



**AVIDITY**<sup>®</sup>  
BIOSCIENCES

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# Delivering on the RNA Revolution

**September 2024**

NASDAQ: RNA | [aviditybio.com](https://aviditybio.com)



# Forward-Looking Statements

We caution the reader that this presentation contains forward-looking statements that involve substantial risks and uncertainties. All statements other than statements of historical fact contained in this presentation are forward-looking statements. Forward-looking statements include, but are not limited to, statements regarding: our business strategy; the anticipated timing, costs, design, goals and conduct of our ongoing and planned preclinical studies and clinical trials; the timing of release of data from our ongoing clinical programs and the announcement of new programs; the timing of additional cohorts to existing clinical trials, including dosage levels and other details thereof; the characterization of data and results from preclinical studies and clinical trials and conclusions drawn therefrom; research and development plans; plans and projected timelines for delpacibart etedesiran (*del-desiran*, formerly AOC 1001), delpacibart braxlosiran (*del-brax*, formerly AOC 1020) and delpacibart zotadirsen (*del-zota*, formerly AOC 1044); safety and tolerability profiles of our product candidates; efficacy or functional data demonstrated by our product candidates; our plans regarding our DMD franchise; the potential of the AOC platform and specific product candidates; the regulatory pathways of our product candidates; the status and potential of our product candidates as first-in-class and/or best-in-class; the ability of our product candidates to treat rare diseases; timing and likelihood of success; product approvals; plans and objectives of management for future operations; collaborations with third parties and expected benefits therefrom; the partial clinical hold related to *del-desiran*; and our cash position and our ability to fund our planned operations. In some cases, the reader can identify forward-looking statements by terms such as “may,” “will,” “should,” “expect,” “plan,” “anticipate,” “could,” “intend,” “target,” “project,” “contemplates,” “believes,” “estimates,” “predicts,” “potential” or “continue” or the negative of these terms or other similar expressions. The inclusion of forward-looking statements should not be regarded as a representation by Avidity that any of our plans will be achieved. Actual results may differ from those set forth in this presentation due to the risks and uncertainties inherent in our business based on factors beyond our control, including, without limitation: we may not be able to fully resolve the partial clinical hold related to *del-desiran*; additional requests for data by the FDA or other regulatory authorities may result in significant additional expense and timing delays; data delivered to the FDA may not be satisfactory to the FDA; additional participant data related to our product candidates that continues to become available may be inconsistent with the data produced as of the most recent respective date cutoffs, and further analysis of existing data and analysis of new data may lead to conclusions different from those established as of such date cutoffs; unexpected adverse side effects or inadequate efficacy of our product candidates may delay or limit their development, regulatory approval and/or commercialization, or may result in additional clinical holds, recalls or product liability claims; we are early in our development efforts; our approach to the discovery and development of product candidates based on our AOC platform is unproven, and we do not know whether we will be able to develop any products of commercial value; the results of preclinical studies and early clinical trials are not necessarily predictive of future results; potential delays in the commencement, enrollment and completion of clinical trials, or of designations conferred by regulatory authorities; our dependence on third parties in connection with preclinical and clinical testing and product manufacturing; we may not realize the expected benefits of our collaborations with third parties, our existing collaborations may terminate earlier than expected or we may not be able to form new collaborations; regulatory developments in the United States and foreign countries, including acceptance of INDs and similar foreign regulatory submissions and our proposed design of future clinical trials; Fast Track or Breakthrough Designation by the FDA may not lead to a faster development or regulatory review or approval process; our ability to obtain and maintain intellectual property protection for our product candidates and proprietary technologies; we may exhaust our capital resources sooner than we expect and fail to raise additional needed funds; and other risks described under the heading “Risk Factors” in our Form 10-K for the year ended December 31, 2023, filed with the SEC on February 28, 2024, and in subsequent filings with the SEC. The reader is cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise. All forward-looking statements are qualified in their entirety by this cautionary statement, which is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995.

This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and the reader is cautioned not to give undue weight to such estimates. In addition, projections, assumptions, and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk. These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties and by us. This presentation shall not constitute an offer to sell or the solicitation of an offer to buy securities, nor shall there be any sale of securities in any state or jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such state or jurisdiction.



**Luke**  
Living with DM1

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## OUR VISION

**To profoundly improve  
people's lives by  
revolutionizing  
the delivery of  
RNA therapeutics**

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# Building a New Class of RNA Therapeutics

Well positioned for next phase of growth

## BROAD & DISRUPTIVE PLATFORM

- AOC platform led to historical first-ever successful delivery of RNA to muscle with *del-desiran*; repeated with *del-brax* and *del-zota* with unprecedented data across all three clinical programs
- Expanding our therapeutic expertise, particularly in precision cardiology, through research collaborations and internal discovery efforts

## WORLD CLASS TEAM OF RNA & RARE DISEASE EXPERTS

- Committed to innovative science matched by passion to improve people's lives
- Building an integrated and diverse company in service of our patients

## STRONG FINANCIALS & INVESTOR CONFIDENCE

- Solid cash position of ~\$1.6 billion provides funding into mid 2027\*
- Advancing our three clinical development programs for *del-desiran*, *del-brax* and *del-zota* into pivotal studies and further expanding our DMD franchise and AOC platform, including precision cardiology programs

# Delivering in 2024: 3 Data Readouts in 3 Clinical Programs in 3 Rare Diseases

## *Del-desiran* in DM1

>40,000 patients in U.S.



