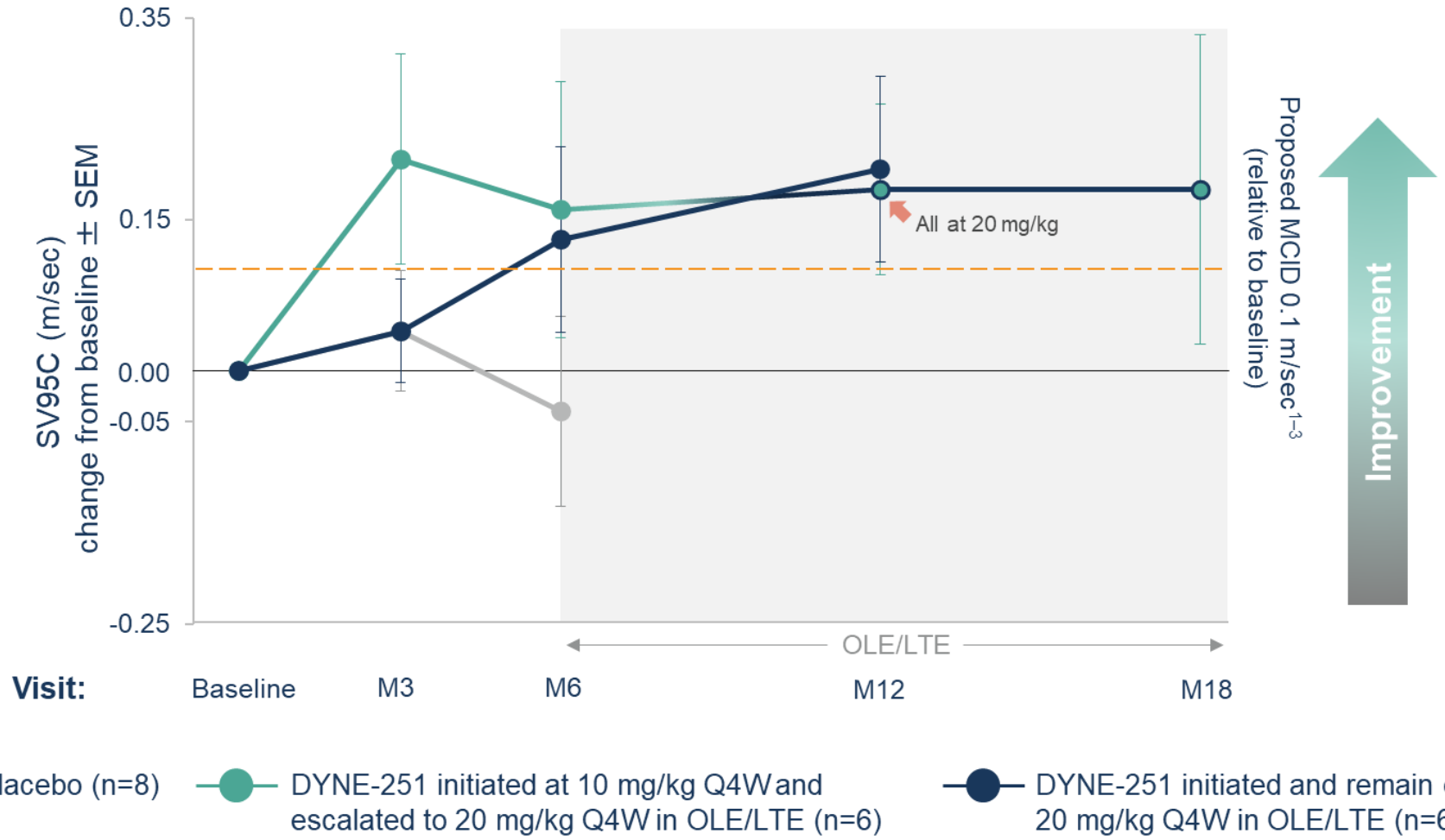


EMA, European Medicines Agency; DMD, Duchenne muscular dystrophy; MCID, minimal clinically important difference; 6MWT, 6-minute walk test; NSAA, North Star Ambulatory Assessment; 4SC, 4-stair climb.

1. EMA. Opinion on SV95C. July 2023. Accessed February 11, 2025. https://www.ema.europa.eu/en/documents/scientific-guideline/qualification-opinion-stride-velocity-95th-centile-primary-endpoint-studies-ambulatory-duchenne-muscular-dystrophy-studies_en.pdf; 2. Servais L, et al. *Nat Med*. 2023;29(10):2391–2; 3. Servais L, et al. *Sci Rep*. 2024;14(1):29681; 4. McDonald CM, et al. *Muscle Nerve*. 2013;48(3):357–68; 5. EMA. Opinion on SV95C. April 2019. Accessed February 11, 2025. https://www.ema.europa.eu/en/documents/scientific-guideline/qualification-opinion-stride-velocity-95th-centile-secondary-endpoint-duchenne-muscular-dystrophy-measured-valid-and-suitable-wearable-device_en.pdf.

Early and sustained improvements in SV95C at 20 mg/kg DYNE-251

Robust improvement observed versus baseline through 18 months; Proposed MCID achieved by 6 months



DYNE-251 is an investigational medicine being evaluated in the ongoing DELIVER trial and has not received approval by FDA, EMA, or any other regulatory authorities.

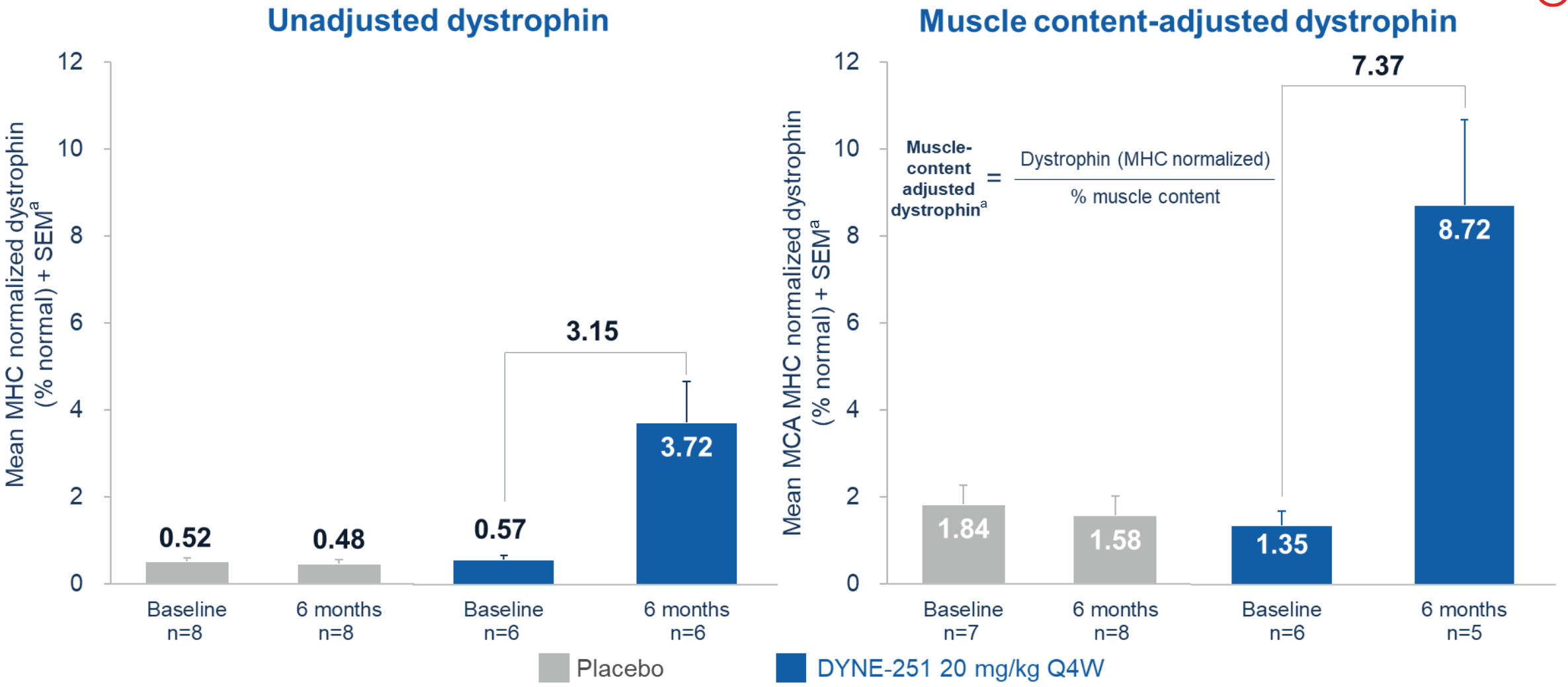
3 months = 85 days; 6 months = 169 days; 12 months = 337 days; 18 months = 505 days.

LTE, long-term extension; m, meter; M, month; MCID, minimal clinically important difference; OLE, open-label extension; Q4W, every 4 weeks; sec, seconds; SEM, standard error of mean; SV95C, stride velocity 95th centile.

1. EMA. Opinion on SV95C. July 2023. Accessed February 11, 2025. https://www.ema.europa.eu/en/documents/scientific-guideline/qualification-opinion-stride-velocity-95th-centile-primary-endpoint-studies-ambulatory-duchenne-muscular-dystrophy-studies_en.pdf; 2. Servais L, et al. *Sci Rep.* 2024;14(1):29681; 3. EMA. Opinion on SV95C. April 2019. Accessed February 11, 2025. https://www.ema.europa.eu/en/documents/scientific-guideline/qualification-opinion-stride-velocity-95th-centile-secondary-endpoint-duchenne-muscular-dystrophy-measured-valid-and-suitable-wearable-device_en.pdf.

Phan H, et al. Oral presentation at the MDA Clinical and Scientific Conference, Dallas, TX, USA, March 16–19, 2025. Oral O83.

DYNE-251 achieved robust dystrophin expression at 6 months



DYNE-251 is an investigational medicine being evaluated in the ongoing DELIVER trial and has not received approval by FDA, EMA, or any other regulatory authorities.

a. DELIVER biopsy taken approximately 28 days after most recent dose; 6 months = Week 25 for DELIVER.

MCA, muscle content-adjusted; MHC, myosin heavy chain; Q4W, every 4 weeks; SEM, standard error of the mean.

Phan H, et al. Oral presentation at the MDA Clinical and Scientific Conference, Dallas, TX, USA, March 16–19, 2025. Oral O83.

DYNE-251 safety profile is consistent with expectations for the DMD population

Summary of treatment-emergent adverse events (TEAEs)[a]

TEAE category	Participants with ≥1 TEAE – n (%)								
	0.7 mg/kg Q4W N=6	1.4 mg/kg Q4W N=6	2.8 mg/kg Q4W N=6	5 mg/kg Q4W N=6	10 mg/kg Q4W N=8	20 mg/kg Q4W N=8	40 mg/kg Q8W N=8	40 mg/kg Q4W N=6	Overall N=54
Any TEAE	6 (100)	6 (100)	6 (100)	6 (100)	7 (87.5)	8 (100)	8 (100)	6 (100)	53 (98.1)
Any related TEAE	3 (50.0)	3 (50.0)	2 (33.3)	6 (100)	2 (25.0)	4 (50.0)	2 (25.0)	3 (50.0)	25 (46.3)
Any serious TEAE	0	0	1 (16.7)	0	0	1 (12.5)	2 (25.0)	3 (50.0)	7 (13.0)
Any serious related TEAE	0	0	0	0	0	0	0	2 (33.3)	2 (3.7)
Any TEAE leading to withdrawal from study	0	0	0	0	0	0	0	0	0
Any TEAE leading to death	0	0	0	0	0	0	0	0	0

Potentially related serious TEAEs

- Acute kidney injury; thrombocytopenia[b]
- Pancytopenia[c]

Most frequent TEAEs[d]

- Pyrexia (48%)
- Headache and vomiting (each 37%)
- Fall (35%)
- Nasopharyngitis (33%)
- Cough (26%)
- Infusion-related reaction[e] (24%)

Additional safety data

- Other than two participants with serious TEAEs in the 40 mg/kg Q4W cohort:
  - No participants have demonstrated persistent related anemia or thrombocytopenia
  - No participants have demonstrated kidney injury
- No participants have demonstrated clinically meaningful changes in electrolytes, including magnesium

970 doses of study drug administered to date over a period of 77.1 patient-years of follow-up[a]
546 doses of study drug at 20 mg/kg dose level administered to date[f]

DYNE-251 is an investigational medicine being evaluated in the ongoing DELIVER trial and has not received approval by FDA, EMA, or any other regulatory authorities.

a. Data as of February 7, 2025, all participants, placebo-controlled period, open-label period, long-term extension period; b. Events have same day of onset in a single participant with a non-serious related TEAE of anemia in the context of fever, hemolysis, diarrhea, and positive blood in stool; together these events are consistent with hemolytic uremic syndrome with a possible infectious etiology; c, Participant has a history of hemolytic anemia of unidentified etiology; presented with fever and tonsilitis; symptoms resolved without therapeutic intervention; d. All cohorts combined; preferred terms are reported; e. All infusion-related reactions have been mild or moderate in intensity; dosing has continued in all participants; f. Data as of February 21, 2025. AE, adverse event; Q4W, every 4 weeks; Q8W, every 8 weeks.

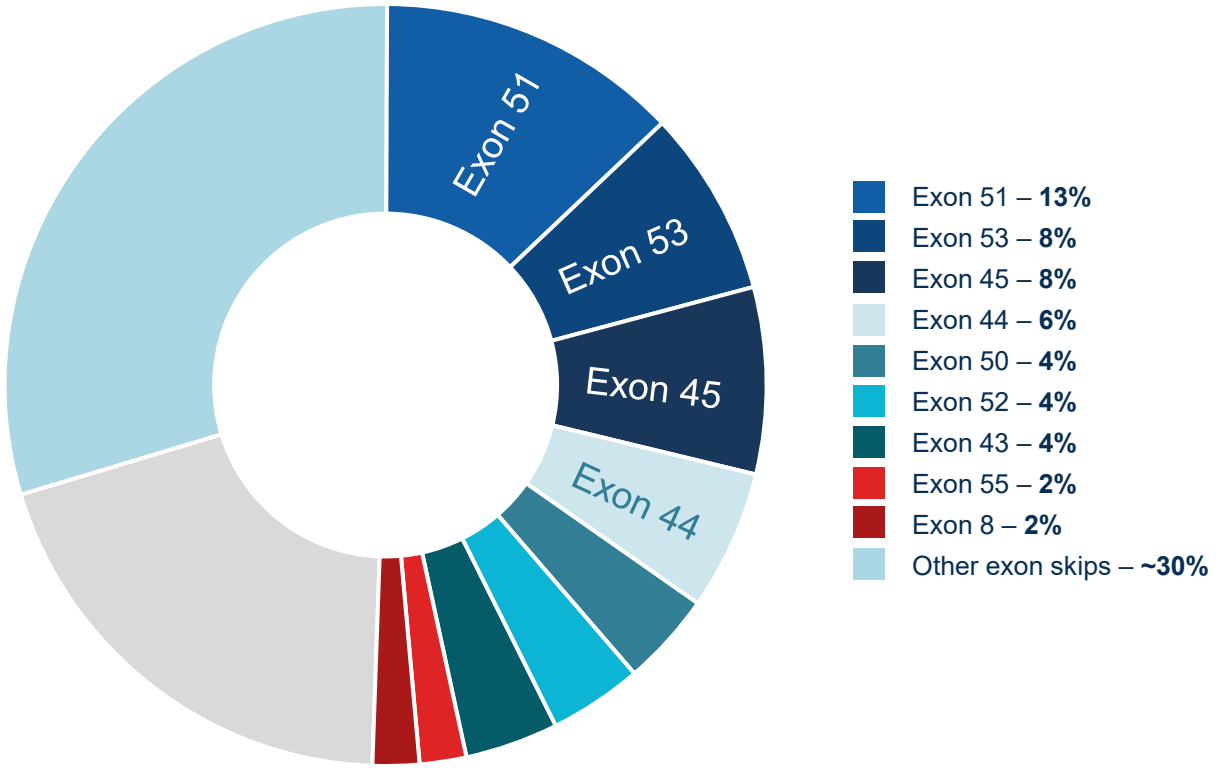
Phan H, et al. Oral presentation at the MDA Clinical and Scientific Conference, Dallas, TX, USA, March 16–19, 2025. Oral O83.

DMD pipeline expansion includes exons 53, 45, and 44

Approximately

80% of all *DMD* mutations

are amenable to exon skipping



DMD, Duchenne muscular dystrophy.

Aartsma-Rus A, et al. *Hum Mutat*. 2009;30(3):293–9.

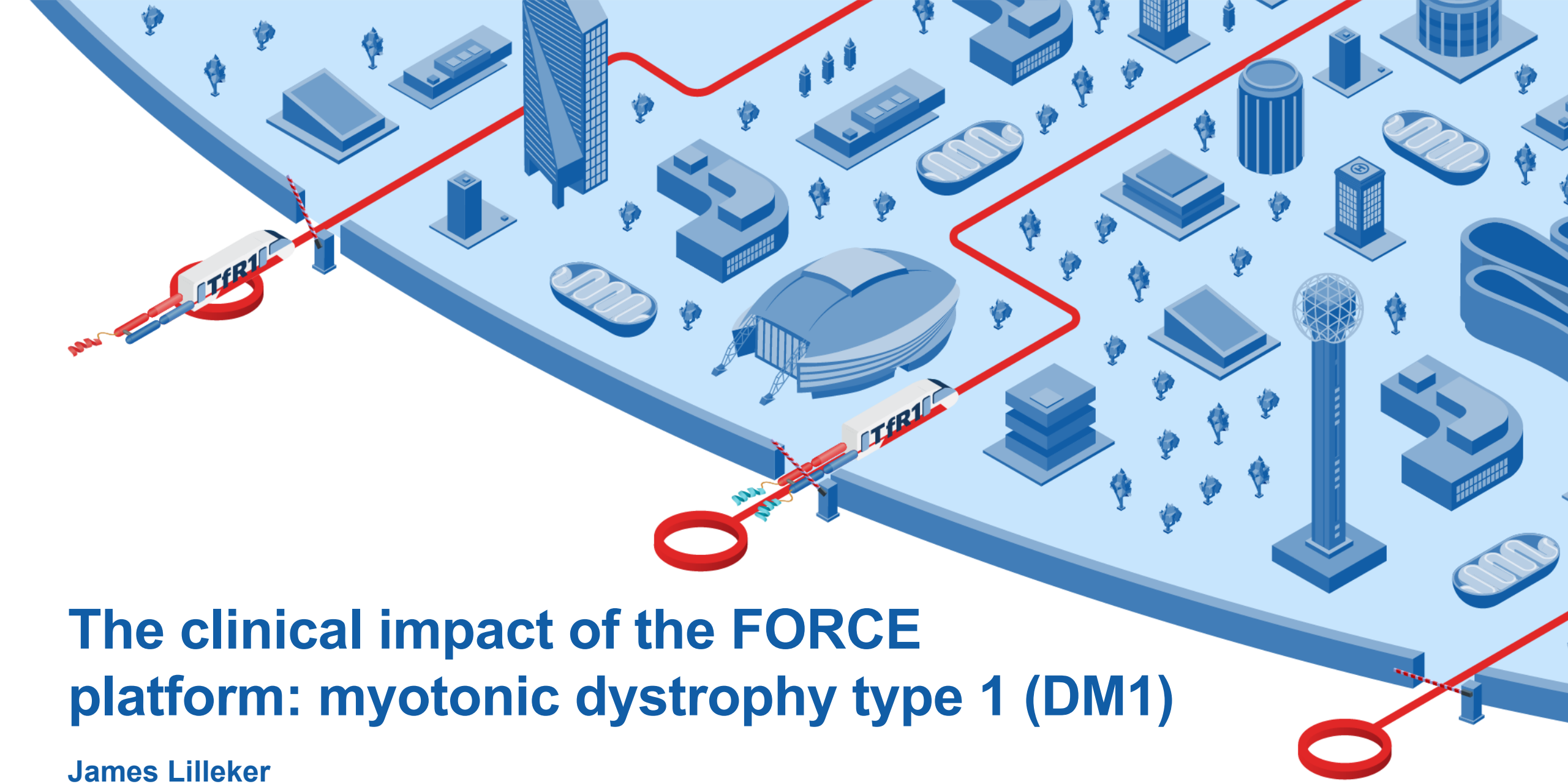
Summary

- **DYNE-251** is designed to deliver an **exon 51 skipping PMO** to muscles via TfR1[1,2]
- The FORCE platform achieved **broad distribution to key muscles such as cardiac and skeletal (including diaphragm), as well as the CNS** in preclinical models of DMD[1,3]
- The Phase 1/2 **DELIVER** trial is an ongoing, randomized, placebo-controlled global trial of DYNE-251 in ambulant and non-ambulant males with DMD with mutations amenable to exon 51 skipping therapy[2]
- **The safety profile of DYNE-251 is favorable to date**, with up to ~2.5 years of follow-up[a,4]
- **Robust expression of near full-length dystrophin** following treatment with DYNE-251[4]
- **Early and sustained benefit** of treatment with DYNE-251 consistently seen on clinical and real-world functional outcomes, including SV95C, NSAA, TTR, and 10MRW, through 18 months[4]
  - **Improvement versus baseline in SV95C**, a reliable measure of continuous real-world function, demonstrated **at the registrational dose level of 20 mg/kg**[4]
  - **Proposed MCID for SV95C achieved by 6 months**[4]
- The registrational cohort (20 mg/kg Q4W) of DELIVER (N=32) is **fully enrolled**
  - Data planned for late 2025[5]
- DELIVER data support the **DMD pipeline expansion**, including the development of therapies for patients with DMD mutations amenable to skipping of exons 53, 45, and 44[2,6]

The FORCE platform and DYNE-251 are investigational or otherwise in development and have not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.

a. Data as of February 7, 2025. 10MRW, 10-meter run/walk test; CNS, central nervous system; DMD, Duchenne muscular dystrophy; MCID, minimal clinically important difference; NSAA, North Star Ambulatory Assessment; PMO, phosphorodiamidate morpholino oligomers; Q4W, every 4 weeks; SV95C, stride velocity 95th centile; TfR1, transferrin receptor 1; TTR, time to rise.