- ✓ MARINA-OLE™ data (Q1 2024)
- ✓ Initiation of global Phase 3 HARBOR trial (Q2 2024)

## *Del-brax* in FSHD

~16,000-38,000 patients in U.S.



- ✓ Phase 1/2 FORTITUDE initial data (Q2 2024)

Initiate Phase 3 cohorts

- Biomarker cohort (2H 2024)
- Functional cohort (1H 2025)

## *Del-zota* in DMD44

~900 patients in U.S.



- ✓ Phase 1/2 EXPLORE44 5mg/kg patient data (Q3 2024)

# Revolutionizing New Class of Targeted RNA Therapeutics

AOC platform delivers reproducible, consistent data across muscle disease programs

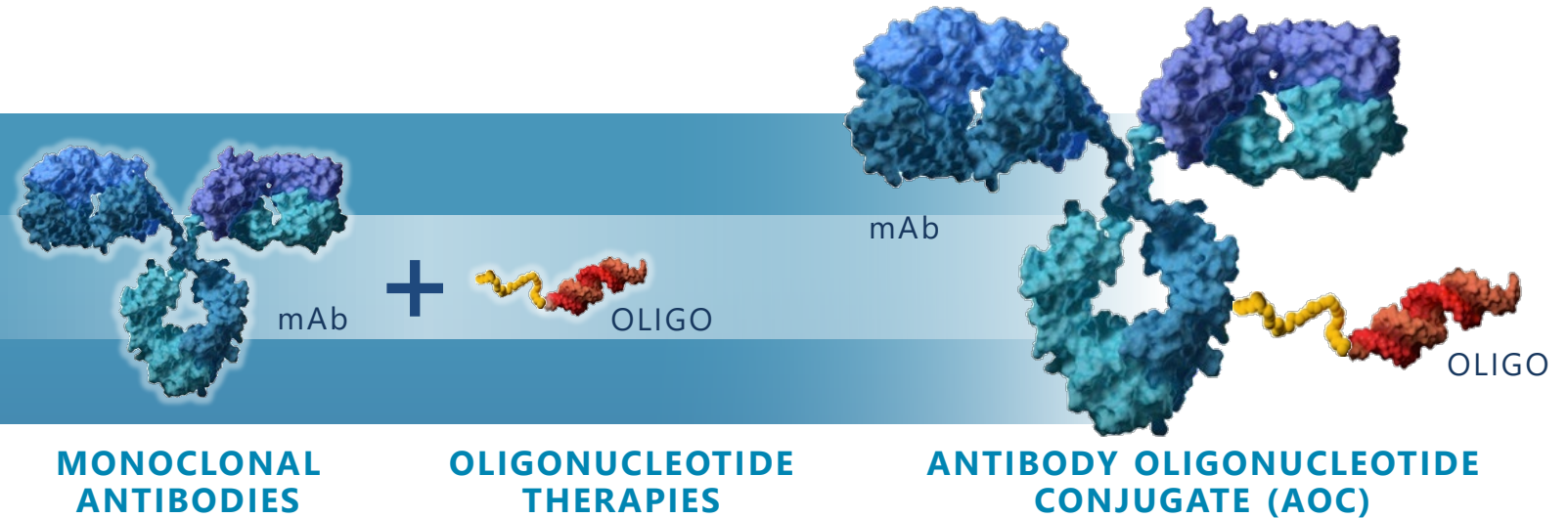
Rare Muscle Disease Therapies	Clinical Program	Safety & Tolerability	Delivery to Muscle	Target Engagement	Functional Improvement
<b><i>Del-desiran</i></b> Myotonic Dystrophy Type 1 (DM1)	 MARINA <sup>®</sup> MARINA <sup>OLE</sup> <sup>™</sup> HARBOR <sup>™</sup>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
<b><i>Del-brax</i></b> Facioscapulohumeral Muscular Dystrophy (FSHD)	 FORTITUDE <sup>™</sup>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
<b><i>Del-zota</i></b> Duchenne Muscular Dystrophy (DMD44)	 explore 44 <sup>™</sup>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	

# Delivering on the RNA Revolution

PROGRAM / INDICATION	TARGET	LEAD OPTIMIZATION	IND ENABLING	PHASE 1/2	PHASE 3
Myotonic Dystrophy Type 1 (DM1)	DMPK	<i>Del-desiran</i> <sup>TM</sup> (AOC 1001)			HARBOR <sup>TM</sup>
Facioscapulohumeral Muscular Dystrophy (FSHD)	DUX4	<i>Del-brax</i> <sup>TM</sup> (AOC 1020)			FORTITUDE <sup>TM</sup>
Duchenne Muscular Dystrophy (DMD)	Exon 44	<i>Del-zota</i> <sup>TM</sup> (AOC 1044)			explore 44 <sup>TM</sup>
DMD Exon 45	Exon 45				
Additional DMD Programs	Undisclosed				
Rare Skeletal Muscle	Undisclosed				
Rare Precision Cardiology	To be disclosed in Q4 24				

# Key to Our Success: Proprietary AOC™ Platform

Combining the specificity of mAbs with the precision of oligonucleotide therapies

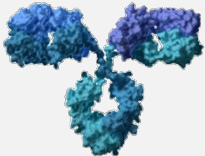

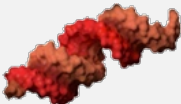



## AOC platform advantages:

- ✓ Ability to target new tissue and cell types beyond the liver
- ✓ Flexibility to select and deploy the most potent oligonucleotides (e.g., siRNAs, PMOs)
- ✓ Maximizes therapeutic durability, enabling infrequent dosing
- ✓ Readily reproducible and scalable

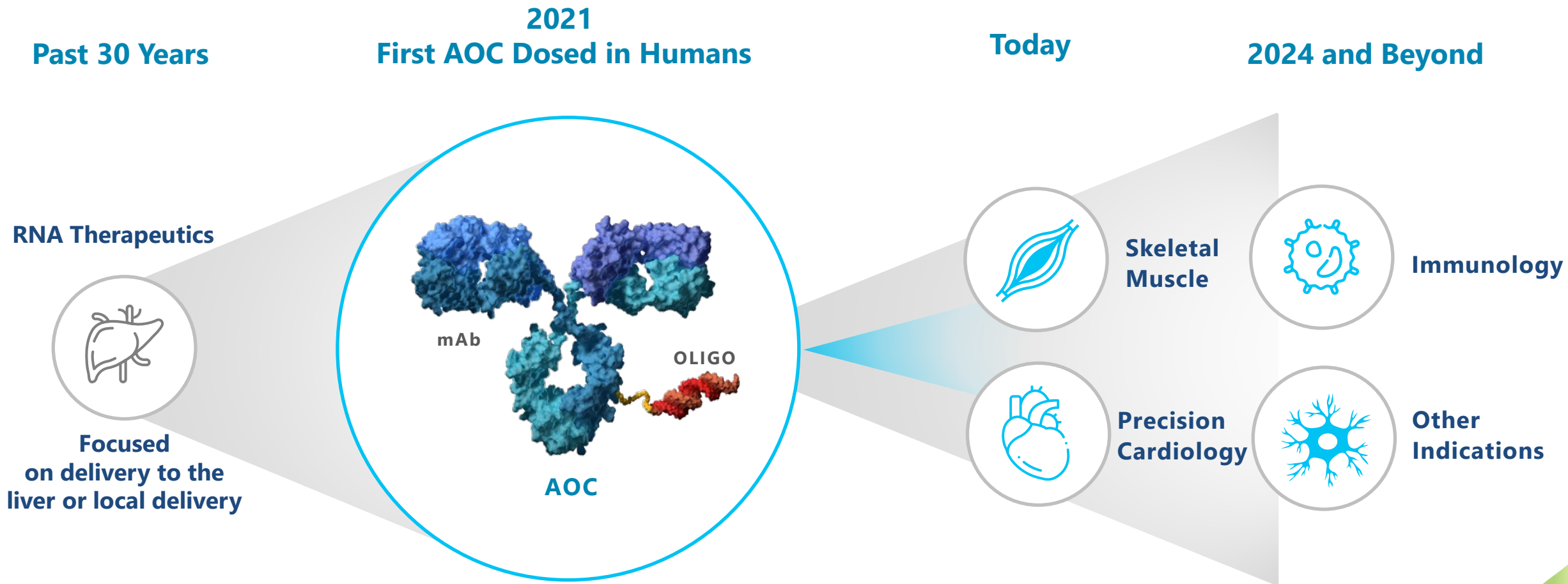


# The Optimal AOC for Each Target

AOC COMPONENTS		DATA-DRIVEN COMPONENT CHARACTERISTICS	OUR ENGINEERING IMPACT
mAb		<ul style="list-style-type: none"> <li>Well-established safety profile</li> <li>High specificity and affinity</li> <li>Long half-life</li> </ul>	<ul style="list-style-type: none"> <li>Designed to be effector function null</li> <li>Epitope selection designed for optimal activity</li> </ul>
Linker		<ul style="list-style-type: none"> <li>Known linker</li> <li>Applicable to multiple oligo modalities</li> </ul>	<ul style="list-style-type: none"> <li>Enhanced for durability</li> <li>Engineered sites of conjugation</li> <li>Optimized ratio of oligonucleotides to mAbs</li> </ul>
Oligonucleotide	siRNA 	<ul style="list-style-type: none"> <li>Attractive safety profiles</li> <li>Potency in the nanomolar range</li> <li>Sustained activity in the cytoplasm and nucleus</li> </ul>	<ul style="list-style-type: none"> <li>Engineered to withstand lysosomal enzymes</li> <li>Selected and modified to diminish off-target effects</li> </ul>
	PMO 	<ul style="list-style-type: none"> <li>Attractive safety profile</li> <li>Potency in the nanomolar range</li> <li>Sustained activity</li> </ul>	<ul style="list-style-type: none"> <li>Engineered for efficient delivery to muscle – increased drug to antibody ratio</li> </ul>