1. Desjardins CA, et al. *Nucleic Acids Res.* 2022;50(20):11401–11414; 2. De Waele L, et al. Poster presentation at the World Muscle Society Annual Congress, Prague, Czechia, October 8–12, 2024. Poster 225; 3. Desjardins CA, et al. Poster presentation the 2025 MDA Clinical and Scientific Conference. March 16–19, 2025. Dallas, USA. Poster 004; 4. Phan H, et al. Oral presentation at the MDA Clinical and Scientific Conference, Dallas, TX, USA, March 16–19, 2025. Oral O83; 5. Dyne Therapeutics (February 27, 2025). Dyne Therapeutics Reports Fourth Quarter and Full Year 2024 Financial Results and Recent Business Highlights [Press Release]. Accessed March 13, 2025. https://investors.dyne-tx.com/news-releases/news-release-details/dyne-therapeutics-reports-fourth-quarter-and-full-year-2024; 6. Aartsma-Rus A, et al. *Hum Mutat.* 2009;30(3):293–9.



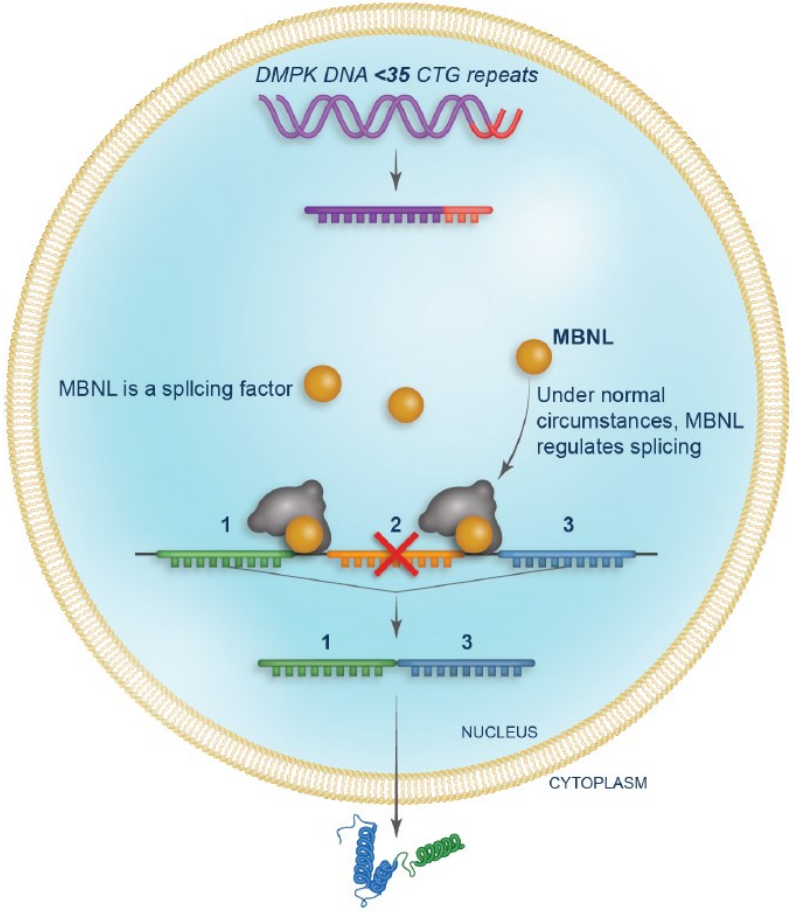
The clinical impact of the FORCE platform: myotonic dystrophy type 1 (DM1)

James Lilleker

Myotonic dystrophy type 1 (DM1) is a spliceopathy

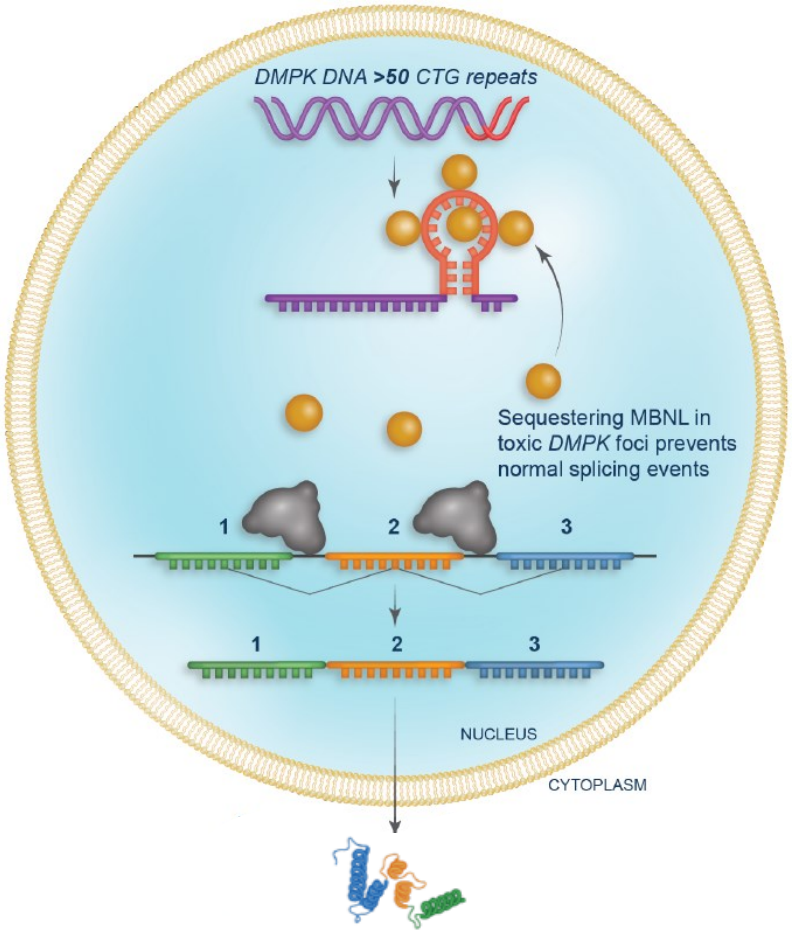
Targeting missplicing in the nucleus may improve function

Normal splicing



Normal splicing leads to **appropriate protein synthesis**

DM1 spliceopathy



Disrupted splicing **impairs** normal **protein synthesis**

CTG, cytosine, thymine, and guanine; DMPK dystrophia myotonica protein kinase; MBNL, muscleblind-like.

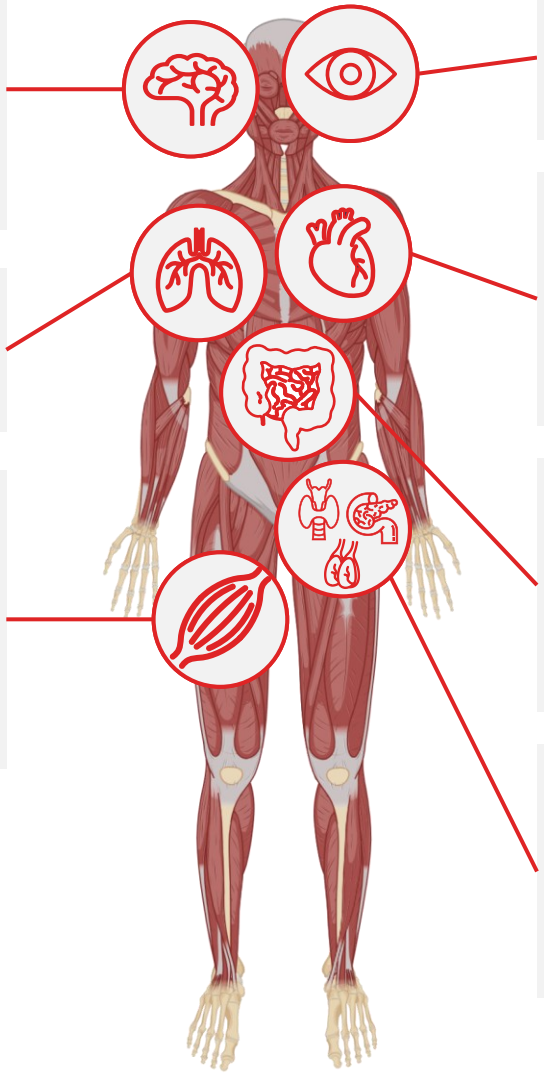
López-Martínez A, et al. *Genes (Basel)*. 2020;11(9):1109.

Abnormal splicing in multiple tissues drives multisystem disease manifestations

CNS[1–4]
- Fatigue
- Excessive daytime sleepiness
- Difficulty concentrating
- Behavioral/personality changes

Skeletal muscle (respiratory)[1–4]
- Restrictive ventilatory pattern
- Shortness of breath

Skeletal muscle[1–4]
- Muscle weakness
- Myotonia
- Balance issues
- Muscle pain
- Atrophy



Ocular[1–4]
- Cataracts
- Ptosis

Cardiac[1–4]
- Conduction disturbances
- Arrythmia
- Cardiomyopathy
- Sudden death

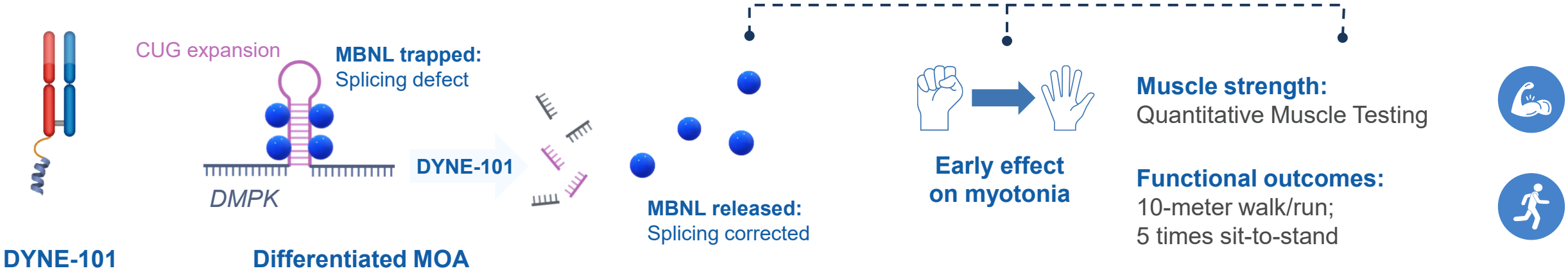
Smooth muscle[1–4]
- Dysphagia
- Constipation
- Heartburn
- Regurgitation

Endocrine[1–4]
- Thyroid disorders
- Diabetes
- Male hypogonadism
- Vitamin D deficiency

Slide does not represent an exhaustive list of symptoms.
CNS, central nervous system.
1. Thornton CA. *Neurol Clin.* 2014;32(3):705–719; 2. Ho G, et al. *World J Clin Pediatr.* 2015;4(4):66–80;
3. Hagerman KA, et al. *Muscle Nerve.* 2019;59(4):457–464; 4. Gutierrez Gutierrez G, et al. *Neurologia (Engl Ed).* 2020;35(3):185–206.

DYNE-101 addresses the central pathobiology of DM1 to enable broad functional improvement

Robust and widespread delivery → ***DMPK* degradation in the nucleus** → **MBNL release and splicing correction** → **Early clinical effect** → **Broad functional improvement**



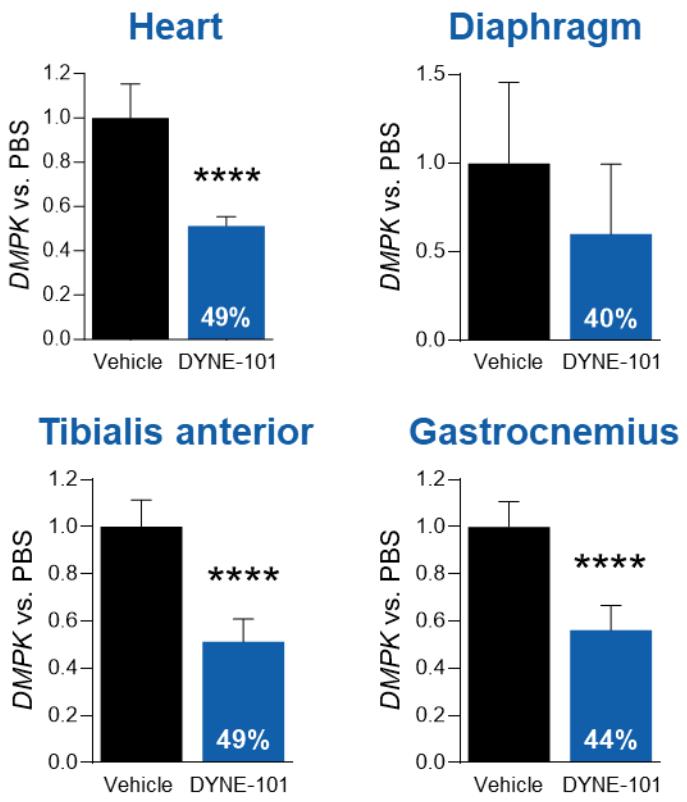
DYNE-101 **Differentiated MOA**

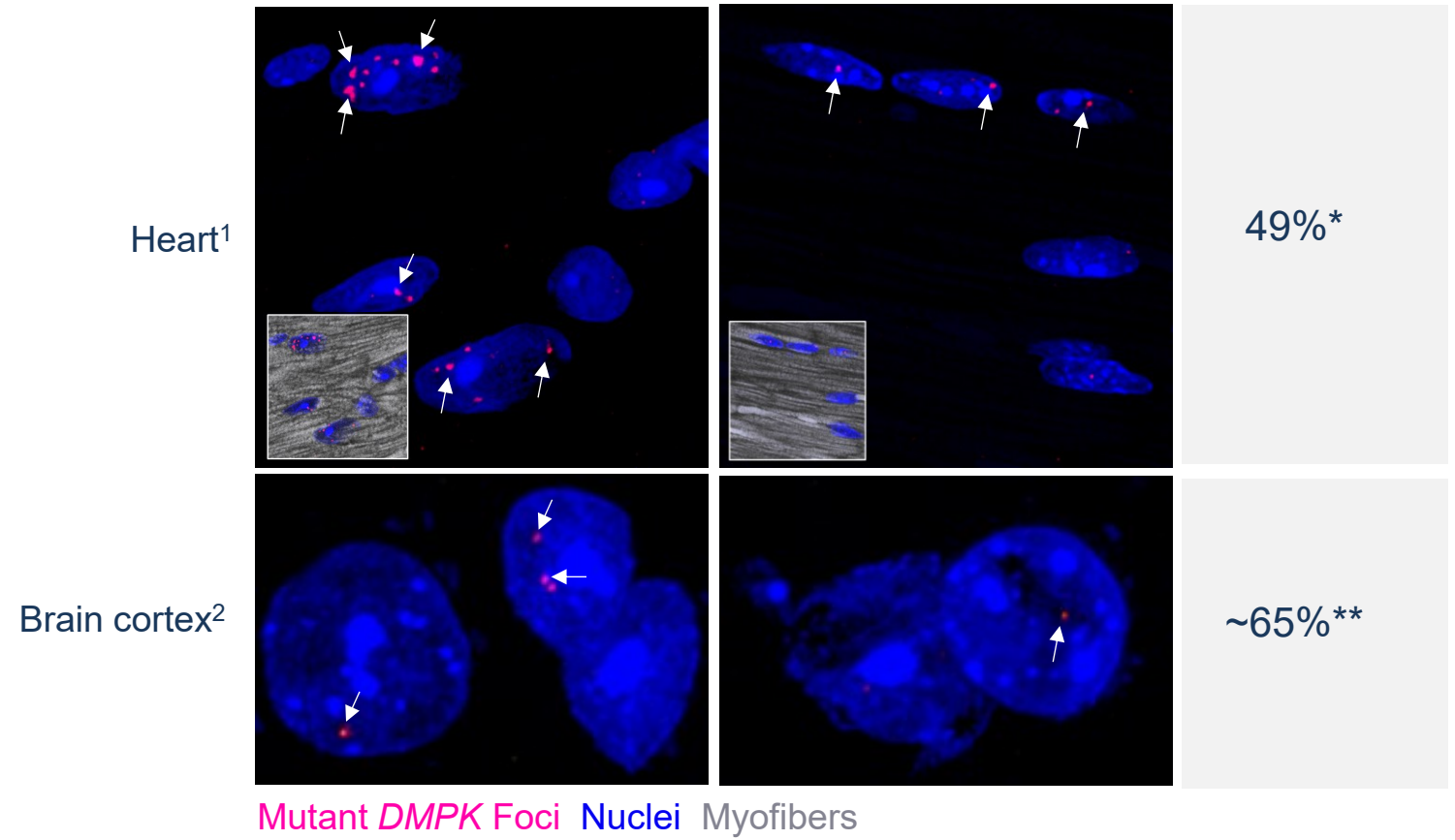
Image depicts the intended DYNE-101 mechanism of action.

DYNE-101 is investigational or otherwise in development and has not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.
Image depicts the intended DYNE-101 mechanism of action.
DM1, myotonic dystrophy type 1; DMPK, dystrophia myotonica protein kinase; MBNL, muscleblind-like; MOA, mechanism of action.
Lilleker J, et al. Oral presentation at the MDA Clinical and Scientific Conference, Dallas, TX, USA, March 16–19, 2025. Oral O44.

The FORCE platform has demonstrated broad distribution and pharmacodynamic efficacy in a preclinical model of DM1

Total *DMPK* expression (%KD)[1]





The FORCE platform and DYNE-101 are investigational or otherwise in development and have not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.

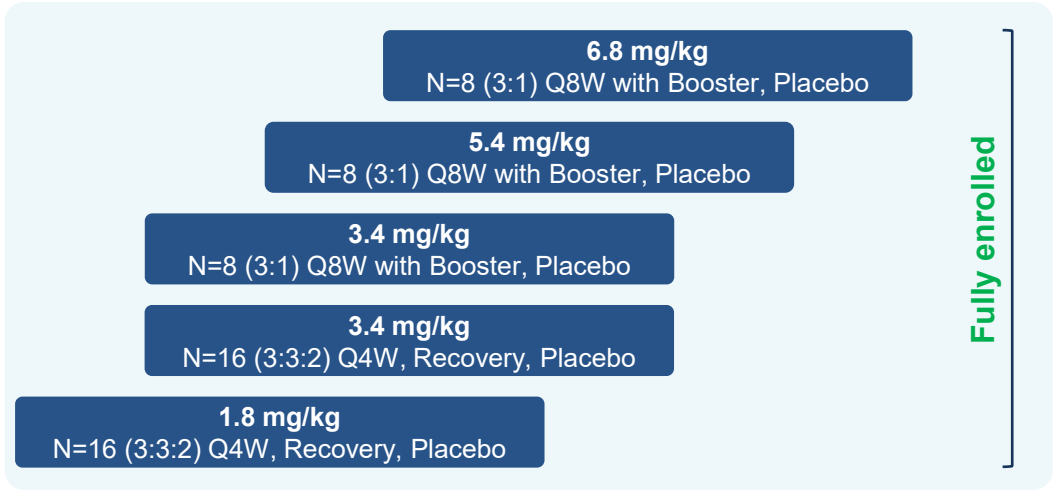
hTfR1/DMSXL homozygous mice. 10 mg/kg DYNE-101 or FORCE on d0 and d7, analyzed d28 or d35 (brain cortex only). *p<0.05, **p<0.01. ****p<0.0001 significant by t-test.

DM1, myotonic dystrophy type 1; DMPK, dystrophia myotonica protein kinase; hTfR1, humanized transferrin receptor 1; KD, knock down; PBS, phosphate buffered saline.

1. Zanotti S. Presentation at the 25th American Society of Gene & Cell Therapy Annual Meeting. May 16, 2022. Washington DC, USA. Abstract 17;
2. Zanotti S. Presentation at the 26th American Society of Gene & Cell Therapy Annual Meeting. May 17, 2023. Los Angeles, USA. Abstract 82.

ACHIEVE trial of DYNE-101 in adults with DM1

Placebo-controlled period (MAD cohorts)



Muscle biopsies at baseline, 12, and 24 weeks

Transition to 6.8 mg/kg[a]

Open-label extension (OLE)

Long-term extension (LTE)

Population

- Ages 18–49 years

Primary endpoints

- Safety and tolerability

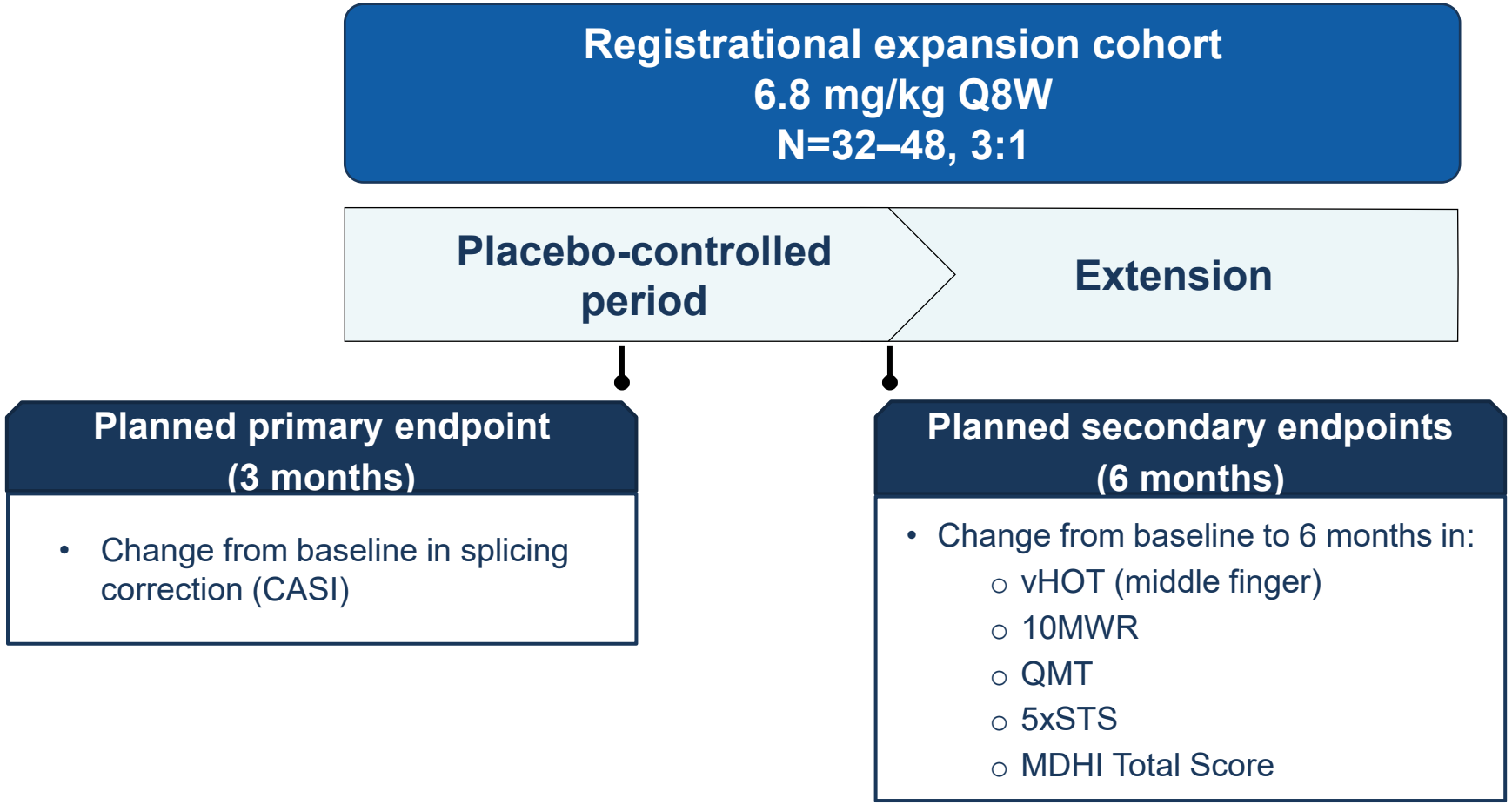
Additional endpoints

- Pharmacokinetics
- Change from baseline of:
  - Splicing
  - *DMPK* RNA expression
  - Multiple assessments of muscle strength and function
  - Patient-reported outcomes, including MDHI

Registrational dose and dose regimen selected at 6.8 mg/kg Q8W; Registrational expansion cohort planned (N=32–48, 3:1 randomization)

DYNE-101 is investigational or otherwise in development and has not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.
Doses provided refer to antisense oligonucleotide (ASO) component of DYNE-101. Recovery cohort Q4W x 2 doses then placebo for the remainder of the 24W placebo-controlled period. Q8W with booster includes Q4W x 3 doses then Q8W dosing. Additional endpoints include select secondary and exploratory endpoints. a. Transition to 6.8 mg/kg dose occurs at non-uniform times during OLE or LTE.
DM1, myotonic dystrophy type 1; DMPK, dystrophia myotonica protein kinase; MAD, multiple ascending dose; MDHI, Myotonic Dystrophy Health Index; Q4W, every 4 weeks; Q8W, every 8 weeks.
Wolf D, et al. Poster presentation at the World Muscle Society Annual Congress, Prague, Czechia, October 8–12, 2024. Poster 221P;
Lilleker J, et al. Oral presentation at the MDA Clinical and Scientific Conference, Dallas, TX, USA, March 16–19, 2025. Oral O44.

ACHIEVE trial: Planned registrational expansion cohort



Full enrollment of registrational expansion cohort planned for mid-2025

DYNE-101 is investigational or otherwise in development and has not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.
Dose provided refers to antisense oligonucleotide (ASO) component of DYNE-101. Cohort randomized to active arm or placebo.
5xSTS, 5 times sit-to-stand; 10MWR, 10-meter walk/run; MDHI, myotonic dystrophy health index; Q8W, every 8 weeks; QMT, quantitative muscle testing; vHOT, video hand opening time.
Lilleker J, et al. Oral presentation at the MDA Clinical and Scientific Conference, Dallas, TX, USA, March 16–19, 2025. Oral O44.

ACHIEVE baseline participant characteristics: 6.8 mg/kg Q8W cohort

Mean (SD) or n (%)	Placebo (N=14)	6.8 mg/kg Q8W (N=6)
Age (years)	32.6 (9.6)	37.2 (9.7)
BMI (kg/m^2)	24.4 (4.7)	23.4 (5.6)
CASI-22	0.68 (0.20)	0.74 (0.25)
CTG repeats	597 (246)	542 (191)
vHOT (middle finger) (sec)	7.5 (3.0)	7.8 (3.8)
QMT total (% predicted)	51.5 (14.3)	51.3 (10.4)
10-meter walk/run (sec)	3.34 (0.48)	3.94 (1.56)
5 times sit-to-stand (sec)	9.24 (2.03)	9.98 (3.33)
MDHI total	18.7 (13.8)	26.5 (13.7)

DYNE-101 is investigational or otherwise in development and has not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.
BMI, body mass index; CASI, composite alternative splicing index; CTG, cytosine, thymine and guanine; MDHI, Myotonic Dystrophy Health Index; Q8W, every 8 weeks; QMT, quantitative muscle testing; SD, standard deviation; sec, seconds; vHOT, video hand opening time.
Lilleker J, et al. Oral presentation at the MDA Clinical and Scientific Conference, Dallas, TX, USA, March 16–19, 2025. Oral O44.

Favorable safety profile with no serious related TEAEs

Summary of treatment-emergent adverse events (TEAEs)[a]

TEAE category	Participants with ≥1 TEAE – n (%)					
	1.8 mg/kg Q4W+Rec. N=16	3.4 mg/kg Q4W+Rec. N=16	3.4 mg/kg Q8W N=8	5.4 mg/kg Q8W N=8	6.8 mg/kg Q8W N=8	Overall (N=56)
Any TEAE	16 (100)	16 (100)	8 (100)	8 (100)	8 (100)	56 (100)
Any related TEAE	9 (56)	9 (56)	2 (25)	3 (38)	6 (75)	29 (52)
Any serious TEAE	4 (25)	0	1 (13)	0	0	5 (9)
Any serious related TEAE	0	0	0	0	0	0
Any TEAE leading to withdrawal from study	0	0	0	0	0	0
Any TEAE leading to death	0	0	0	0	0	0

Most TEAEs were mild or moderate in intensity[a]

- **6 serious TEAEs unrelated to study drug**
  - Atrioventricular block first degree[b] (1)
  - Pneumonia (2 events in same participant)
  - Pulmonary embolism[c] (1)
  - Hyponatremia (1)
  - Influenza (1)
- **Most common TEAEs (≥20% participant incidence)[d]**
  - Nasopharyngitis (38%)
  - Procedural pain (30%)
  - Influenza (27%)
  - Infusion-related reaction (25%)
  - Diarrhea; headache (each 21%)

Additional safety data

- **Liver enzyme elevations have been observed in a minority of participants**
  - No impact on liver function (bilirubin or coagulation)
  - Interpretation is complicated by underlying disease and elevated baseline values up to ~2.5x greater than the upper limit of normal
- **No participants have demonstrated persistent related anemia or thrombocytopenia**

~855 doses administered to date representing over 72 patient-years of follow-up[a]

DYNE-101 is investigational or otherwise in development and has not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.

a. Data as of December 6, 2024; b. Transient worsening of atrioventricular (AV) block in a participant with ongoing medical history of first-degree AV block;
c. Attributed to risk factors for pulmonary embolism; d. All cohorts combined; preferred terms are reported.
Q4W, every 4 weeks; Q8W, every 8 weeks; TEAE, treatment-emergent adverse event.
Lilleker J, et al. Oral presentation at the MDA Clinical and Scientific Conference, Dallas, TX, USA, March 16–19, 2025. Oral O44.

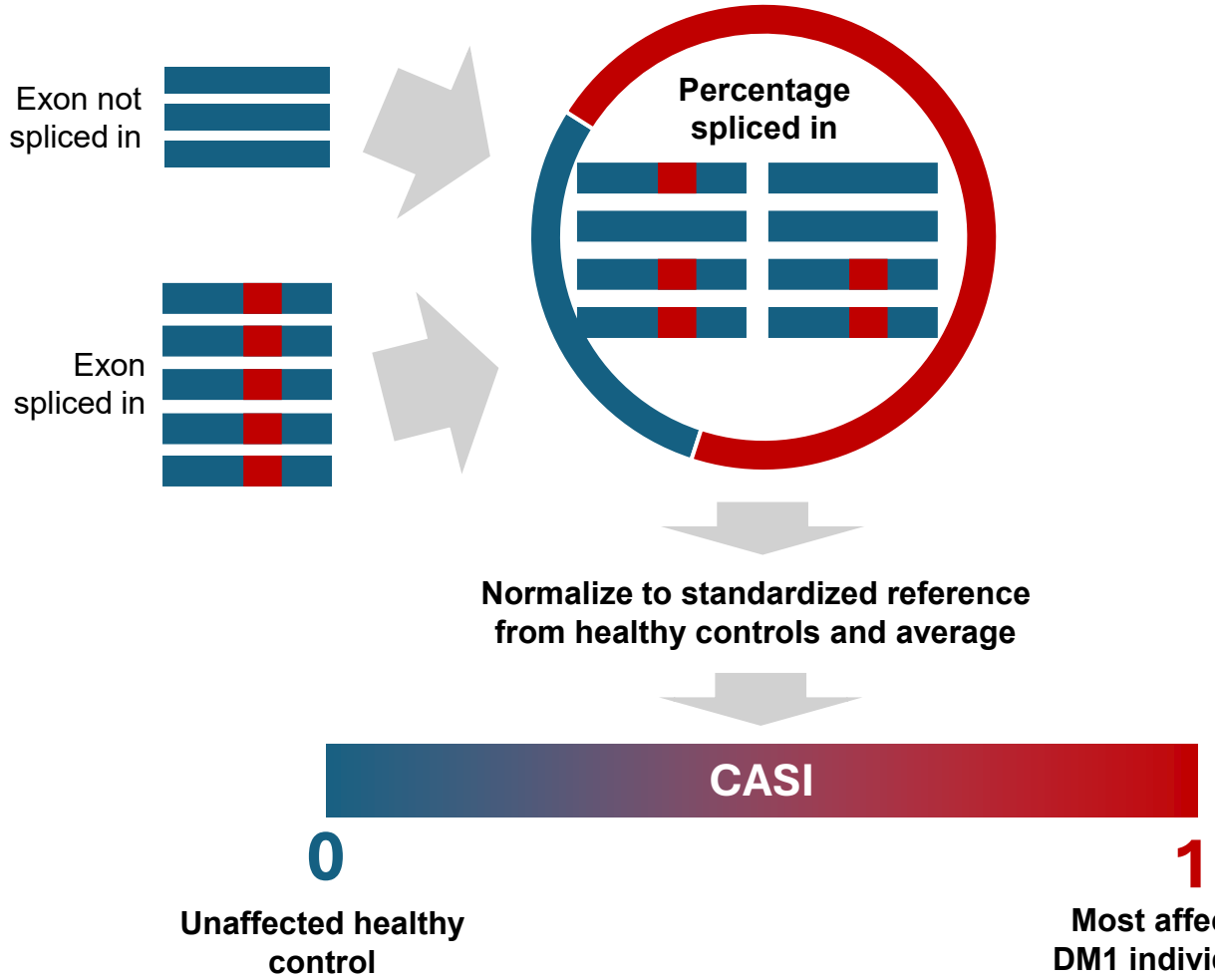
CASI measures therapeutic efficacy in DM1 by quantifying RNA splicing

Muscle weakness and/or altered contraction and relaxation[1,2]	Aberrant mRNA splicing[1,2]
RYR1 (calcium channel) *CACNA1S* (calcium channel) *ATP2A1* (calcium pump) *CLCN1* (chloride channel) *DMD* (muscle structure) *BIN1* (component of T-tubules) *SOS1* (cell cycle regulation) *OPA1* (mitochondrial dynamics)[3]	*MBNL1* (alternative splicing) *MBNL2* (alternative splicing)
	Insulin resistance[1,2]
	INSR (glucose metabolism)

Undefined, regulated by MBNL[1,3]

VPS39 (vesicle fusion)	*ANK2* (membrane targeting)
GOLGA4 (membrane trafficking)	*BEST3* (ion channel)
KIF13A (motor protein)	*CCPG1* (GTPase regulation)
CLASP1 (microtubule dynamics)	*CAPZB* (actin filament assembly)
GFPT1 (glucose metabolism)[2]	*NFIX* (extracellular matrix component)[2]
CAMK2B (calcium signalling)	

Calculating CASI[4]

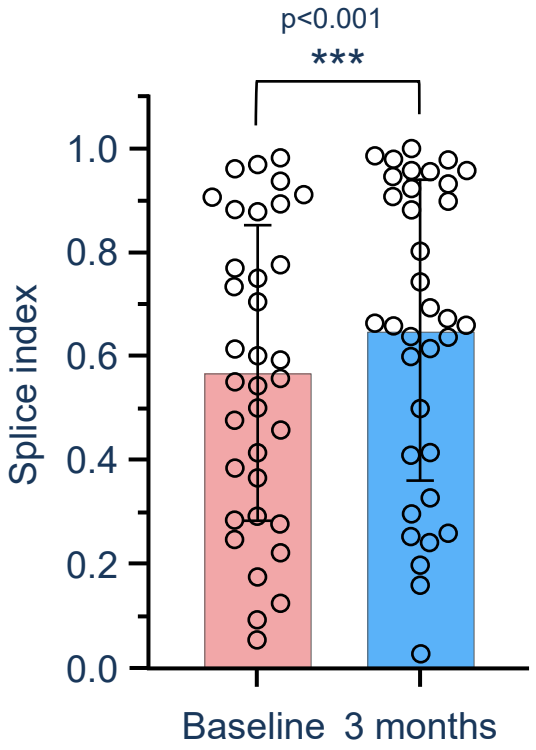


CASI, composite alternative splicing index; DM1, myotonic dystrophy type 1; MBNL, muscleblind-like; mRNA, messenger ribonucleic acid.

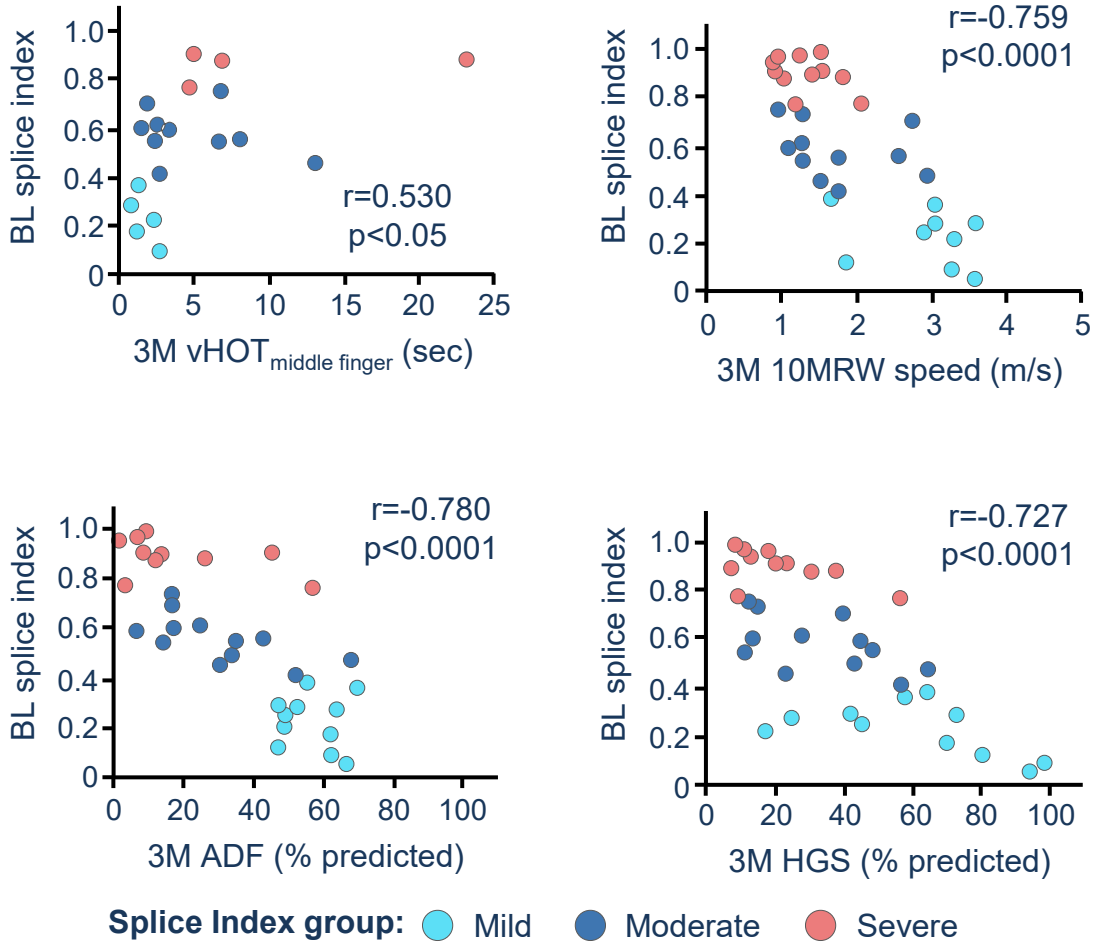
1. Wang W. 2017. University of Rochester School of Medicine and Dentistry PhD thesis. Accessed March 13, 2025. http://hdl.handle.net/1802/32572; 2. López-Martínez A, et al. *Genes (Basel).* 2020;11(9):1109;
3. Gene functions from AmiGO 2. Accessed March 13, 2025. https://amigo.geneontology.org/amigo; 4. Provenzano M, et al. *J Clin Invest.* 2025:e185426.

The Splice Index is a prognostic biomarker that predicts clinical benefit

Worsening in Splice Index is observed in as little as 3 months in the NH cohort (N=35)[a]

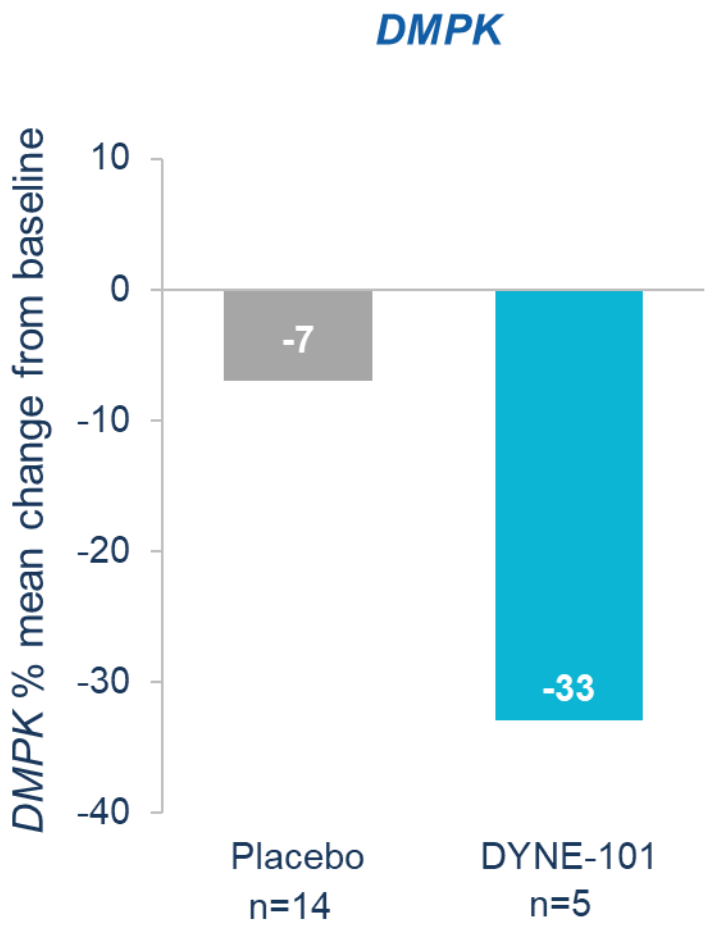


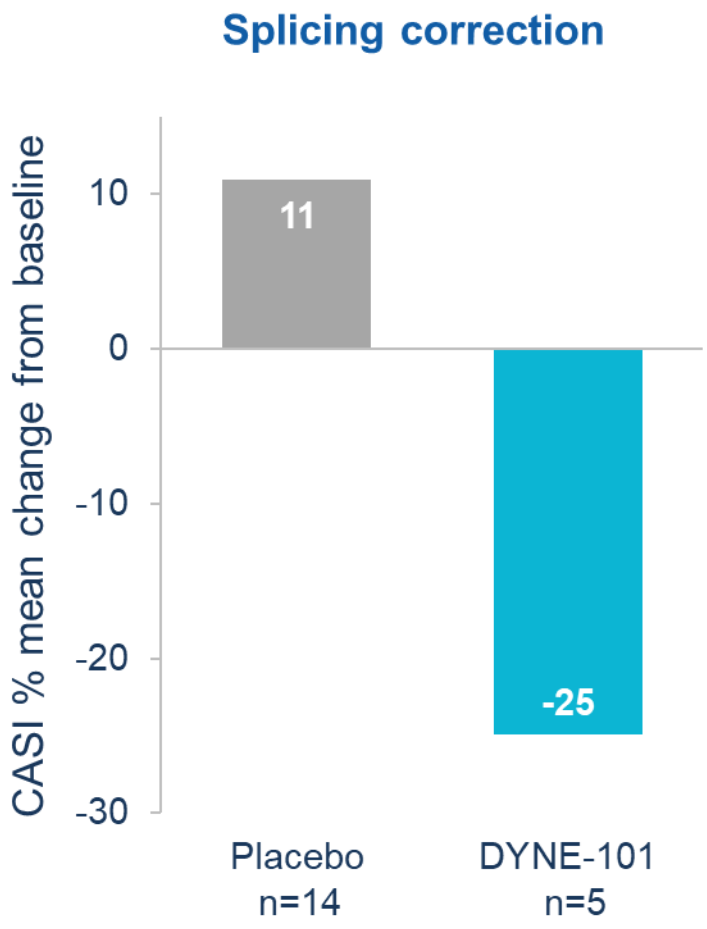
The Splice Index is predictive of function



a. Data represent mean ±standard deviation.
3M, 3 month; 10MWR, 10-meter walk/run; ADF, ankle dorsiflexion; BL, baseline; DM1, myotonic dystrophy type 1; HGS, hand grip strength; NH, natural history; vHOT, video hand opening time.
Provenzano M, et al. *J Clin Invest.* 2025:e185426.