# Avidity Is Opening the Possibilities of RNA Delivery

First-ever company to demonstrate successful targeted delivery of RNA to muscle





## ***Del-desiran (AOC 1001) Program for Myotonic Dystrophy Type 1 (DM1)***

***“Some days I don’t have the energy to take another step.”***

*— Karin, living with DM1*

# DM1: Significant Patient Burden and Unmet Need

>40,000

PEOPLE WITH DM1 IN THE US

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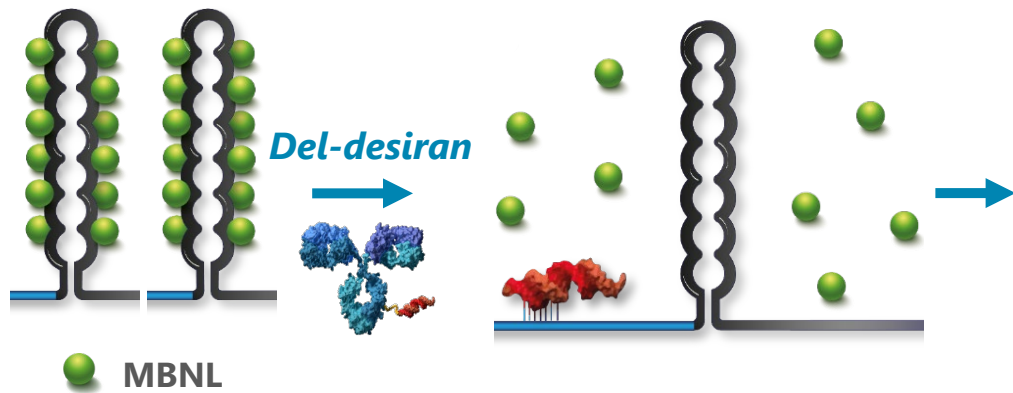
APPROVED THERAPIES

- Underrecognized, progressive & often fatal neuromuscular disease that primarily affects skeletal, cardiac & smooth muscle
- Increases in severity from generation to generation
- Significant impact on quality of life
- *Del-desiran* is designed to address root cause of DM1



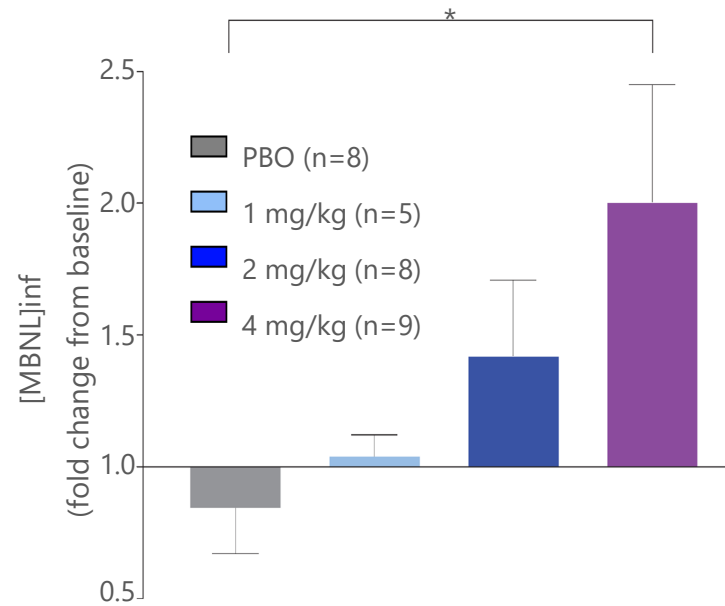
Loraine,  
Kristl & Zen  
Living with DM1

# Del-desiran Designed to Address Underlying Cause of Myotonic Dystrophy by Liberating Free MBNL



MBNL sequestered by CUG repeats of mutant DMPK

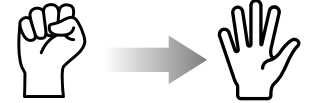
*Del-desiran* (AOC 1001) treatment Reduced mutant DMPK



\**Del-desiran* (AOC 1001) Leads to Dose-dependent increase in MBNL

MARINA<sup>®</sup>  
MARINA<sup>OLE</sup><sup>™</sup>

Video Hand Opening Time (vHOT)



MYOTONIA

Hand Grip Quantitative Muscle Testing



STRENGTH



DM1-Activ



ACTIVITIES OF DAILY LIVING

## Recent *del-desiran* Program Updates

- Initiated and began administration of *del-desiran* in the global Phase 3 HARBOR™ trial in people living with myotonic dystrophy type 1 (DM1)
- In May 2024, received Breakthrough Therapy designation from the FDA for *del-desiran* for the treatment of DM1
- Secured regulatory agreement with FDA, EMA and other global regulatory authorities on the Phase 3 HARBOR™ trial design
- All MARINA-OLE™ study participants moving to 4 mg/kg of *del-desiran*
- In March 2024, presented first-look at long-term efficacy and safety data from MARINA-OLE™ trial in people living with DM1 at MDA Clinical & Scientific Conference
  - Data from MARINA-OLE™ showed reversal of disease progression in multiple functional measures in people living with DM1 compared to END-DM1 natural history data
  - Data demonstrated consistent and durable improvements in myotonia, muscle strength and activities of daily living in people with DM1 in new long-term data from MARINA-OLE™