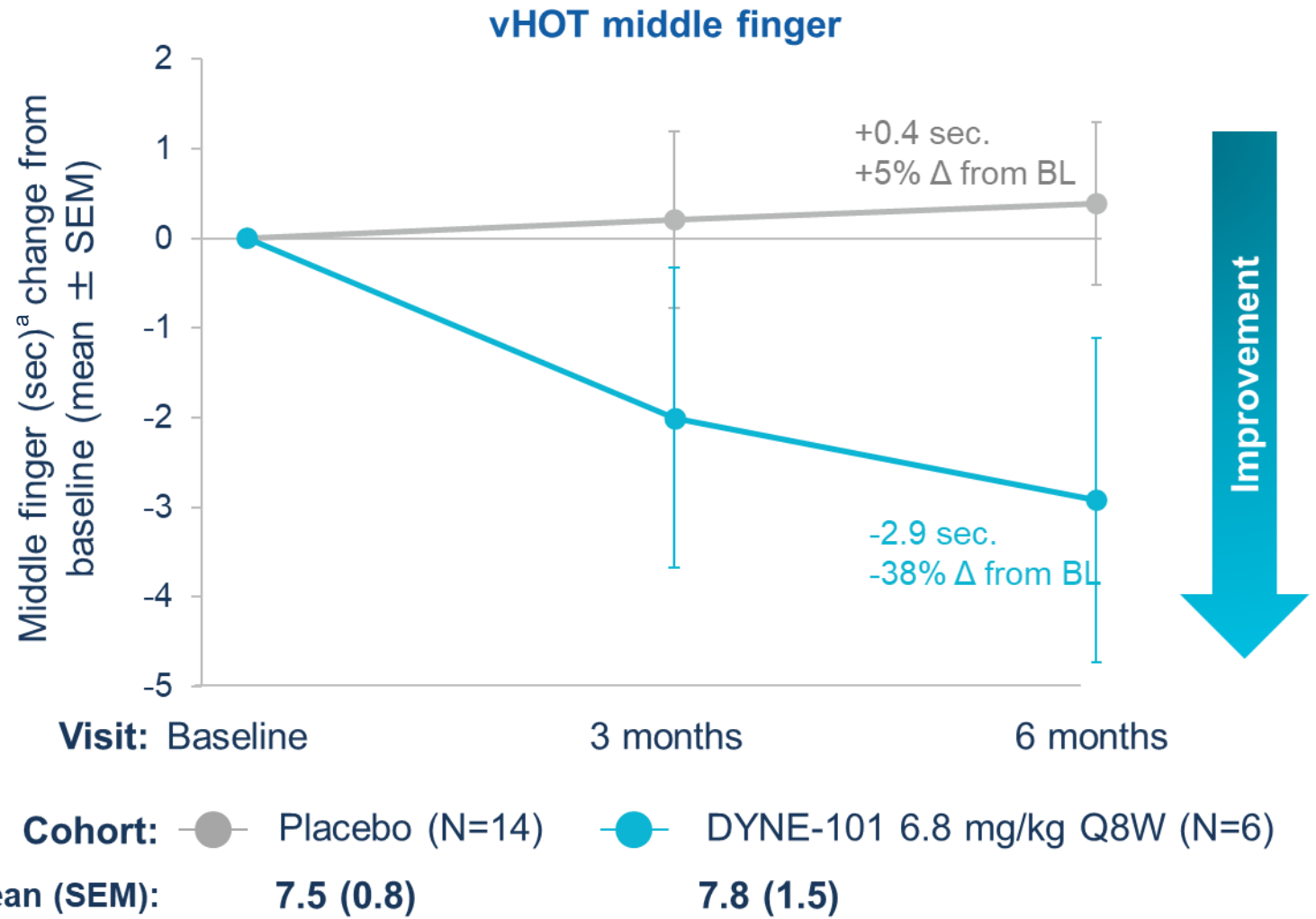
DYNE-101 at 6.8 mg/kg Q8W improved the foundational pathobiology of DM1 at 3 months





DYNE-101 is investigational or otherwise in development and has not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.
One baseline sample in 6.8 mg/kg treatment group not included as the sample did not meet quality control criteria. 3 months = 85 days.
CASI, composite alternative splicing index; DM1, myotonic dystrophy type 1; DMPK, dystrophia myotonica protein kinase; Q8W, every 8 weeks.
Lilleker J, et al. Oral presentation at the MDA Clinical and Scientific Conference, Dallas, TX, USA, March 16–19, 2025. Oral O44.

Treatment with 6.8 mg/kg Q8W DYNE-101 resulted in early and robust improvement in functional myotonia at 6 months



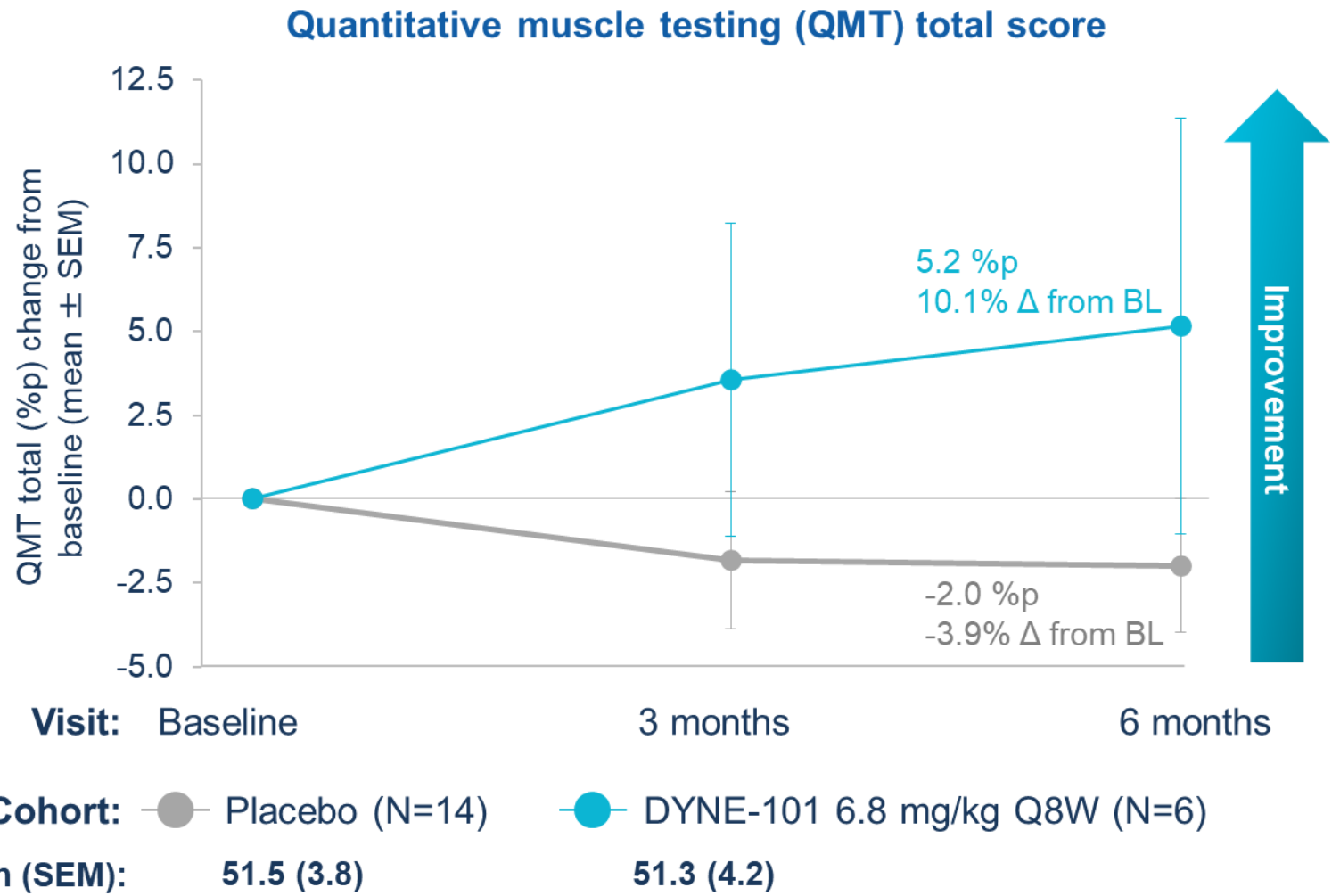
DYNE-101 is investigational or otherwise in development and has not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.

a. vHOT middle finger (sec) is the average of all myotonia trials for an individual participant in ACHIEVE. 3 months = 85 days; 6 months = 169 days.

BL, baseline; Q8W, every 8 weeks; SEM, standard error of mean; vHOT, video hand opening time.

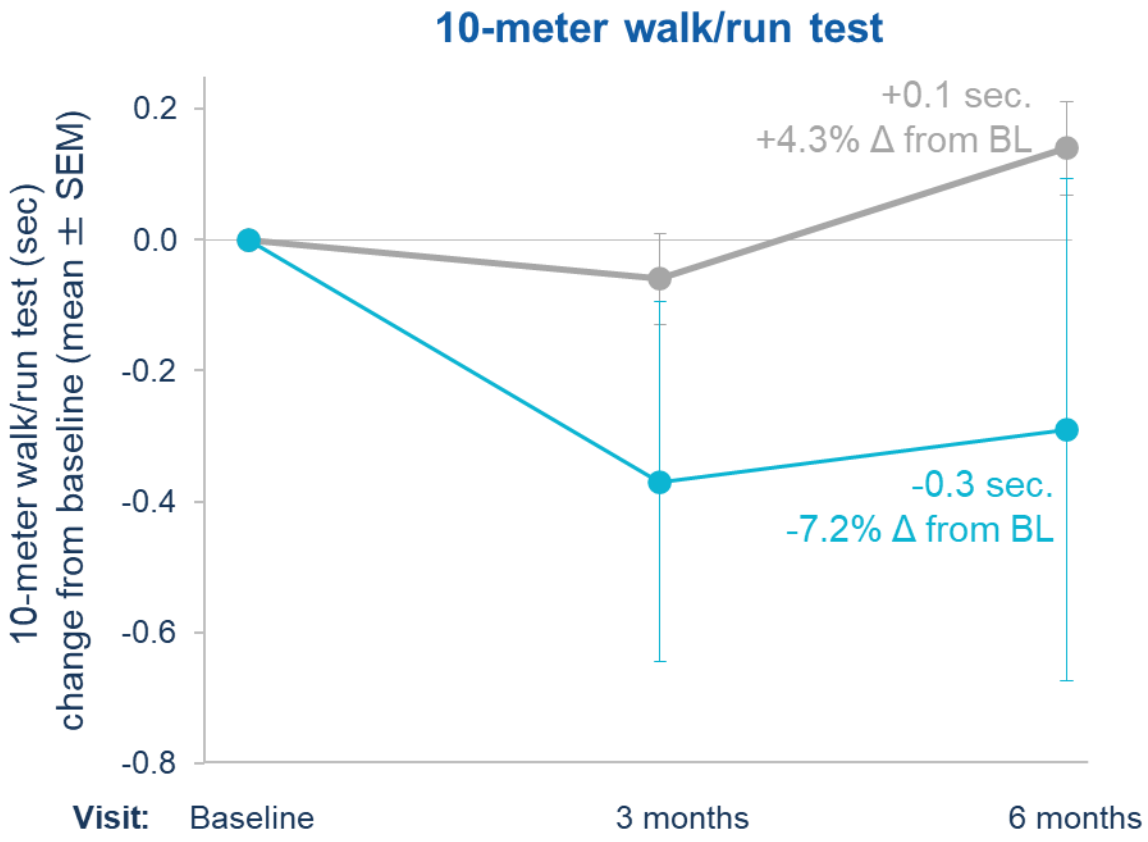
Lilleker J, et al. Oral presentation at the MDA Clinical and Scientific Conference, Dallas, TX, USA, March 16–19, 2025. Oral O44.

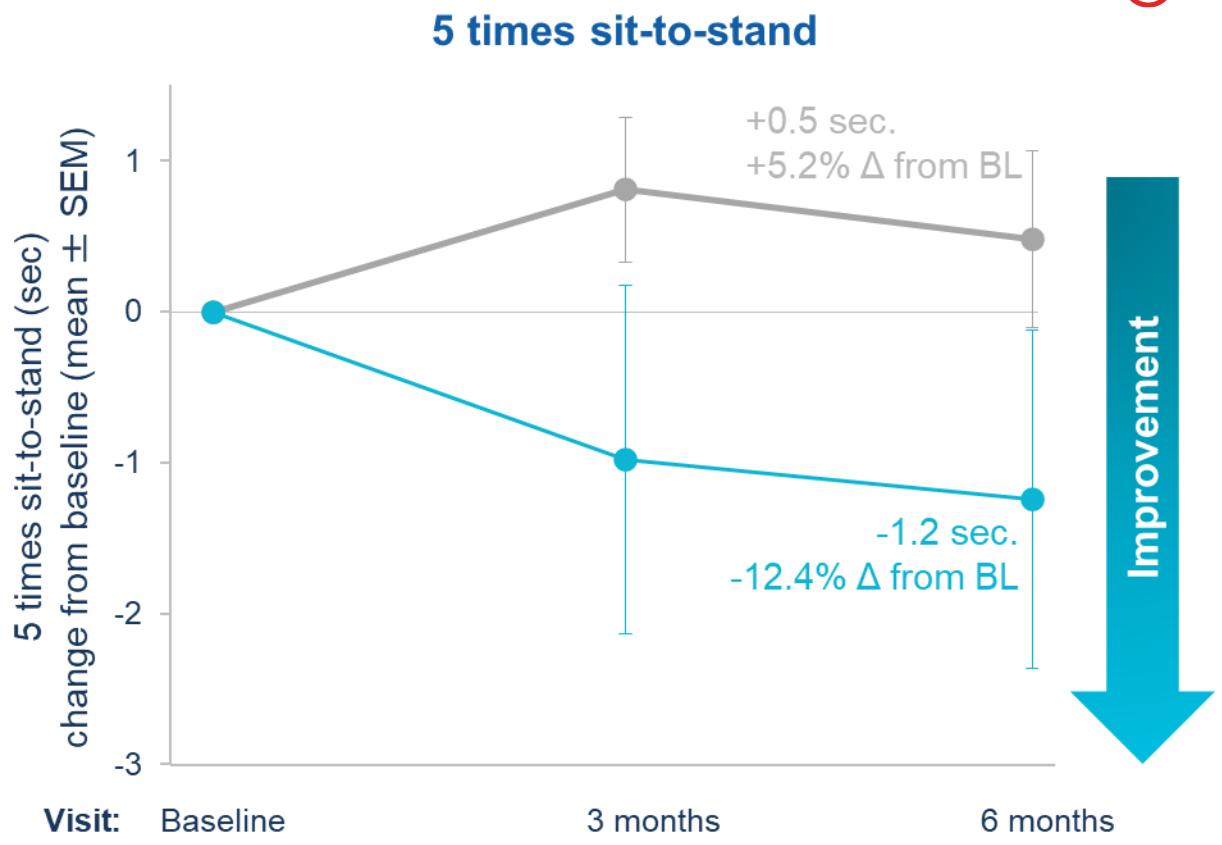
DYNE-101 improved muscle strength at 6 months



DYNE-101 is investigational or otherwise in development and has not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.
QMT total is a composite score of 6 muscle groups, including handgrip, ankle dorsiflexion, knee extension, knee flexion, elbow extension, and elbow flexion. 3 months = 85 days; 6 months = 169 days.
BL, baseline; Q8W, every 8 weeks dosing.
Lilleker J, et al. Oral presentation at the MDA Clinical and Scientific Conference, Dallas, TX, USA, March 16–19, 2025. Oral O44.

Treatment with DYNE-101 led to early and robust benefit across multiple timed function tests



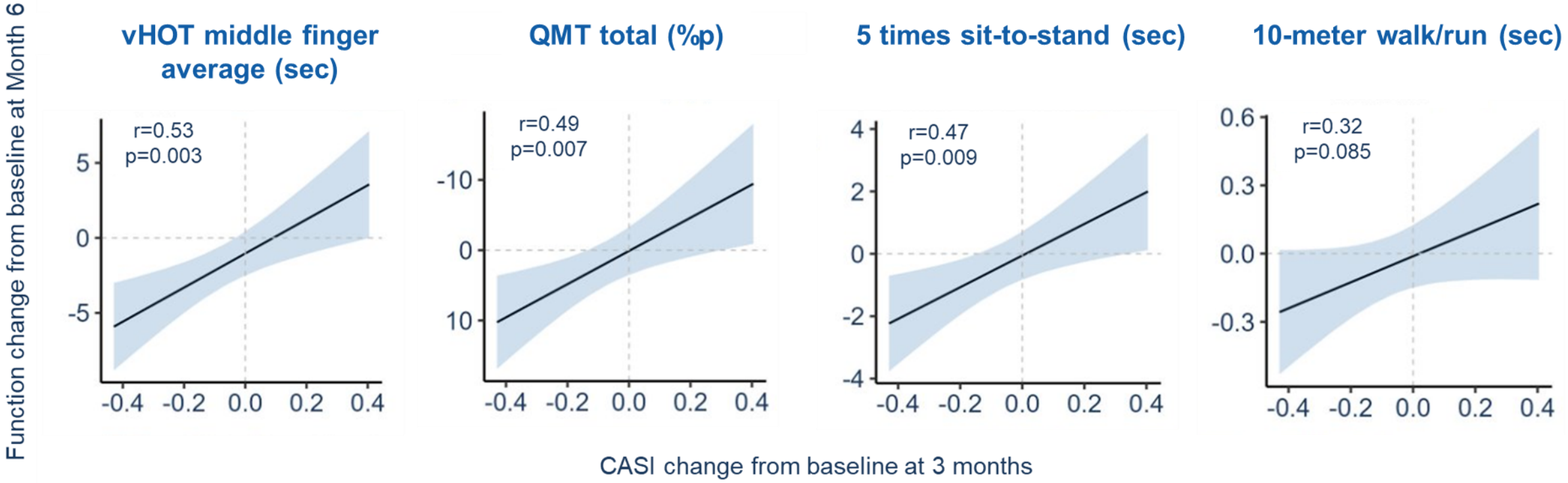


DYNE-101 is investigational or otherwise in development and has not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.

3 months = 85 days; 6 months = 169 days. BL, baseline; Q8W, every 8 weeks dosing.

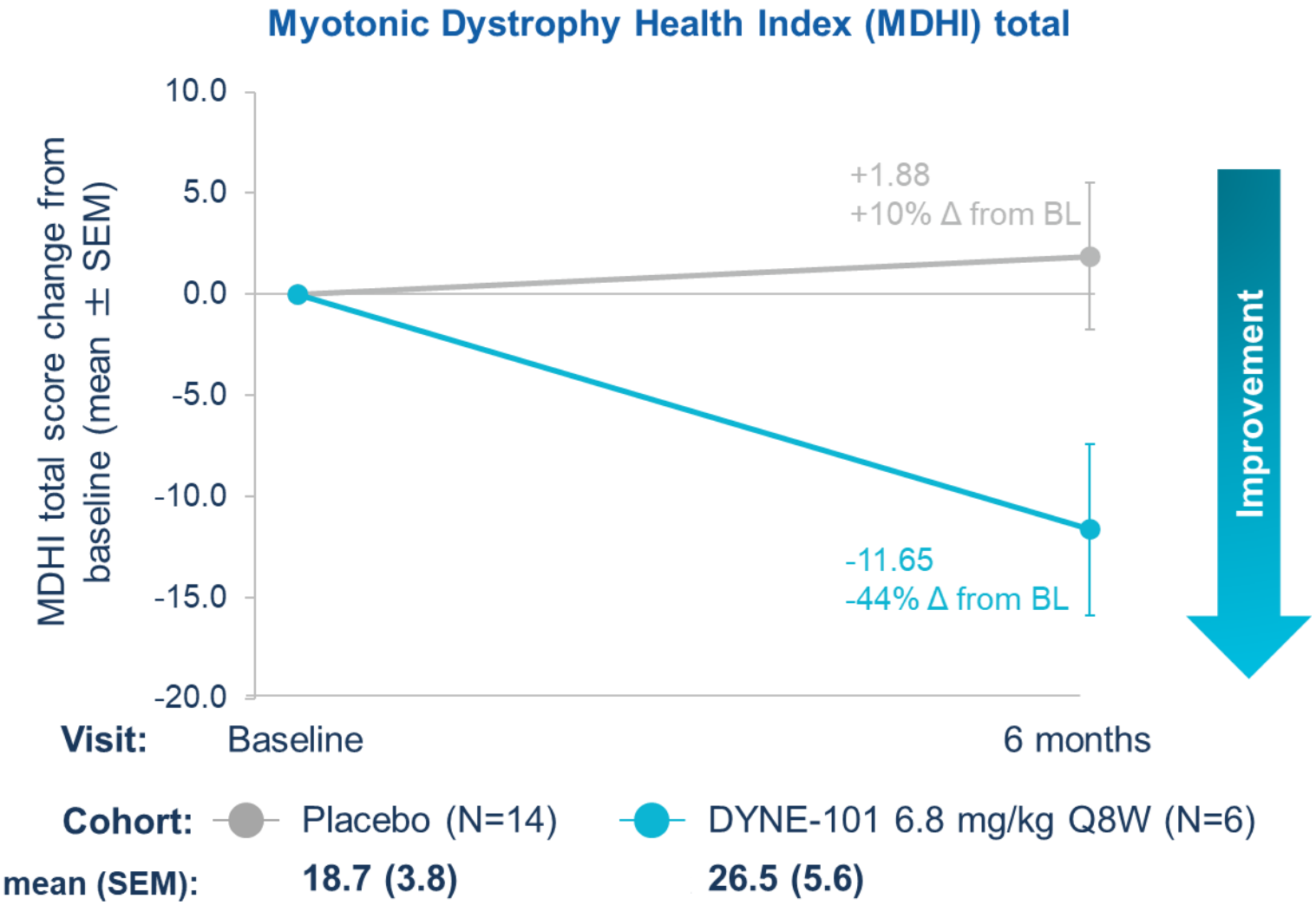
Lilleker J, et al. Oral presentation at the MDA Clinical and Scientific Conference, Dallas, TX, USA, March 16–19, 2025. Oral O44.

In ACHIEVE, 3-month CASI predicted 6-month functional outcomes



DYNE-101 is investigational or otherwise in development and has not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.
Shown are linear regression lines and correlation analysis for pooled 3.4 mg/kg Q4W, 5.4 mg/kg Q8W and 6.8 mg/kg Q8W and Placebo (N=24). Band for model predicted mean with 95% CI.
3 months = 85 days; 6 months = 169 days. CASI, composite alternative splicing index; Q4W, every 4 weeks; Q8W, every 8 weeks; QMT, quantitative muscle testing; sec, seconds; vHOT, video hand opening time.
Lilleker J, et al. Oral presentation at the MDA Clinical and Scientific Conference, Dallas, TX, USA, March 16–19, 2025. Oral O44.

Improvement in MDHI total score with DYNE-101 indicates encouraging patient-reported outcome trends

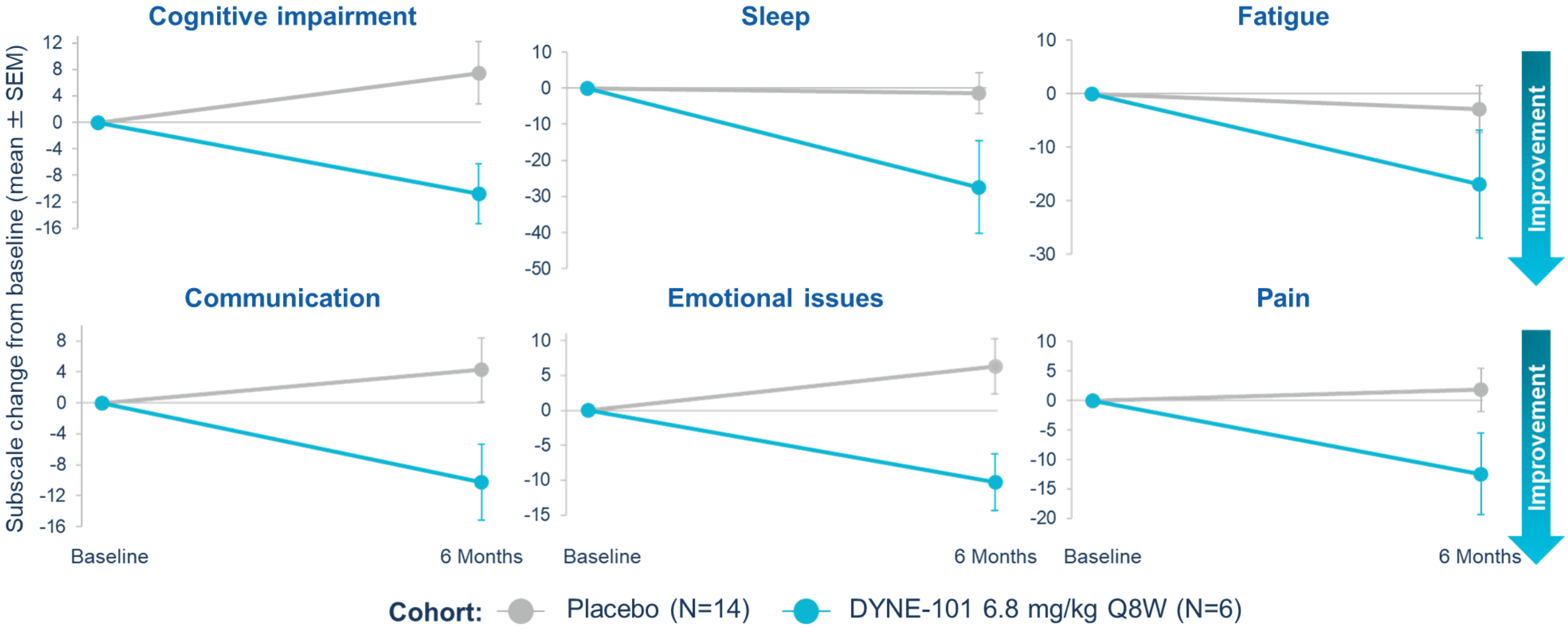


DYNE-101 is investigational or otherwise in development and has not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.

Patient-reported outcomes (PRO) including MDHI collected at baseline and 6 months (169 days). BL, baseline; MDHI, Myotonic Dystrophy Health Index; Q8W, every 8 weeks; SEM, standard error of mean.

Lilleker J, et al. Oral presentation at the MDA Clinical and Scientific Conference, Dallas, TX, USA, March 16–19, 2025. Oral O44.

Improvement in CNS-related MDHI subscales was shown with DYNE-101

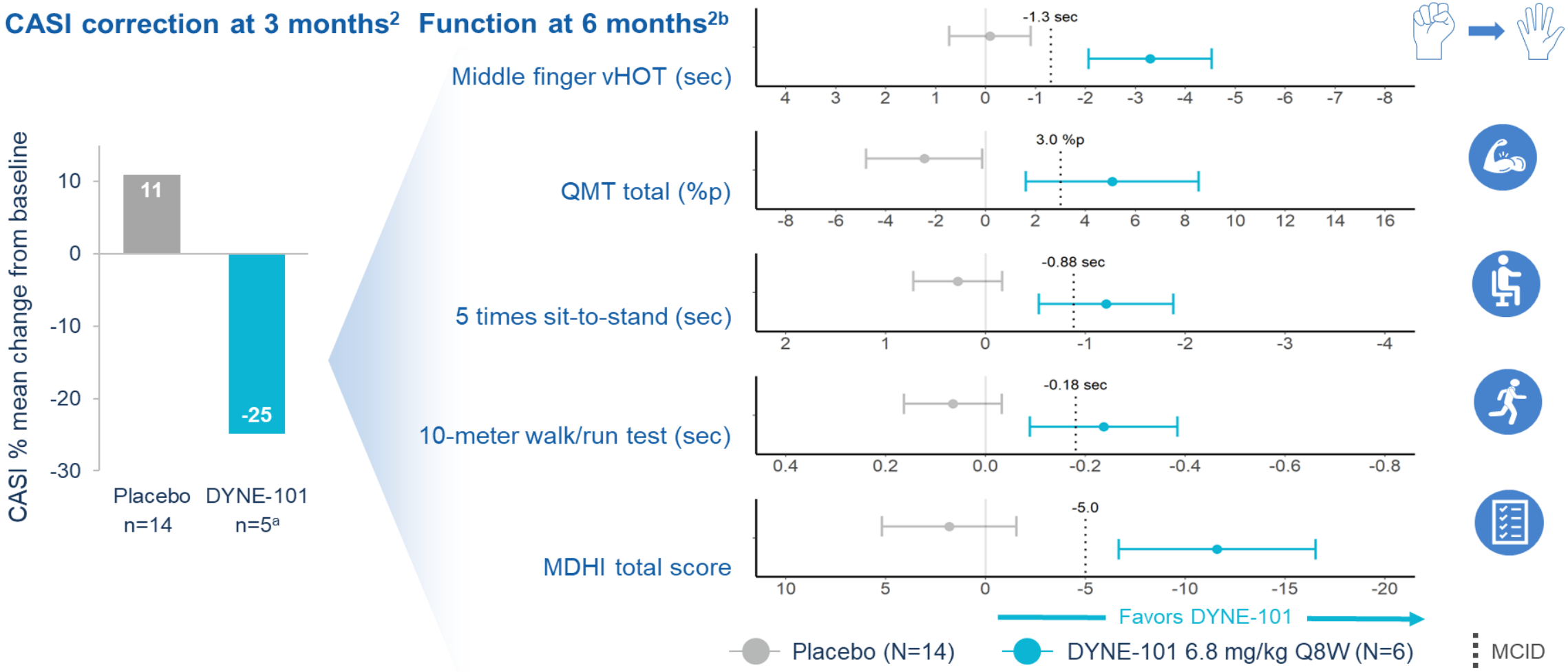


DYNE-101 is investigational or otherwise in development and has not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.

Patient-reported outcomes (PRO) including MDHI collected at baseline and 6 months (169 days). CNS, central nervous system; MDHI, Myotonic Dystrophy Health Index; Q8W, every 8 weeks; SEM, standard error of mean.

Lilleker J, et al. Oral presentation at the MDA Clinical and Scientific Conference, Dallas, TX, USA, March 16–19, 2025. Oral O44.

DYNE-101 demonstrates improvements in areas that patients find most impactful: muscle function and CNS-related manifestations[1]



DYNE-101 is investigational or otherwise in development and has not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.

a. One baseline sample in 6.8 mg/kg treatment group not included within splicing assay as the sample did not meet quality control criteria. b. Mixed model for repeated measures (MMRM): fixed effects: dose, visit, baseline, dose by visit interaction, baseline by visit interaction. Data: all dose groups except recovery group; excluding placebo data after 6 months; Data presented are least squares (LS) mean change from baseline ±SE. MCID estimate is calculated as the average of 2 distribution-based methods using ACHIEVE data (0.2 SD of baseline [N=56] and 0.5 SD placebo change from baseline at 6 months [n=14]). 3 months = 85 days; 6 months = 169 days. Q8W, every 8 weeks; CASI, composite alternative splicing index; CNS, central nervous system; MCID, minimal clinically important difference; MDHI, Myotonic Dystrophy Health Index; QMT, quantitative muscle testing; SD, standard deviation; SE, standard error; vHOT, video hand opening time.

1. Hagerman KA, et al. *Muscle Nerve* 2019;59(4):457–64; 2. Lilleker J, et al. Oral presentation at the MDA Clinical and Scientific Conference, Dallas, TX, USA, March 16–19, 2025. Oral O44.

Summary

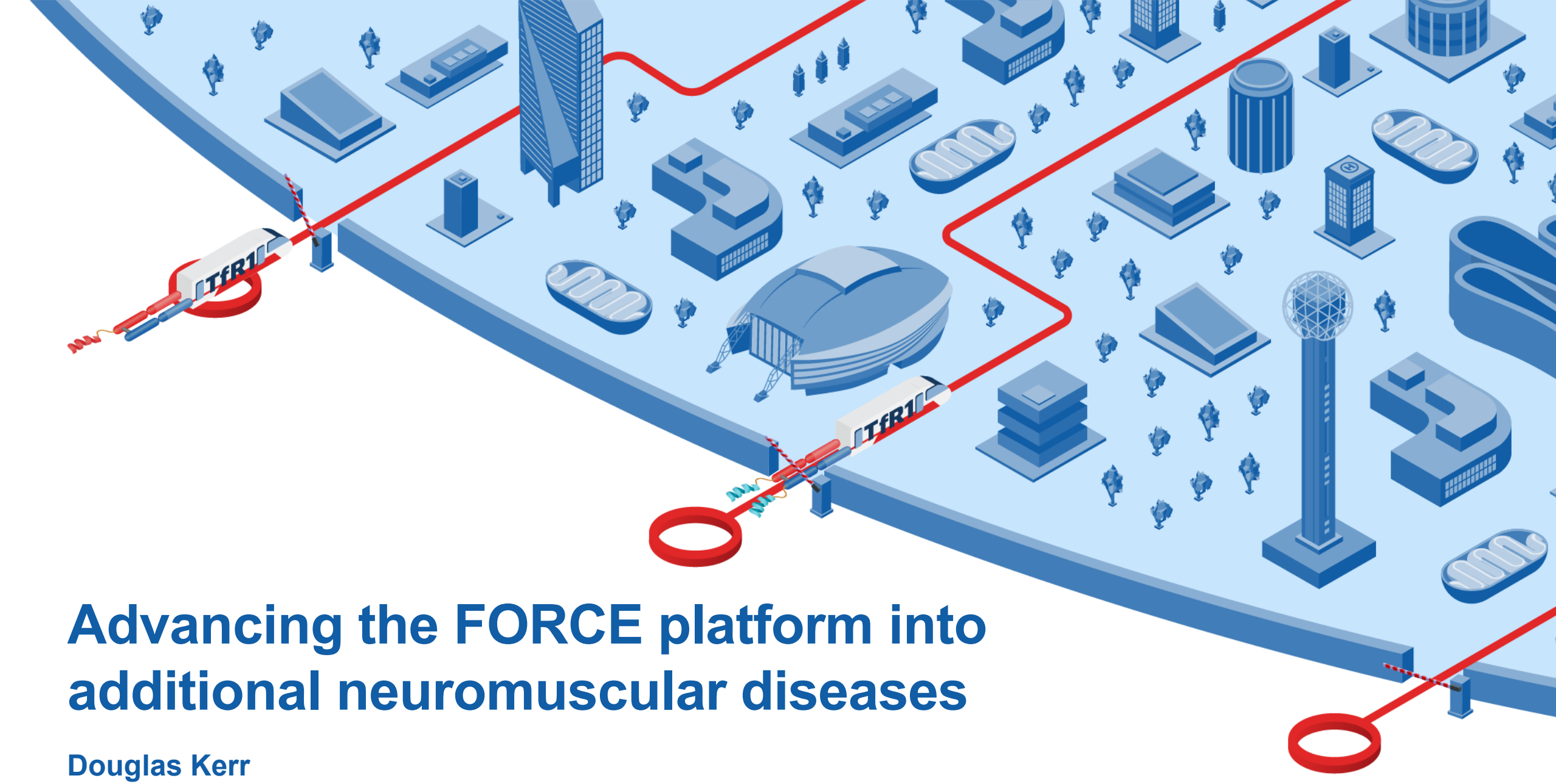
- **DYNE-101** is designed to target mutant **nuclear** *DMPK* RNA with the goal of **correcting the abnormal splicing** to improve the **multisystem disease manifestations** of **DM1**[1,2]
- The FORCE platform achieves **broad distribution to key muscles such as cardiac, skeletal (including diaphragm), and smooth, as well as the brain**[2,3]
- **The safety profile of DYNE-101 is favorable to date**[a]
- DYNE-101 **addresses the underlying pathobiology** (dysregulated splicing) of DM1 and at 6.8 mg/kg Q8W has demonstrated **clinically meaningful improvements on measurements of strength, mobility and QoL, including CNS manifestations**
  - Splicing correction at 3 months with DYNE-101 was predictive of functional benefit at 6 months
- The MAD portion of ACHIEVE is completed; **6.8 mg/kg Q8W** has been selected as the **registrational dose/dose regimen** of DYNE-101

DYNE-101 is investigational or otherwise in development and has not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.

a. Data as of December 6, 2024.

CNS, central nervous system; DM1, myotonic dystrophy type 1; DMPK, dystrophia myotonica protein kinase; Q8W, every 8 weeks; QoL, quality of life.

1. López-Martínez A, et al. *Genes (Basel).* 2020;11(9):1109; 2. Zanotti S. Presentation at the 25th American Society of Gene & Cell Therapy Annual Meeting. May 16, 2022. Washington DC, USA. Abstract 17;
3. Zanotti S. Presentation at the 26th American Society of Gene and Cell Therapy Annual Meeting. May 17, 2023. Los Angeles, USA. Abstract 82.

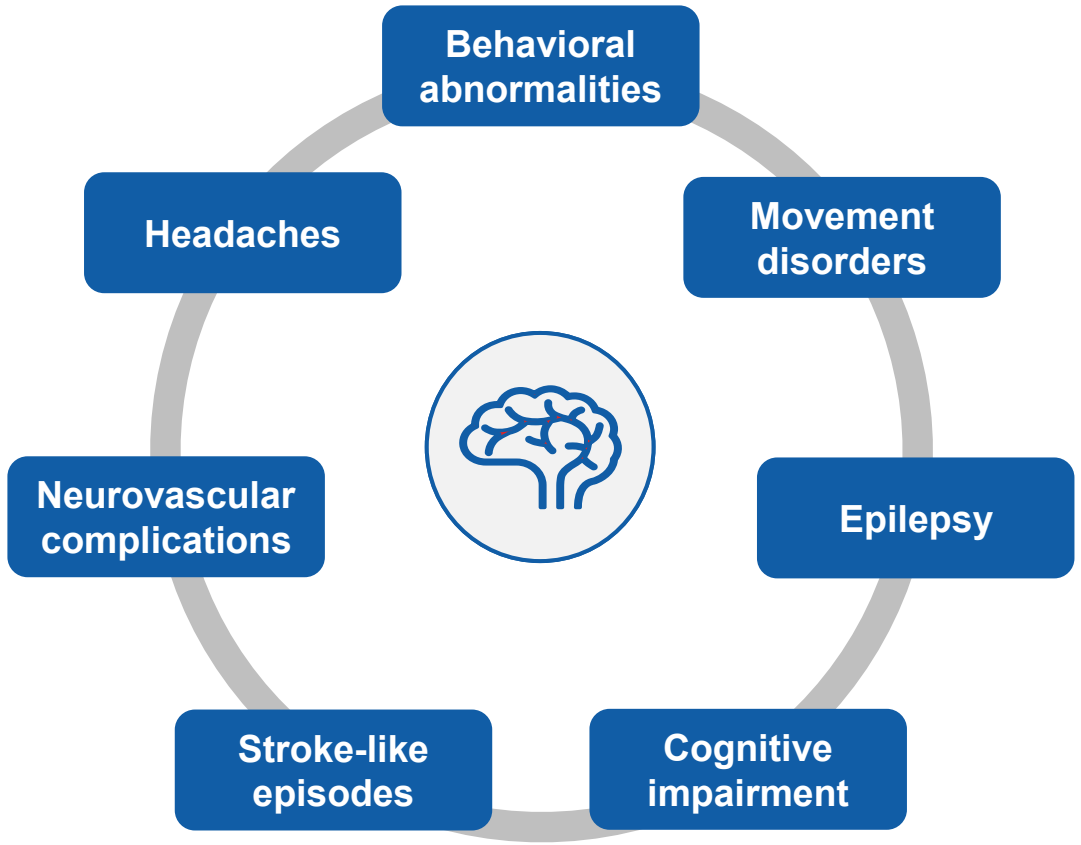


Advancing the FORCE platform into additional neuromuscular diseases

Douglas Kerr

In addition to muscle, CNS involvement is common in many NMDs

CNS involvement is highly variable across NMDs[1]



DM1 (adult-onset)[2]

Neurocognitive

- Lower IQ scores, frontal dysexecutive syndrome, apathy, theory of mind deficit, fatigue, EDS

Neuropsychiatric

- Avoidant personality, social interaction problems

DMD[3]

Neurocognitive

- Executive functions, working memory, intellectual functioning

Academic

- Reading and arithmetic

Emotional

- Anxiety and depression

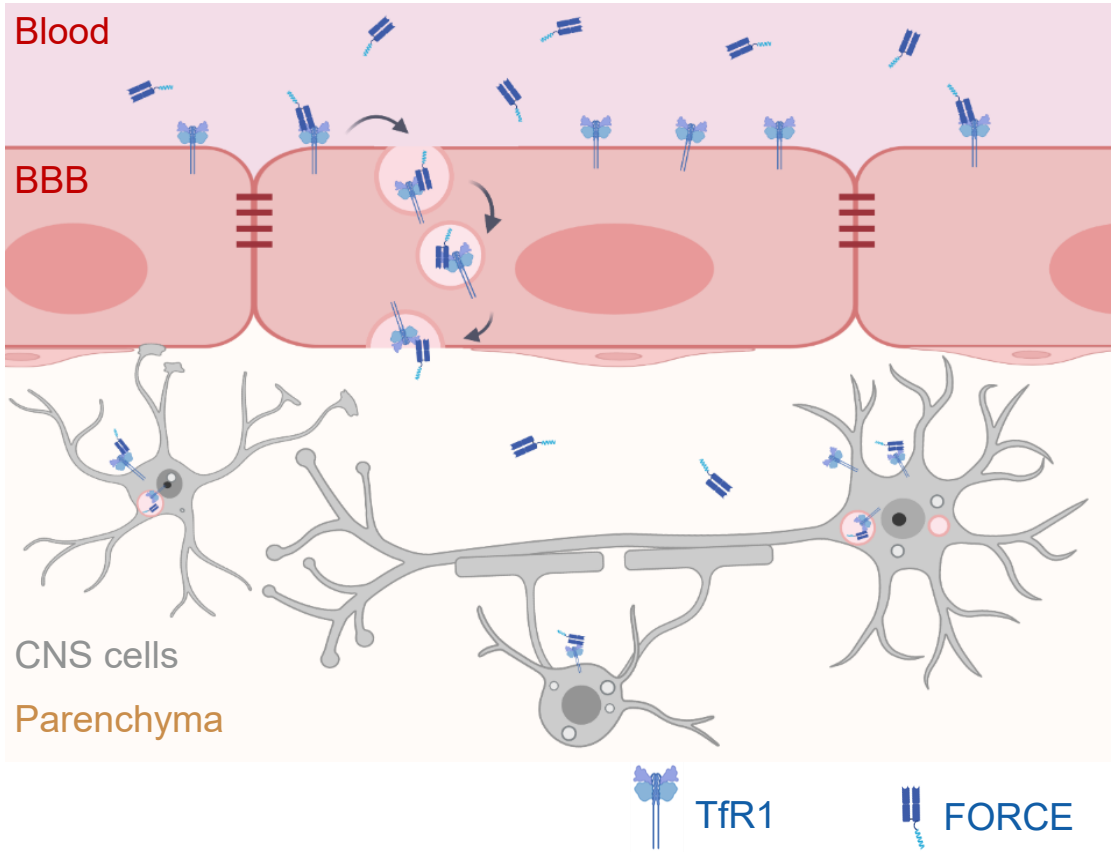
Neuropsychiatric

- Autism, ADHD, OCD

Slide does not represent an exhaustive list of symptoms.
ADHD, attention-deficit hyperactivity disorder; CNS, central nervous system; EDS: excessive daytime sleepiness; NMD, neuromuscular disease; OCD: obsessive-compulsive disorder.
1. Reimann J, Kornblum C. *J Neuromuscul Dis.* 2020;7(4):367–393; 2. Gourdon G, Meola G. *Front Cell Neurosci.* 2017;11:101; 3. Vaillend C, et al. *Nat Commun.* 2025;16(1):1298.