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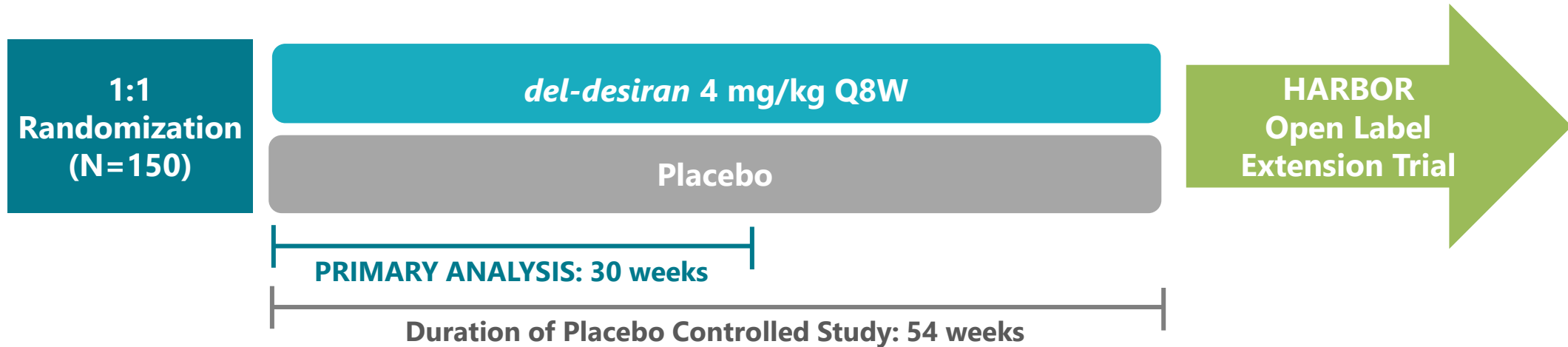
## **Global Phase 3 HARBOR™ Trial Design for Myotonic Dystrophy Type 1 (DM1)**

**March 2024**



# HARBOR™ Initiating Global Phase 3 Study

- Initiated Phase 3 HARBOR™ Study
- FDA, EMA and other global regulatory authorities in agreement on study design
- HARBOR™ study designed for efficiency and speed of execution





# HARBOR™ Phase 3 Trial: Design & Objectives

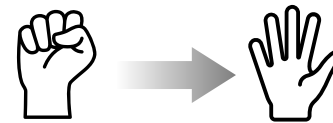
Optimized for efficiency and speed of execution

## Pivotal Study Design

- 4 mg/kg every 8 weeks; first dose of 2 mg/kg
- N=150; Ages 16+
- 1:1 randomization
- Primary analysis at Week 30; Placebo-control out to week 54
- Participants eligible to roll-over into an open label extension
- ~40 global sites

## Primary Endpoint

### Video Hand Opening Time (vHOT)



MYOTONIA

## Key Secondary Endpoints

### Hand Grip



STRENGTH

### Quantitative Muscle Testing



### DM1-Activ



ACTIVITIES OF DAILY LIVING

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## **MARINA-OLE™ Long-term Safety & Efficacy Data in Patients with DM1 Presented at MDA Scientific Conference**

**March 2024**

# Phase 1/2 MARINA<sup>®</sup> and MARINA-OLE<sup>™</sup> Trial Design

MARINA<sup>®</sup>

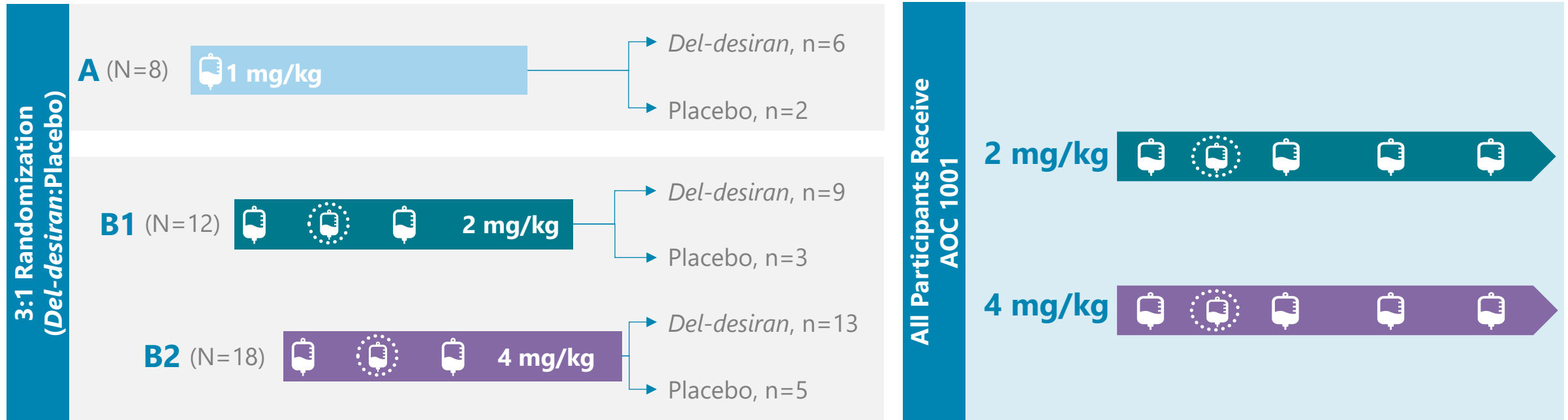


Dose



Booster

MARINA-OLE<sup>™</sup>



- In MARINA, one participant receiving 4 mg/kg *del-desiran* discontinued treatment due to SAE
- All eligible participants (N=37) have enrolled in the MARINA-OLE<sup>™</sup>