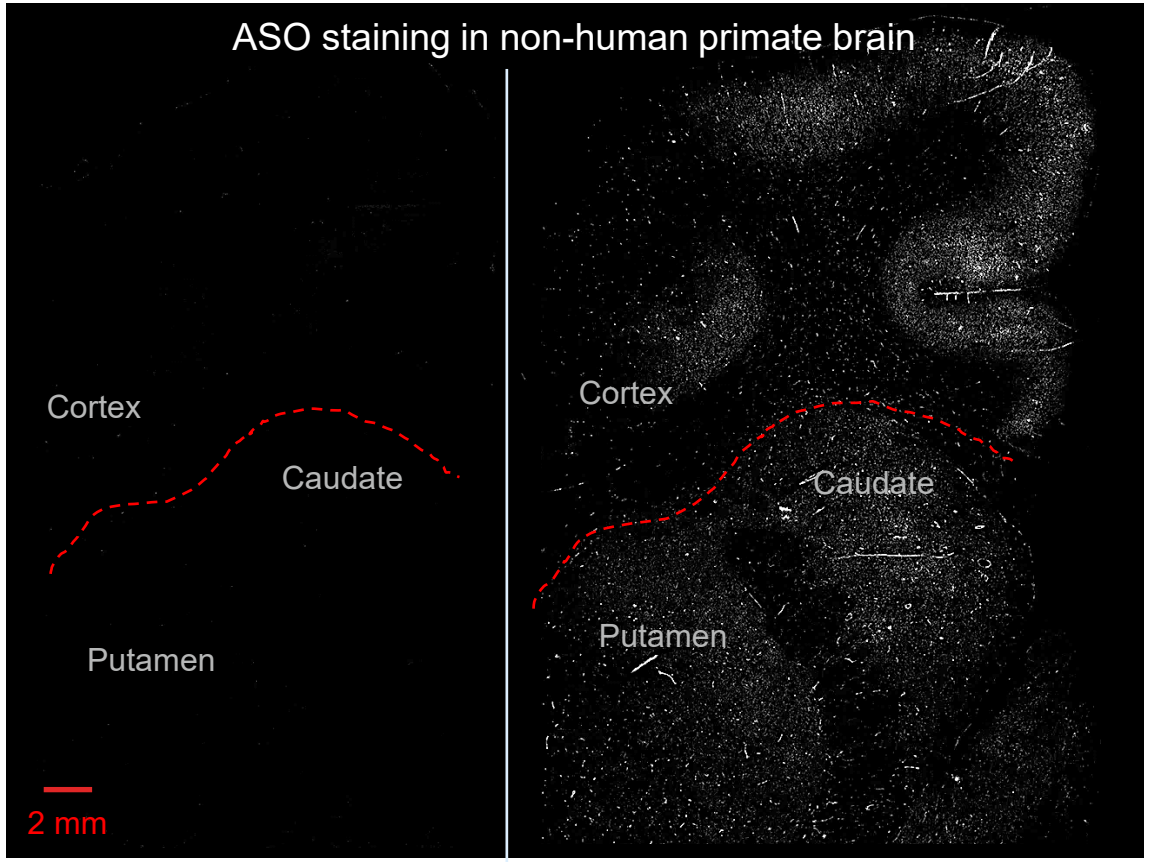
The FORCE platform can cross the blood–brain barrier and achieve widespread brain delivery

TfR1-mediated transcytosis: potential for crossing the BBB



Naked ASO, IV
No ASO delivery

FORCE, IV
Widespread ASO delivery



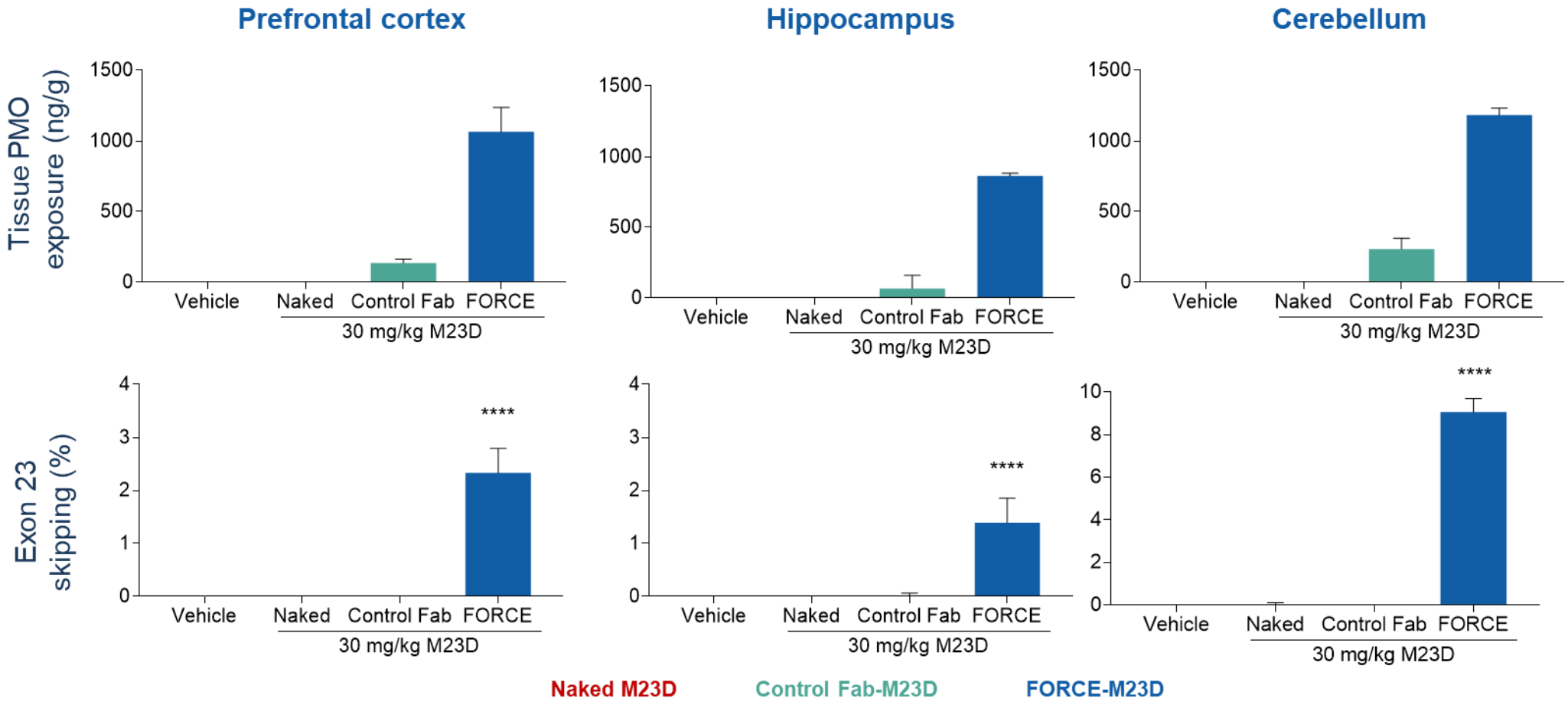
The FORCE platform is investigational or otherwise in development and has not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.

Adapted from Pulgar VM. *Front Neurosci.* 2019;12:1019 and Liu K, et al. *Sci Rep.* 2016;6:21019. Schematic created by BioRender.com.

ASO, antisense oligonucleotide; BBB, blood–brain barrier; CNS, central nervous system; IV, intravenous; TfR1, transferrin receptor 1.

Zanotti S. Presentation at the 26th American Society of Gene and Cell Therapy Annual Meeting. May 17, 2023. Los Angeles, USA. Abstract 82.

The FORCE platform delivers PMO and induces exon skipping in the brain of a DMD mouse



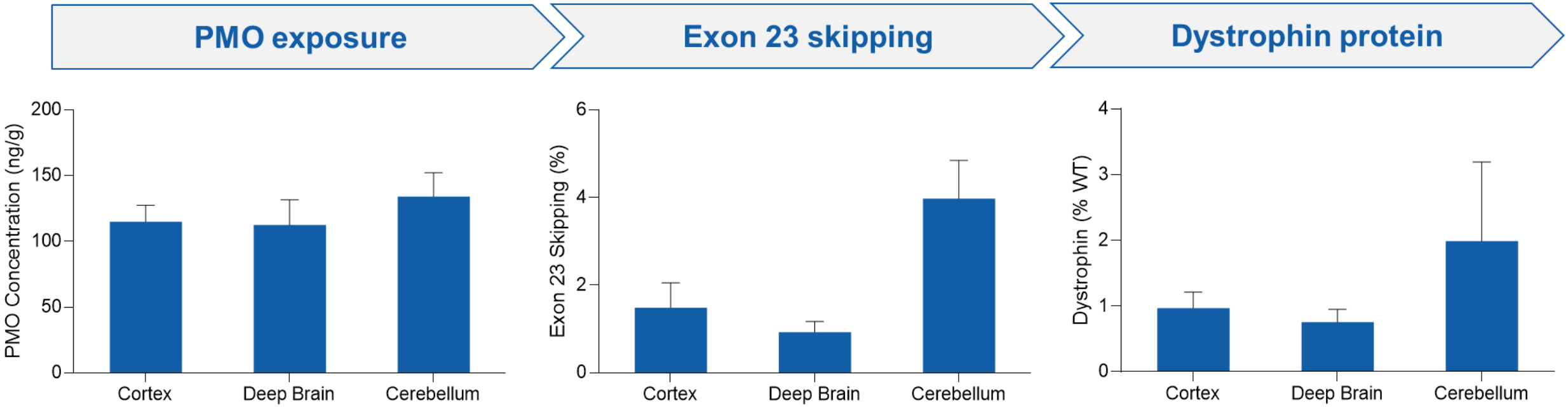
The FORCE platform is investigational or otherwise in development and has not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.

30 mg/kg single IV dose of FORCE-M23D. Analyses at 7 days. Data are means + SD; n=5 per group.

DMD, Duchenne muscular dystrophy; PMO, phosphorodiamidate morpholino oligomer.

Desjardins CA, et al. Poster presentation the 2025 MDA Clinical and Scientific Conference. March 16–19, 2025. Dallas, USA. Poster 004.

The FORCE platform induces durable exon skipping and dystrophin expression in the brain of a DMD mouse

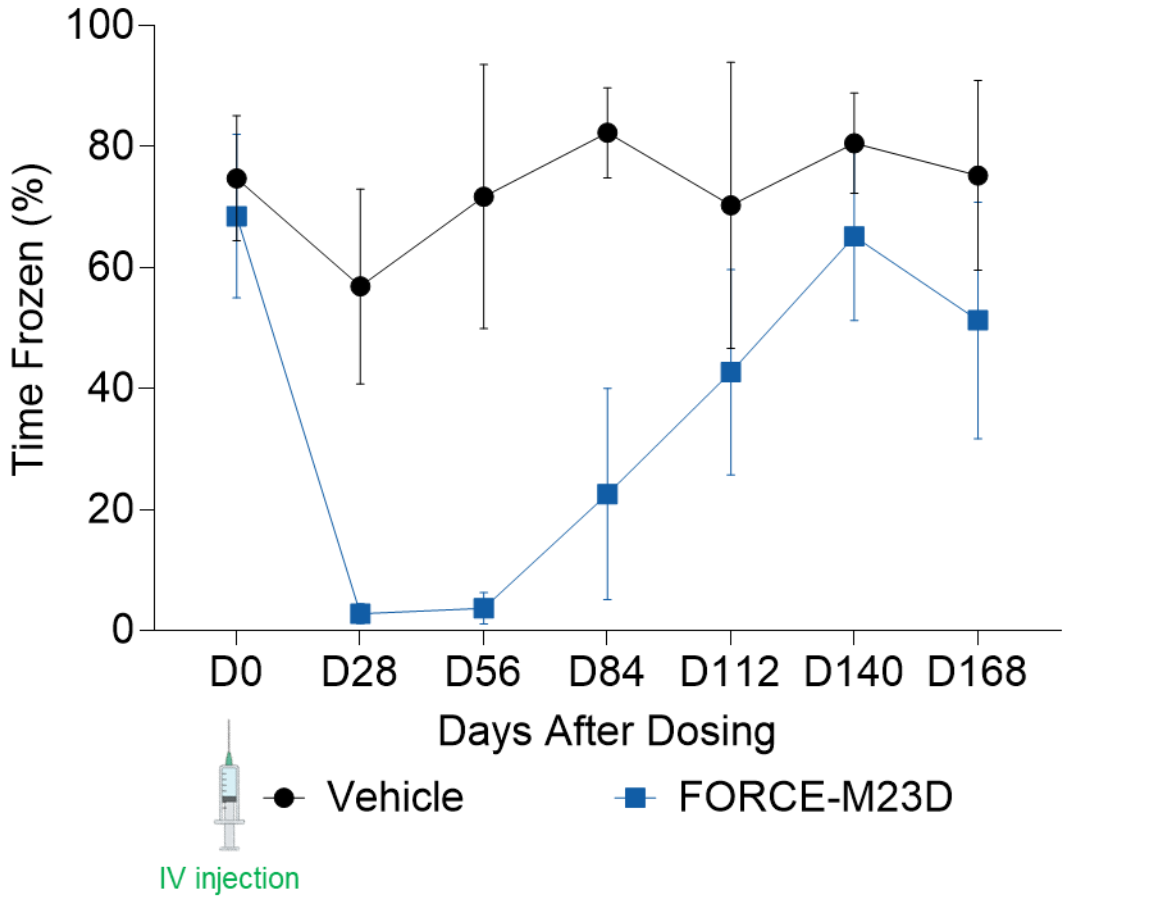


The FORCE platform is investigational or otherwise in development and has not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.
30 mg/kg single IV dose of FORCE-M23D. Analyses at 28 days. Data are means + SD; n=5 per group.
DMD, Duchenne muscular dystrophy; PMO, phosphorodiamidate morpholino oligomer; WT, wild-type.
Desjardins CA, et al. Poster presentation the 2025 MDA Clinical and Scientific Conference. March 16–19, 2025. Dallas, USA. Poster 004.

The FORCE platform corrects CNS-related anxiety in a DMD mouse

Vehicle

FORCE

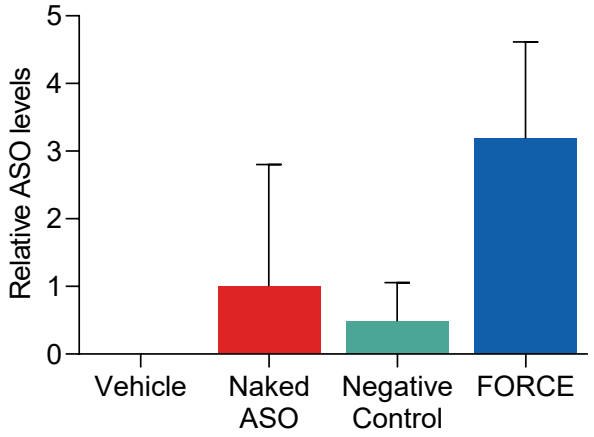


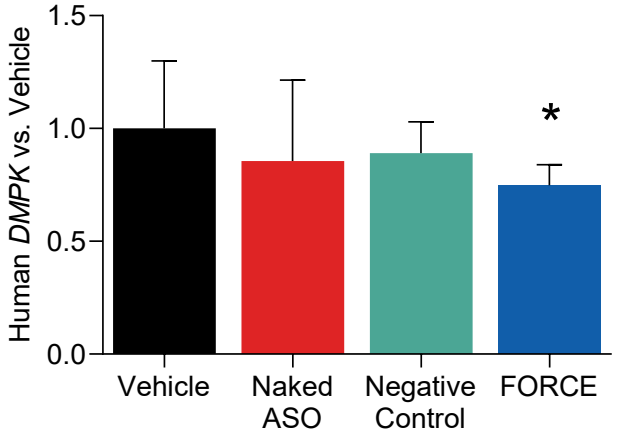
The FORCE platform is investigational or otherwise in development and has not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.
Single 30 mg/kg IV dose of FORCE-M23D. Data are means + SD; n=5–10 per group.
CNS, central nervous system; DMD, Duchenne muscular dystrophy; hTfR1, humanized transferrin receptor 1.
Desjardins CA, et al. Poster presentation the 2025 MDA Clinical and Scientific Conference. March 16–19, 2025. Dallas, USA. Poster 004.

FORCE delivers to the brain in a mouse model of DM1

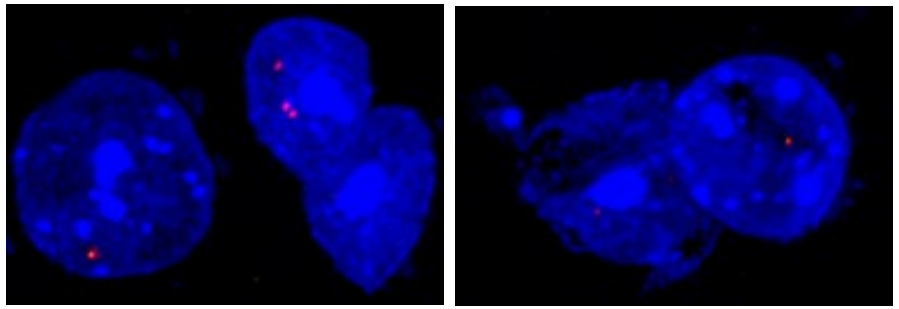
ASO delivery | **Total *DMPK* KD** | **Mutant *DMPK* foci area**

Brain cortex



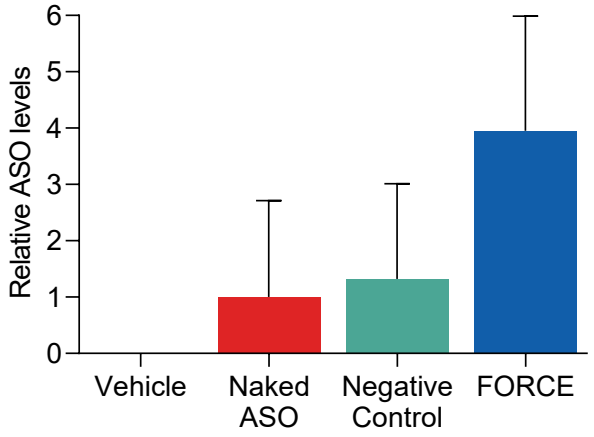


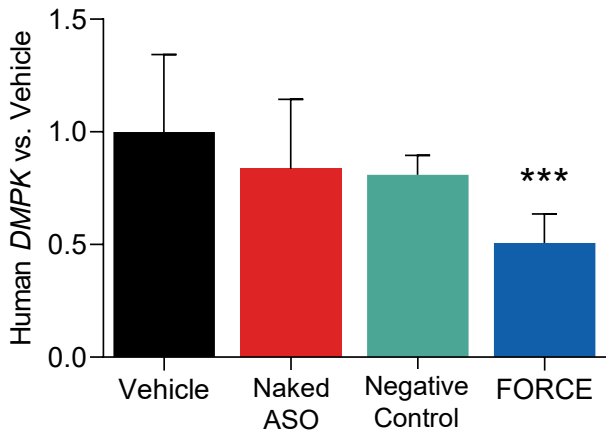
Vehicle | FORCE



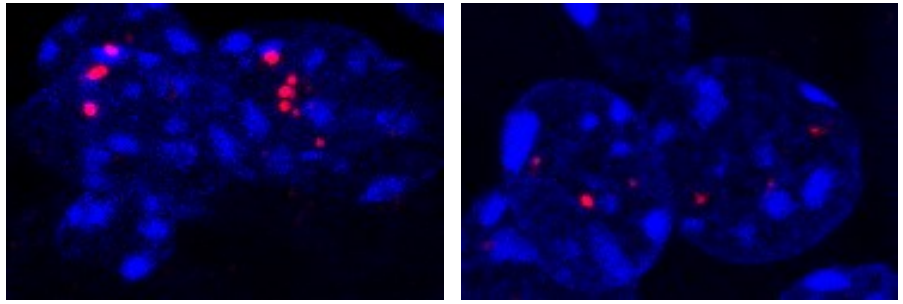
Foci area reduction by ~65%**

Cerebellum





Vehicle | FORCE



Foci area reduction by ~60%*

Nuclei
Mutant *DMPK* foci

The FORCE platform is investigational or otherwise in development and has not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.

hTfR1/DMSXL mice dosed 10 mg/kg on day 0 and day 7, analyzed day 35. Data are mean + SD, n=7. *p<0.05, **p<0.01, ***p<0.001 FORCE vs. vehicle.

ASO, antisense oligonucleotide; DM1, myotonic dystrophy type 1; DMPK, dystrophia myotonica protein kinase; hTfR1, humanized transferrin receptor 1; KD, knock down.

Zanotti S. Presentation at the 26th American Society of Gene and Cell Therapy Annual Meeting. May 17, 2023. Los Angeles, USA. Abstract 82.

Leveraging the FORCE platform to deliver ERT to muscle and the CNS in Pompe disease

DYNE-401 enables TfR1-targeted ERT

Antibody

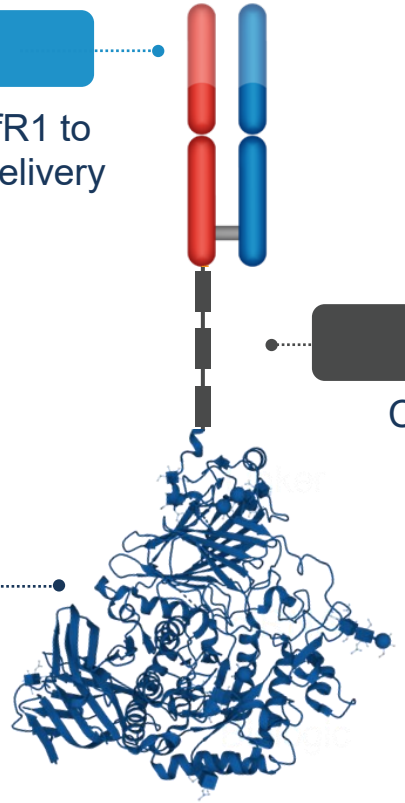
Proprietary Fab targets TfR1 to enable muscle and CNS delivery

Linker

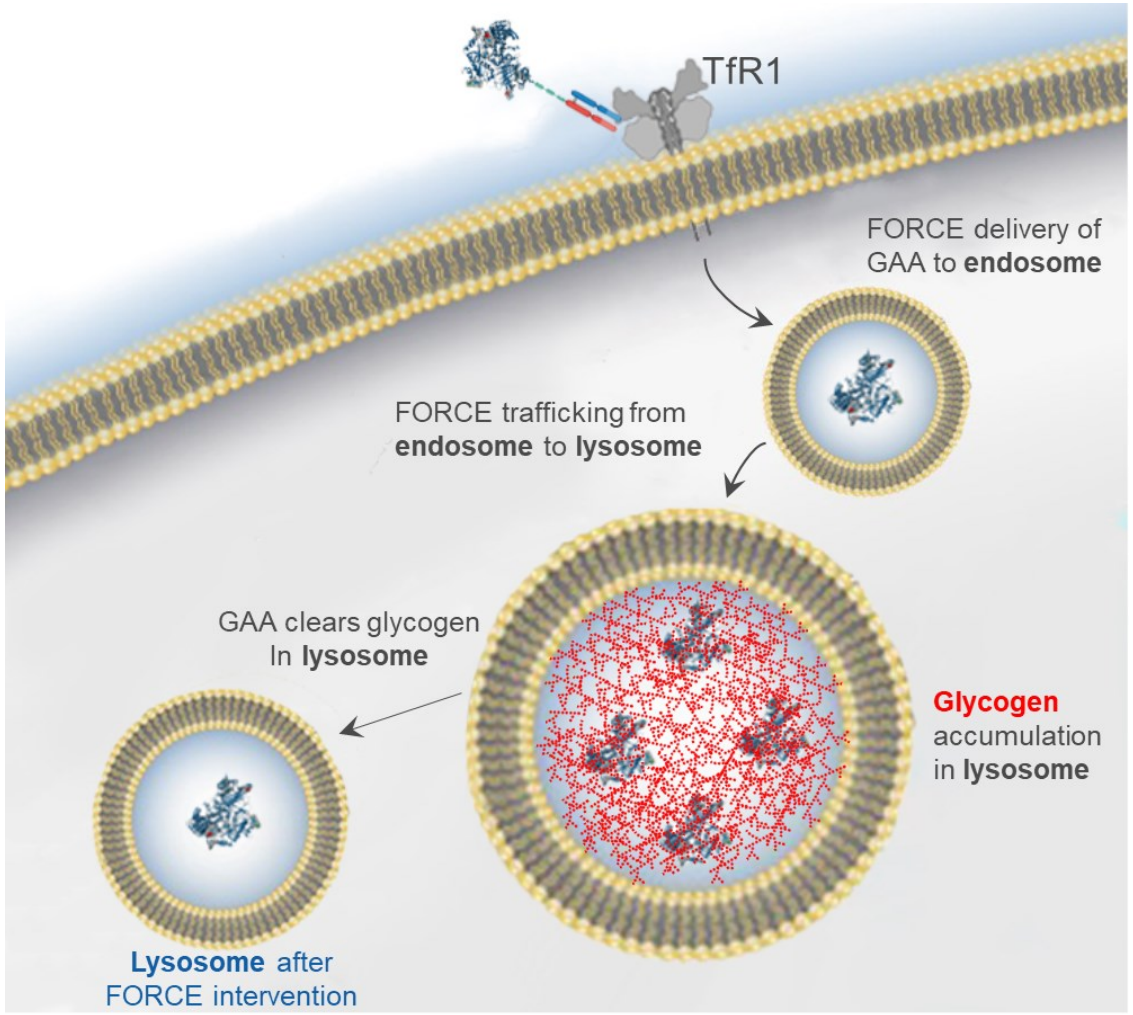
Connects Fab with GAA

Payload

GAA to address Pompe pathology



DYNE-401 delivers to the endo-lysosomal system



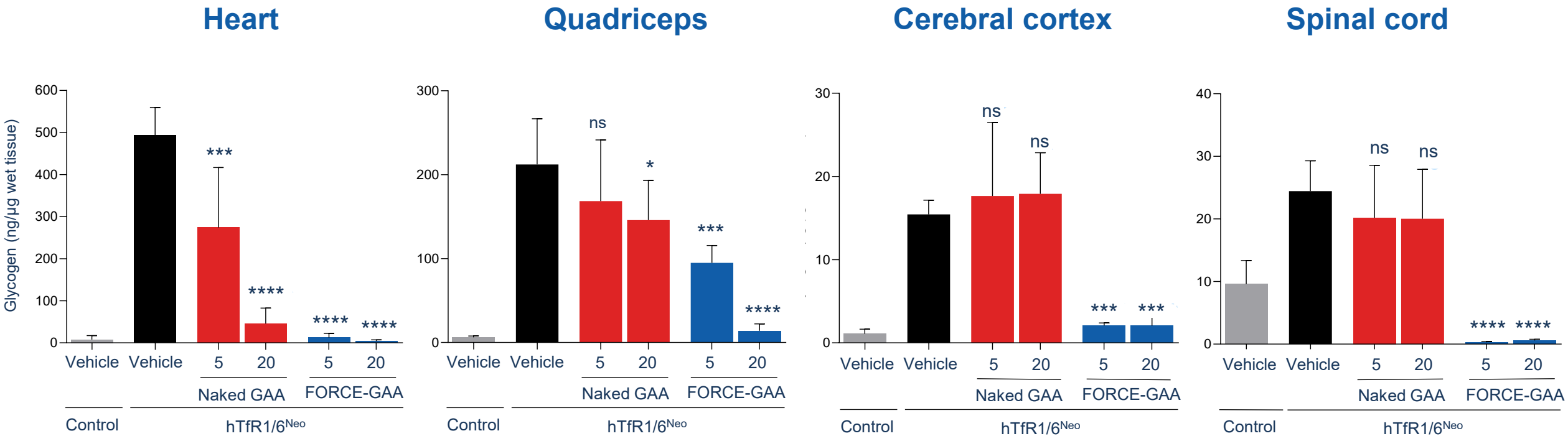
The FORCE platform and DYNE-401 are investigational or otherwise in development and have not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.

Image depicts proposed mechanism of action.

CNS, central nervous system; GAA, acid alpha-glucosidase; ERT: enzyme replacement therapy; Fab, antigen-binding fragment; TfR1, transferrin receptor 1.

Picariello T, et al. Poster presentation at the World Muscle Society Annual Congress, Prague, Czechia, October 8–12, 2024. Poster 669.

FORCE-GAA achieves superior glycogen clearance in muscle and CNS of a Pompe mouse compared to naked GAA using the SOC dosing regimen



FORCE-GAA is investigational or otherwise in development and has not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.

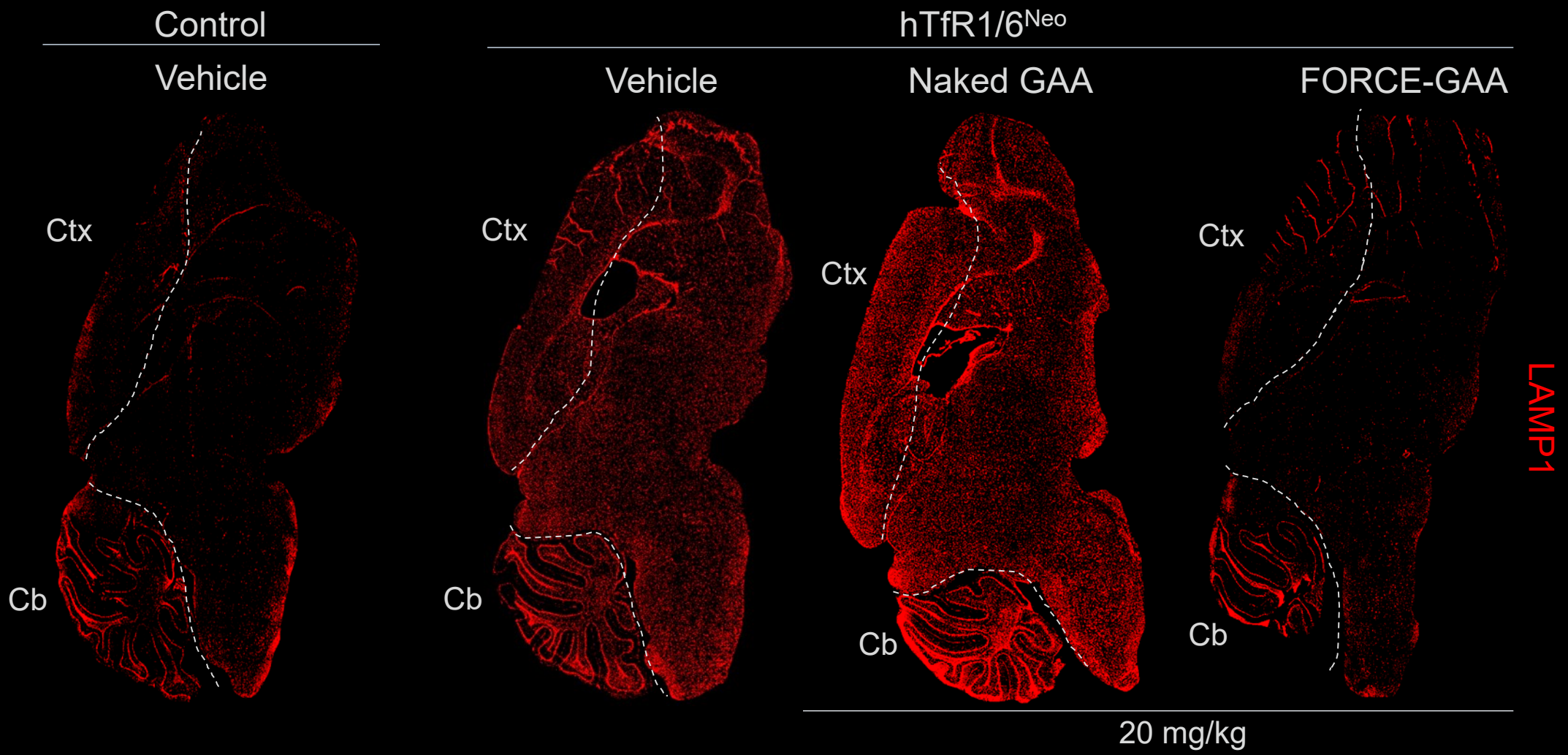
FORCE-GAA is a surrogate of DYNE-401.

Doses are mg/kg GAA-equivalents. Mice were dosed on day 0 and weeks 2, 4, and 6, analyzed on week 8. Data are means + SD; n=4–7. Control mice are hTfR1(Het)/6^{Neo}(Het); hTfR1/6^{Neo} mice are hTfR1(Het)/6^{Neo}(Hom); Statistical significance compared to vehicle treated hTfR1/6^{Neo} mice by ANOVA; *p<0.05, ***p<0.001, ****p<0.0001.

CNS, central nervous system; GAA, acid alpha-glucosidase; hTfR1, humanized transferrin receptor 1; SOC, standard of care.

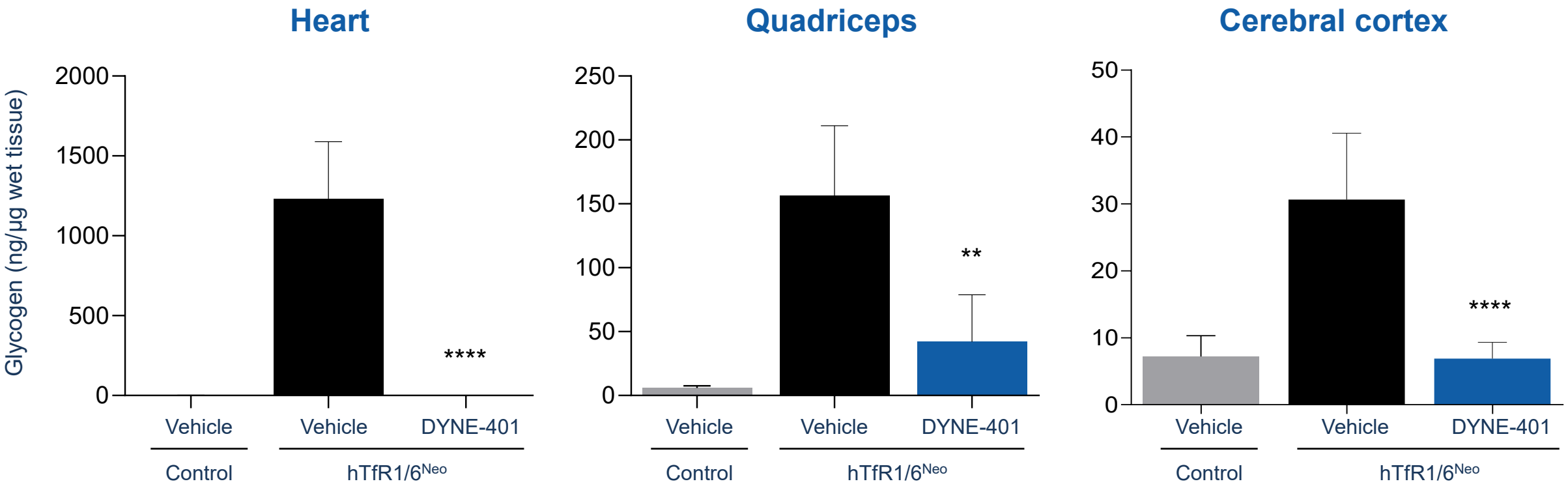
Picariello T, et al. Poster presentation at the World Muscle Society Annual Congress, Prague, Czechia, October 8–12, 2024. Poster 669.

FORCE-GAA achieves widespread lysosomal size normalization in CNS using SOC dosing



FORCE-GAA is investigational or otherwise in development and has not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.
FORCE-GAA is a surrogate of DYNE-401.
Dose is 20 mg/kg GAA-equivalents. Mice were dosed on day 0 and weeks 2, 4, and 6, analyzed on week 8. Control mice are hTfR1(Het)/6^{Neo}(Het); hTfR1/6^{Neo} mice are hTfR1(Het)/6^{Neo}(Hom).
Cb, cerebellum; CNS, central nervous system; Ctx, cortex; GAA, acid alpha-glucosidase; hTfR1, humanized transferrin receptor 1; LAMP1, lysosome associated membrane protein 1; SOC, standard of care.
Picariello T, et al. Presentation at the WorldSymposium, San Diego, USA, February 3–7, 2025.

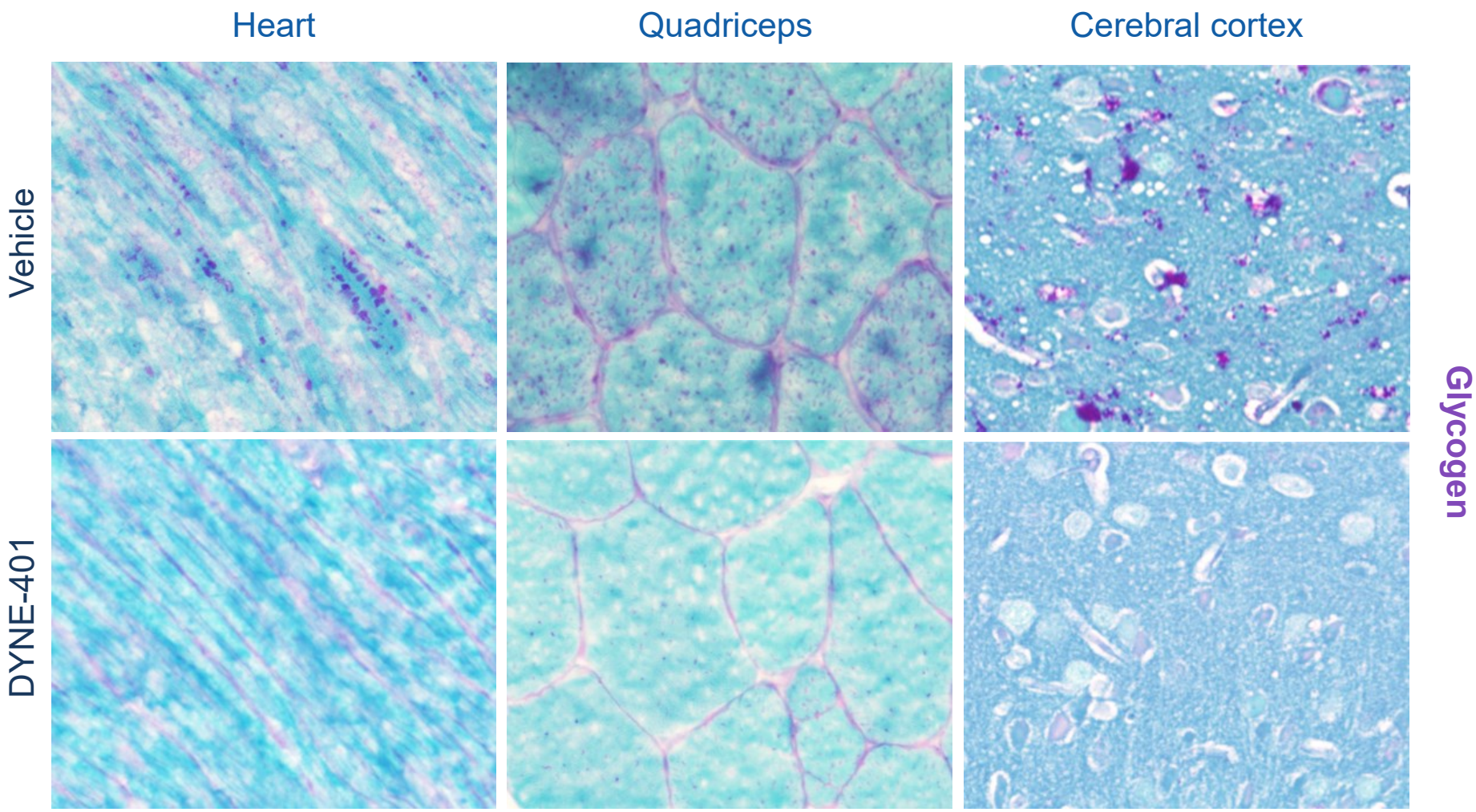
DYNE-401 monthly dosing clears glycogen in muscle and CNS in a Pompe mouse



DYNE-401 is investigational or otherwise in development and has not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.

Dose is 20 mg/kg GAA-equivalents. Mice were dosed on day 0 and week 4 and analyzed on week 8. Control mice are hTfR1(Het)/6^{Neo}(Het); hTfR1/6^{Neo} mice are hTfR1(Het)/6^{Neo}(Hom);
Data are means + SD; n=3 vehicle mice, n=5 treated mice per group. Significantly different from vehicle-treated hTfR1/6^{neo} mice by ANOVA; **p<0.01, ****p<0.0001.
CNS, central nervous system; hTfR1, humanized transferrin receptor 1.
Picariello T, et al. Poster presentation at the World Muscle Society Annual Congress, Prague, Czechia, October 8–12, 2024. Poster 669.

DYNE-401 monthly dosing demonstrates profound glycogen clearance in cardiac and skeletal muscle as well as CNS in a Pompe mouse



DYNE-401 is investigational or otherwise in development and has not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.

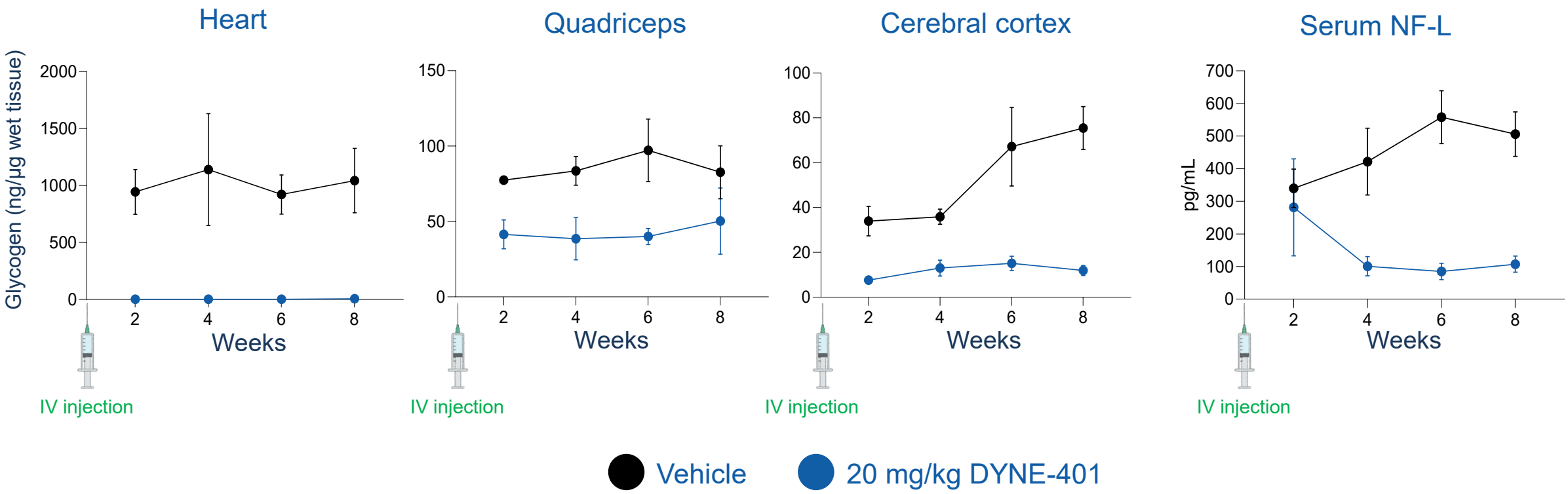
Dose is 20 mg/kg GAA-equivalents. Mice were dosed on day 0 and week 4 and analyzed on week 8. Control mice are hTfR1(Het)/6^{Neo}(Het); hTfR1/6^{Neo} mice are hTfR1(Het)/6^{Neo}(Hom). Sections were stained with Periodic acid-Schiff (PAS) to visualize glycogen (purple) and fast green stain to visualize tissue architecture.

CNS, central nervous system; hTfR1, humanized transferrin receptor 1.

Zanotti S. Presentation at 2024 New Directions in Biology and Disease of Skeletal Muscle Conference. June 23–26, 2024. Fort Lauderdale, USA.