# MARINA-OLE™ Favorable Long-term Safety and Tolerability

Over 265 infusions of *del-desiran* totaling 61.1 patient-years of exposure

MARINA-OLE™	Number (%) with AE N=37
Subjects with ≥ 1 AE	
Any AE	35 (94.6%)
AE related to study drug	9 (24.3%)
Unrelated serious AE (SAE)	4 (10.8)
SAE related to study drug	0
AE leading to treatment discontinuation	0
AE leading to death	0

## MARINA-OLE™

- **All 37 participants enrolled remain on study**
- **All related AEs were mild or moderate**
  - Most common related AEs reported in 2 or more participants:
    - Nausea
    - Headache
  - No discontinuations
  - No study drug related SAEs; unrelated SAEs are consistent with DM1



# END-DM1 Natural History Study: Understanding DM1 Disease Progression

- Ongoing non-interventional NHS aimed to advance the understanding of disease progression in DM1 patients
- Focuses on clinical outcome assessments to support development of therapies for DM1
- 700 patient, 2-year study, ~ 20 centers
- Designed and run by the Myotonic Dystrophy Clinical Research Network (DMCRN)
- Supported by FDA, MDA, MDF; Avidity is one of several sponsoring organizations

# END-DM1 Data Informed Design of the MARINA<sup>®</sup> & Phase 3 HARBOR Trials

Presenting one-year data for the first time today



Same endpoints measured



Clinical trial sites overlap with MARINA<sup>®</sup> & HARBOR



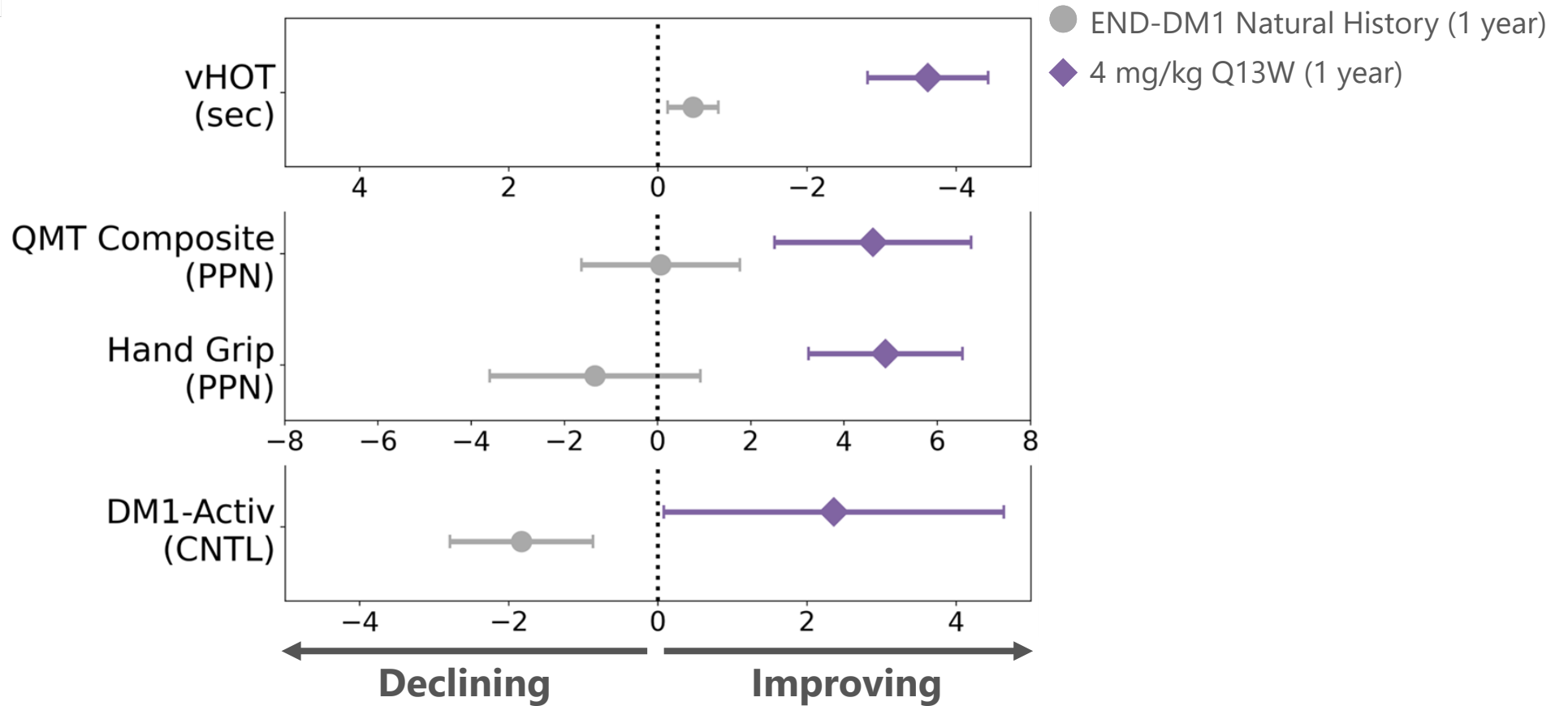
Contemporary data set based upon standard of care