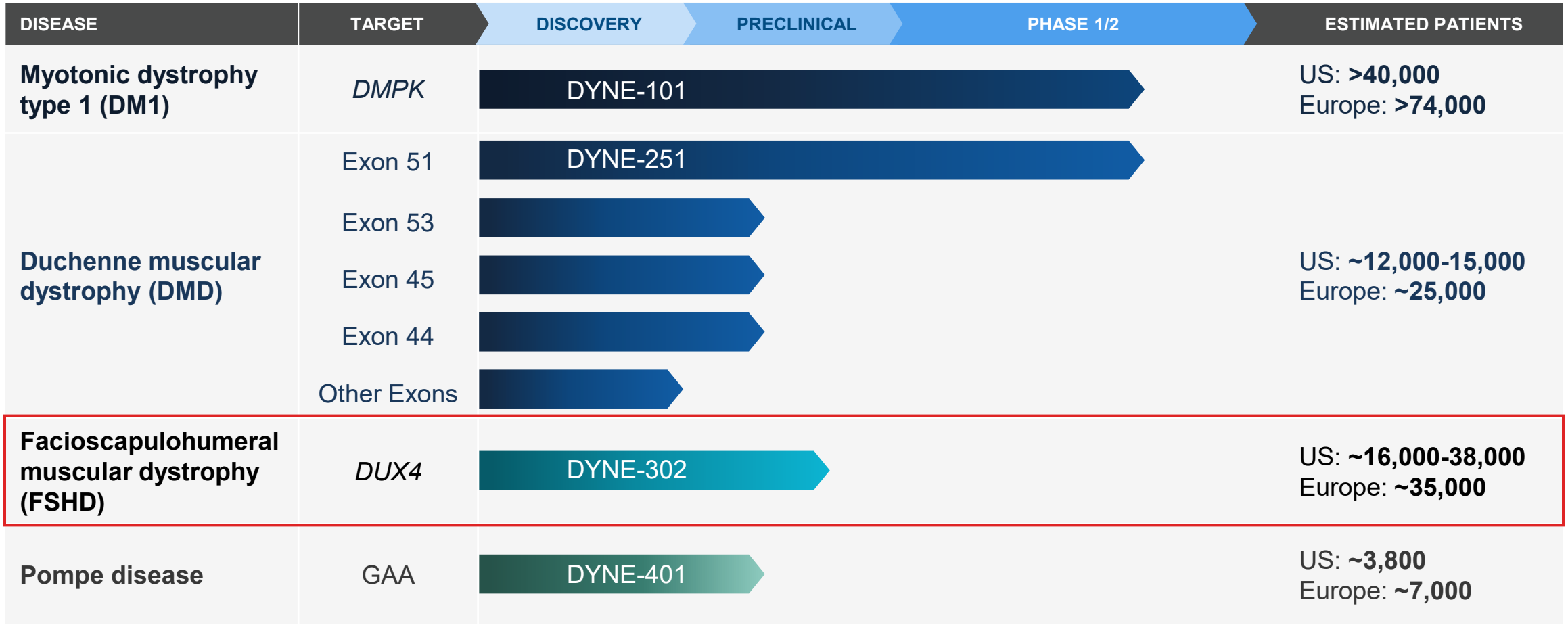
DYNE-401 demonstrates potential for infrequent dosing

DYNE-401 achieves durable glycogen and serum NF-L reduction



DYNE-401 is investigational or otherwise in development and has not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.
Dose is mg/kg GAA-equivalents. Mice were dosed on day 0; analyzed on week 2, 4, 6, and 8. Data are means ±SD; n=3–4.
IV, intravenous; NF-L, neurofilament light polypeptide.
Picariello T, et al. Presentation at the WorldSymposium, San Diego, USA, February 3–7, 2025.

Advancing the FORCE platform for more patients with NMD: pipeline expansion opportunities



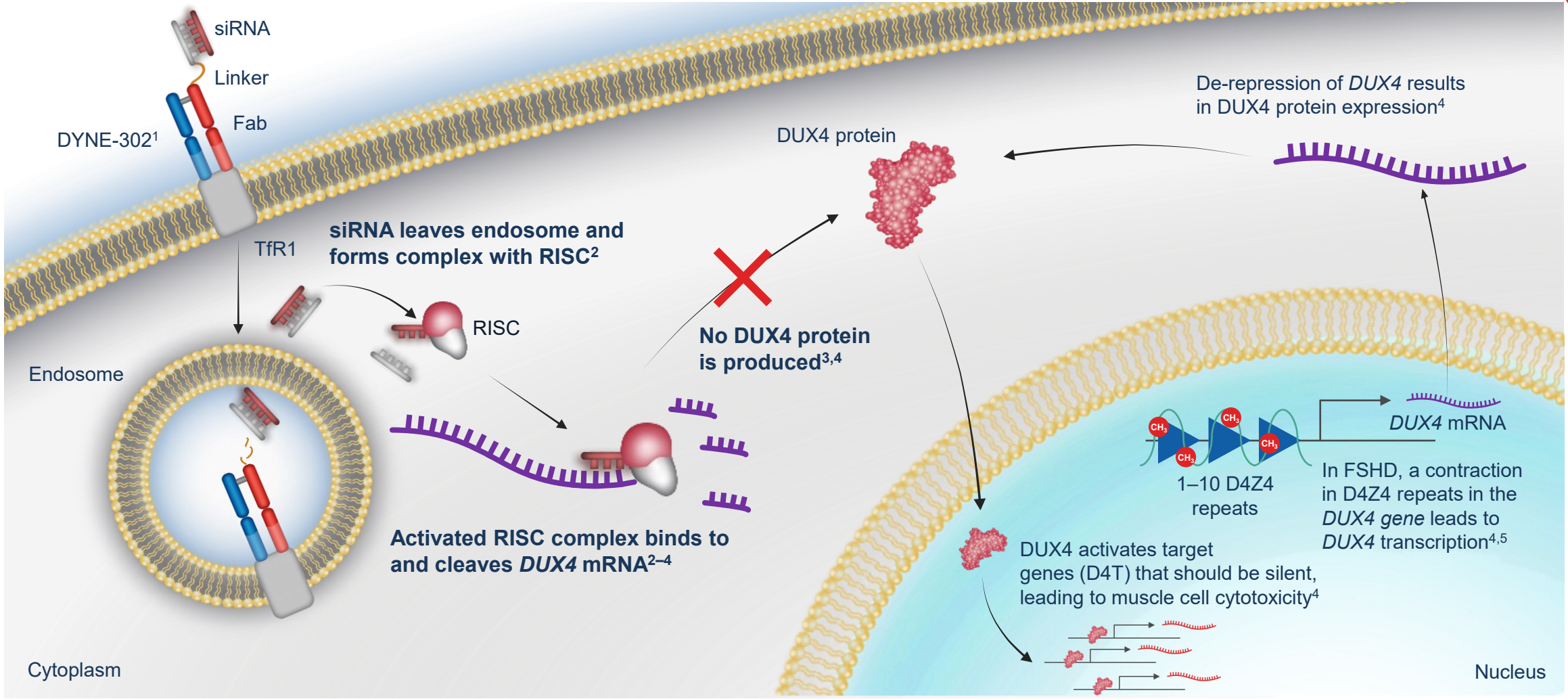
Pipeline expansion opportunities in CNS, rare skeletal, cardiac and metabolic

The FORCE platform, DYNE-251, DYNE-101, DYNE-302 and DYNE-401 are investigational or otherwise in development and have not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.

CNS, central nervous system; DMPK, dystrophia myotonica protein kinase; DUX4, double homeobox 4; GAA, acid alpha-glucosidase; NMD, neuromuscular disease.

Dyne pipeline. Accessed March 13, 2025. https://www.dyne-tx.com/pipeline/.

Targeting *DUX4* mRNA in FSHD with an siRNA FORCE conjugate (DYNE-302)



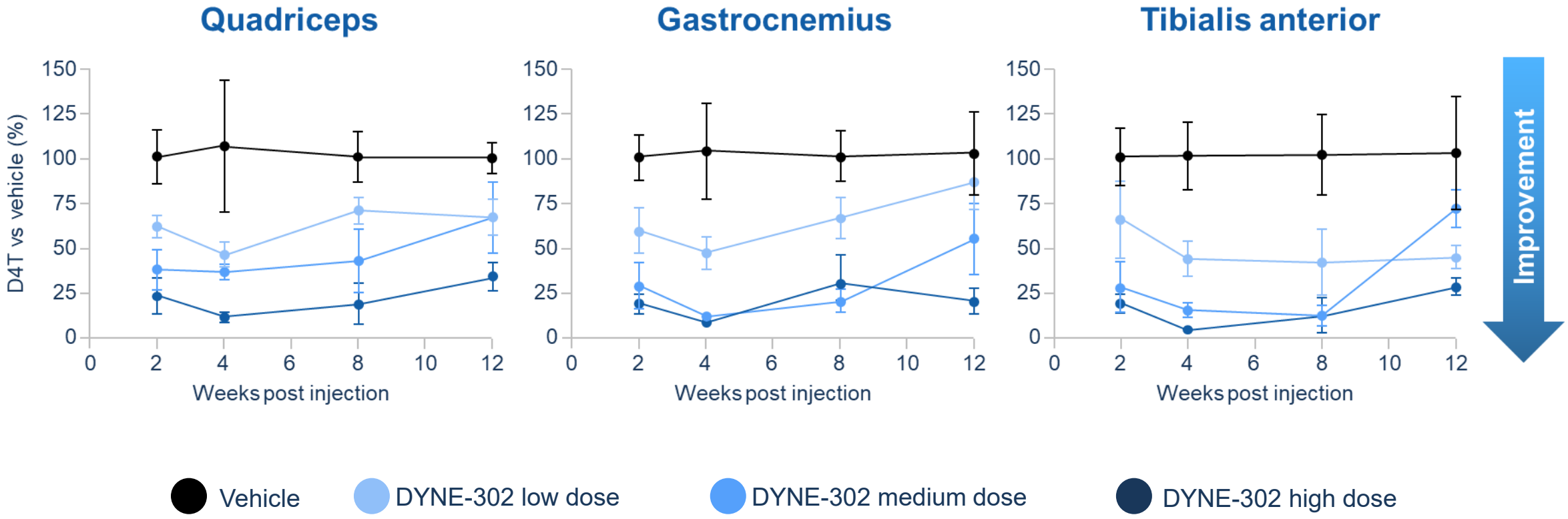
DYNE-302 is investigational or otherwise in development and has not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.

Image depicts intended mechanism of action of DYNE-302.

D4T, *DUX4* transcriptome; *DUX4*, double homeobox 4 gene; FSHD, facioscapulohumeral muscular dystrophy; mRNA, messenger ribonucleic acid; RISC, RNA-induced silencing complex; siRNA, small interfering RNA; TfR1, transferrin receptor 1.

1. Natoli T. Presentation at 31st Annual FSHD Society International Research Congress. June 13–14, 2024. Abstract S2.03; 2. Khvorova A. *JAMA*. 2023;329(4):2185–2186;
3. Lim JW, et al. *Hum Mol Genet*. 2015;24(17):4817–4828; 4. Tihaya MS, et al. *Nat Rev Neurol*. 2023;19(2):91–108; 5. Mul K. *Continuum (Minneap Minn)*. 2022;28(6):1735–1751.

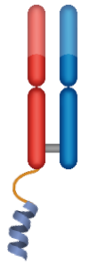
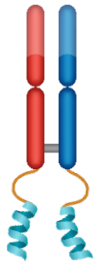
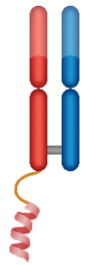
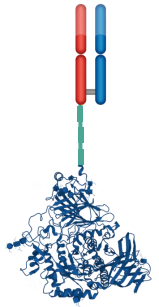
Single dose of DYNE-302 achieves robust, durable, and dose-dependent D4T KD in skeletal muscle of hTfR1/iFLExD FSHD mice



DYNE-302 demonstrates potential for infrequent dosing, out to Q12W

DYNE-302 is investigational or otherwise in development and has not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.
Uninduced hTfR1/iFLExD mice dosed with vehicle or DYNE-302 on day 0, analyzed at indicated weeks. Data are means ± SD; n=4–12. D4T is an average of mouse *Wfdc3*, *Sord*, and *Serpinb6c* mRNA markers.
D4T, DUX4 transcriptome; FSHD, facioscapulohumeral muscular dystrophy; KD, knock down; hTfR1, humanized transferrin receptor 1; Q12W, every 12 weeks.
Natoli T. Presentation at 31st Annual FSHD Society International Research Congress. June 13–14, 2024. Abstract S2.03.

The FORCE platform enables delivery of rationally selected payloads to muscle and CNS to target the genetic basis of disease

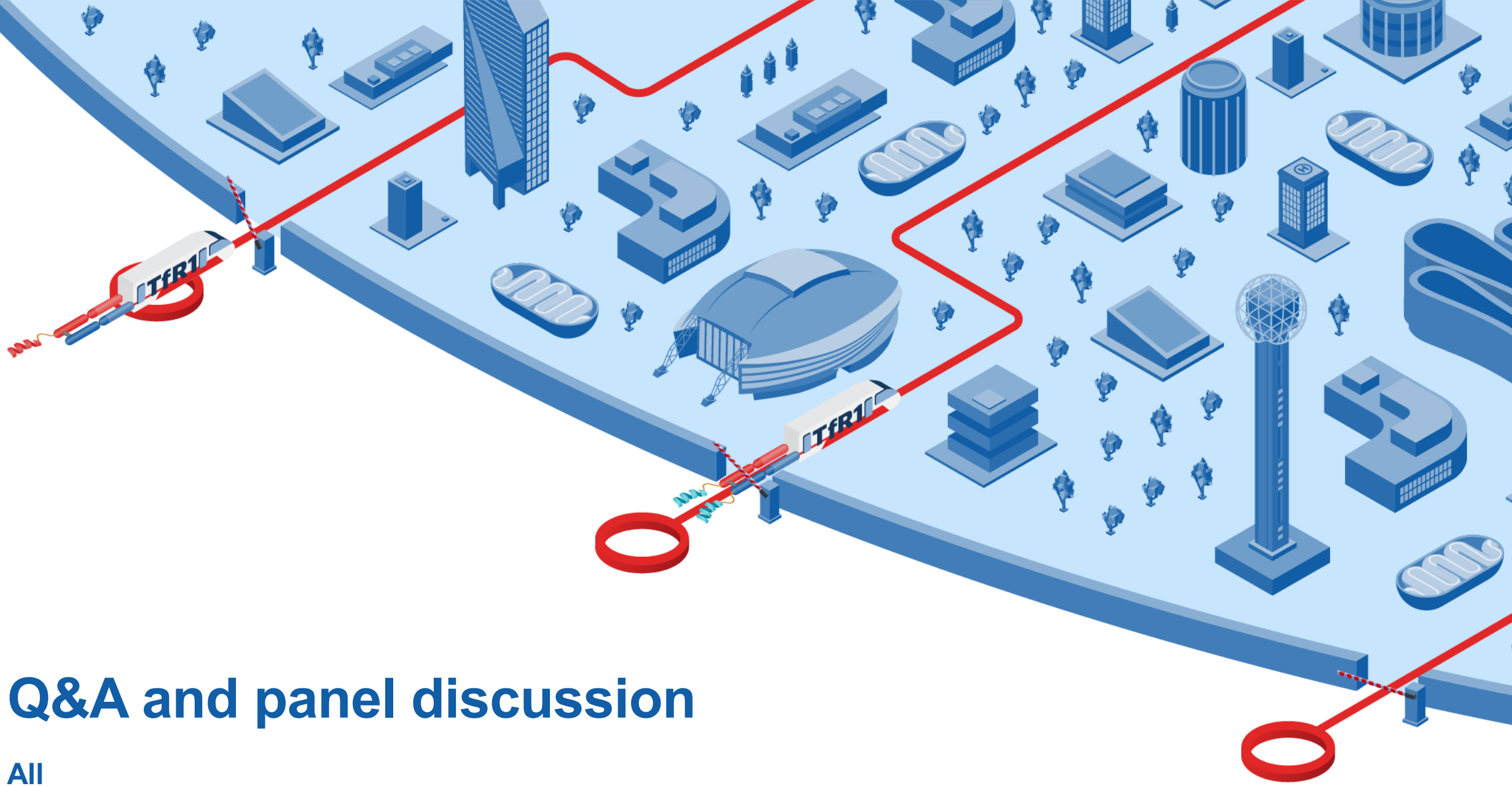
	DYNE-101[1,2]	DYNE-251[3,4]	DYNE-302[5,6]	DYNE-401[7]
				
Payload	ASO	PMO	siRNA	GAA (enzyme)
Disease-modifying target	*DMPK* mRNA	*DMD* exon 51 skipping	*DUX4* mRNA	Lysosomal glycogen accumulation
Localization	Nucleus	Nucleus	Cytoplasm	Lysosome
Demonstrated delivery[a]	• Muscle • CNS[b]	• Muscle • CNS[b]	• Muscle	• Muscle • CNS
Development stage	DM1 (Phase 1/2)	DMD (Phase 1/2)	FSHD (Preclinical)	Pompe disease (Preclinical)

The FORCE platform, DYNE-251, DYNE-101, DYNE-302 and DYNE-401 are investigational or otherwise in development and have not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.

a. Based on clinical and/or preclinical data. b. CNS data in DM1 and DMD generated using surrogate conjugates.

ASO, antisense oligonucleotide; CNS, central nervous system; DM1, myotonic dystrophy type 1; DMD, Duchenne muscular dystrophy; DMPK, dystrophia myotonica protein kinase; DUX4, double homeobox 4; FSHD, facioscapulohumeral muscular dystrophy; GAA, acid alpha-glucosidase; mRNA, messenger ribonucleic acid; PMO, phosphorodiamidate morpholino oligomers; siRNA, small interfering RNA.

1. van Engelen B, et al. Presentation at 14th International Myotonic Dystrophy Consortium Meeting. April 11, 2024; 2. Zanotti S. Presentation at the 26th American Society of Gene and Cell Therapy Annual Meeting. May 17, 2023. Los Angeles, USA. Abstract 82; 3. Desjardins CA, et al. Poster presentation the 2025 MDA Clinical and Scientific Conference. March 16–19, 2025. Dallas, USA. Poster 004; 4. Shieh P. Presentation at 2024 AAN Annual Meeting, April 15, 2024. Abstract 004; 5. Natoli T. Presentation at 31st Annual FSHD Society International Research Congress. June 13–14, 2024. Abstract S2.03; 6. Khvorova A. JAMA. 2023;329(4):2185–2186; 7. Zanotti S. Presentation at 2024 New Directions in Biology and Disease of Skeletal Muscle Conference. June 23–26, 2024. Fort Lauderdale, USA.



Q&A and panel discussion

All

Key scientific highlights

The FORCE platform leverages the natural expression of TfR1 to enable targeted delivery of rationally selected disease-modifying therapies to correct the underlying cause of neuromuscular diseases and achieve broad distribution to tissues relevant to disease pathology	**Payload and distribution matter**
DYNE-251 has a favorable safety profile, with some participants on therapy for 2.5 years[a], and has shown long-term improvement in clinical and real-world functional outcomes in individuals with DMD	**Long-term, sustained efficacy and favorable safety with DYNE-251**
DYNE-101 addresses the underlying pathobiology (dysregulated splicing) of DM1 and has demonstrated a favorable safety profile[b] and clinically meaningful improvements on measures of strength, mobility and QoL, including CNS manifestations – Improvements in areas that patients find most impactful: muscle weakness and CNS-related manifestations[1]	**Splicing correction with DYNE-101 predicts clinically meaningful functional outcomes**
The FORCE platform has the potential to transform the lives of individuals living with neuromuscular disorders by addressing the totality of symptoms experienced by these individuals, including CNS manifestations	**Transformational potential of the FORCE platform**

The FORCE platform, DYNE-251 and DYNE-101 are investigational or otherwise in development and have not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.

a. Data as of February 7, 2025; b. Data as of December 6, 2024.

CNS, central nervous system; DM1, myotonic dystrophy type 1, DMD, Duchenne muscular dystrophy; HCP, healthcare provider; PRO, patient-reported outcome; QoL, quality of life; TfR1, transferrin receptor 1.

1. Hagerman KA, et al. *Muscle Nerve* 2019;59:457–464.

Please remember to complete the meeting evaluation form

By scanning the QR code (also available on the tent card at your table) or completing the printed evaluation form

2025 MDA Clinical & Scientific Conference Industry Forum sponsored by Dyne Therapeutics

Harnessing the FORCE™ Platform to Advance Targeted Therapies for Neuromuscular Diseases

Evaluation Form

Thank you for taking the time to complete our post-symposium survey.
Your feedback is invaluable to us and will help improve future events.

All responses are confidential and anonymous.

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1. Please indicate your field of work:

- ○ Research student
- ○ Research scientist
- ○ Clinician: neuromuscular specialist
- ○ Clinician: adult neurologist
- ○ Clinician: pediatric neurologist
- ○ Clinician: physical therapist
- ○ Clinician: other specialty (e.g. cardiology, pulmonology, etc)
- ○ Industry
- ○ Patient advocacy group, NGO, or charitable organization
- ○ Other _____

2. Please score your understanding and awareness of the following before the symposium for each category (1 = low awareness, 5 = high awareness)

	1	2	3	4	5
Unmet needs in management of neuromuscular diseases	○	○	○	○	○
Design and purpose of the Dyne FORCE platform	○	○	○	○	○
Data from Dyne's investigational therapies using the FORCE platform	○	○	○	○	○

3. Please score your understanding and awareness of the following after the symposium for each category (1 = low awareness, 5 = high awareness)

	1	2	3	4	5
Unmet needs in management of neuromuscular diseases	○	○	○	○	○
Design and purpose of the Dyne FORCE platform	○	○	○	○	○
Data from Dyne's investigational therapies using the FORCE platform	○	○	○	○	○

Please continue the evaluation form overleaf ▸

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was your overall impression of the following? (1 = poor, 5 = excellent) 1 2 3 4 5

- ll quality of the symposium content ○ ○ ○ ○ ○
- ll format of the symposium ○ ○ ○ ○ ○
- ll scientific and clinical relevance of the content ○ ○ ○ ○ ○

likely are you to attend future symposium similar to this one? 1 2 3 4 5
ery unlikely, 5 = very likely) ○ ○ ○ ○ ○

scored lower than 3, please explain why:

e share any additional comments with the organizers in order to help improve future events:

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Visit us at booth #504

to discover more about the FORCE platform and explore our digital content, or scan the QR code for digital handouts on the following topics:

- Think you know DM1?
- What is a spliceopathy?
- One disease, multiple symptoms
- The splice index as a biomarker in DM1
- Understanding dystrophin in DMD
- Motor function assessments in DMD

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Thank you