Hundreds of patients with at least one-year of follow-up in END-DM1 natural history study

# Del-desiran: Reversal of Disease Progression as Measured by MARINA-OLE™ vs. Natural History

Key endpoints to be used in pivotal HARBOR study



Thanks to END-DM1 physicians for reviewing and approving use of this Avidity analysis; END-DM1 subpopulation matched to MARINA® (n ~ 60)

In MARINA-OLE™ data 4 mg/kg, n=12 for vHOT, QMT composite, hand grip; n=11 for DM1-Activ

PPN = Percent predicted normal

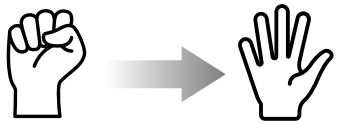
CNTL= percentile

Error bars = SEM (standard error of the mean)

# Del-desiran: Long-term Improvement in Myotonia

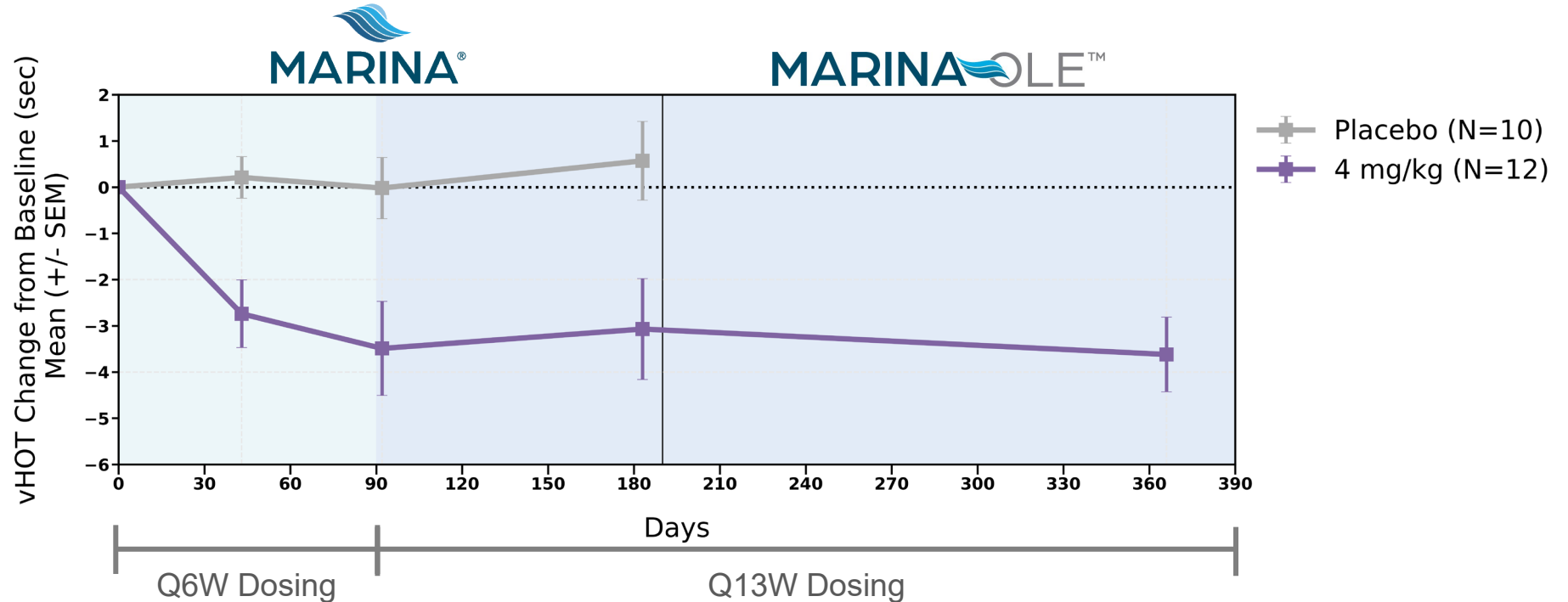
Measured by video hand opening time (vHOT) in MARINA<sup>®</sup> and MARINA-OLE<sup>™</sup>

Video Hand Opening Time (vHOT)



Independently adjudicated

Improvement ↓



**MARINA<sup>®</sup> data statistically significant at all assessment time points\***



# *Del-desiran*: Long-term Improvement in Myotonia

Measured by video hand opening time (vHOT) in MARINA<sup>®</sup> and MARINA-OLE<sup>™</sup>

Participant from  
*del-desiran* 4 mg/kg

Baseline vHOT



MARINA-OLE<sup>™</sup>  
(1 year of 4 mg/kg)



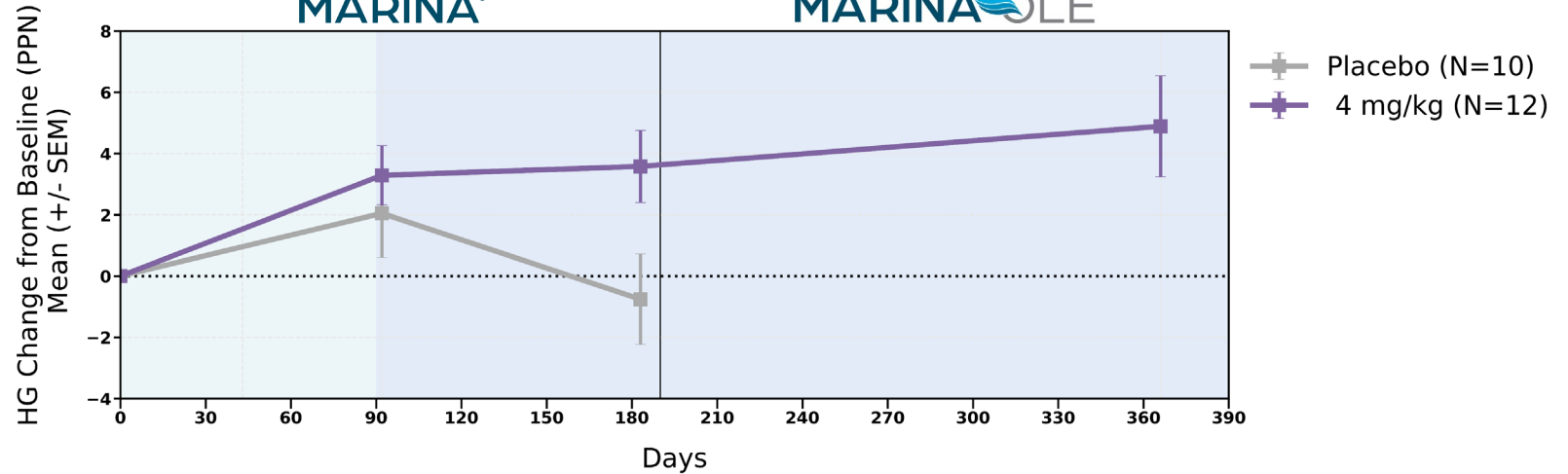
# Del-desiran: Long-term Improvement in Muscle Strength

## Measured by Hand Grip and Quantitative Muscle Testing in MARINA<sup>®</sup> and MARINA-OLE<sup>™</sup>

### Hand Grip Strength



Improvement ↑



### Quantitative Muscle Testing (QMT)



Hand Grip

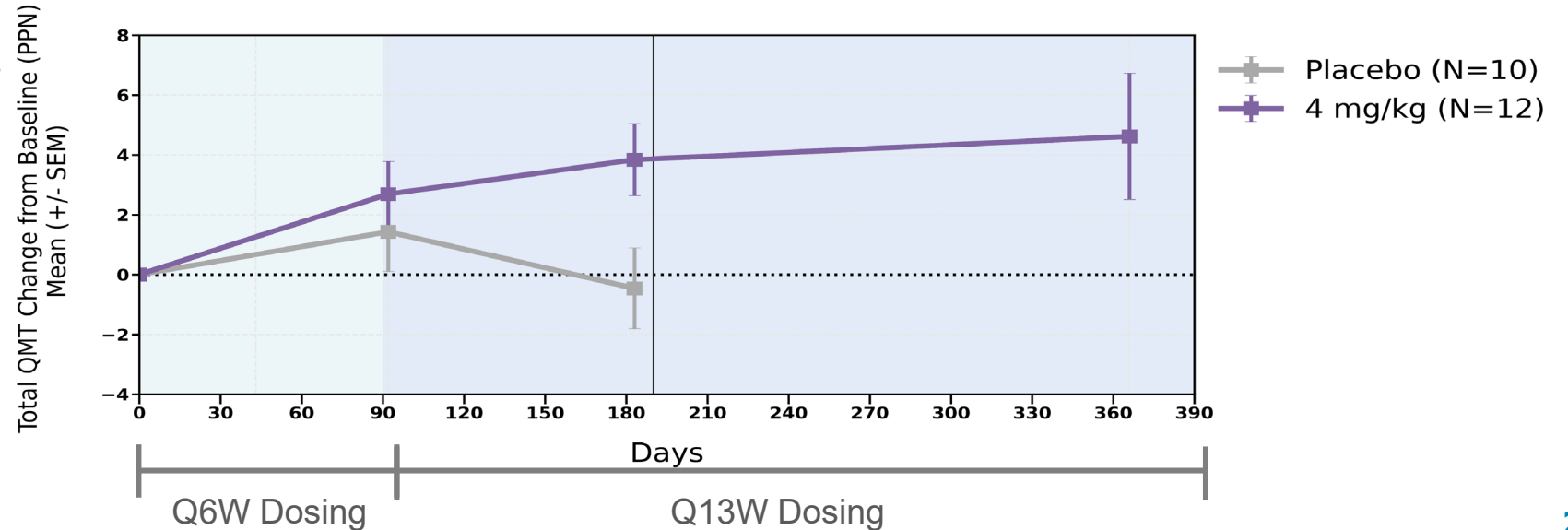
Elbow Extension & Elbow Flexion



Knee Extension & Knee Flexion

Ankle Dorsiflexion

Improvement ↑



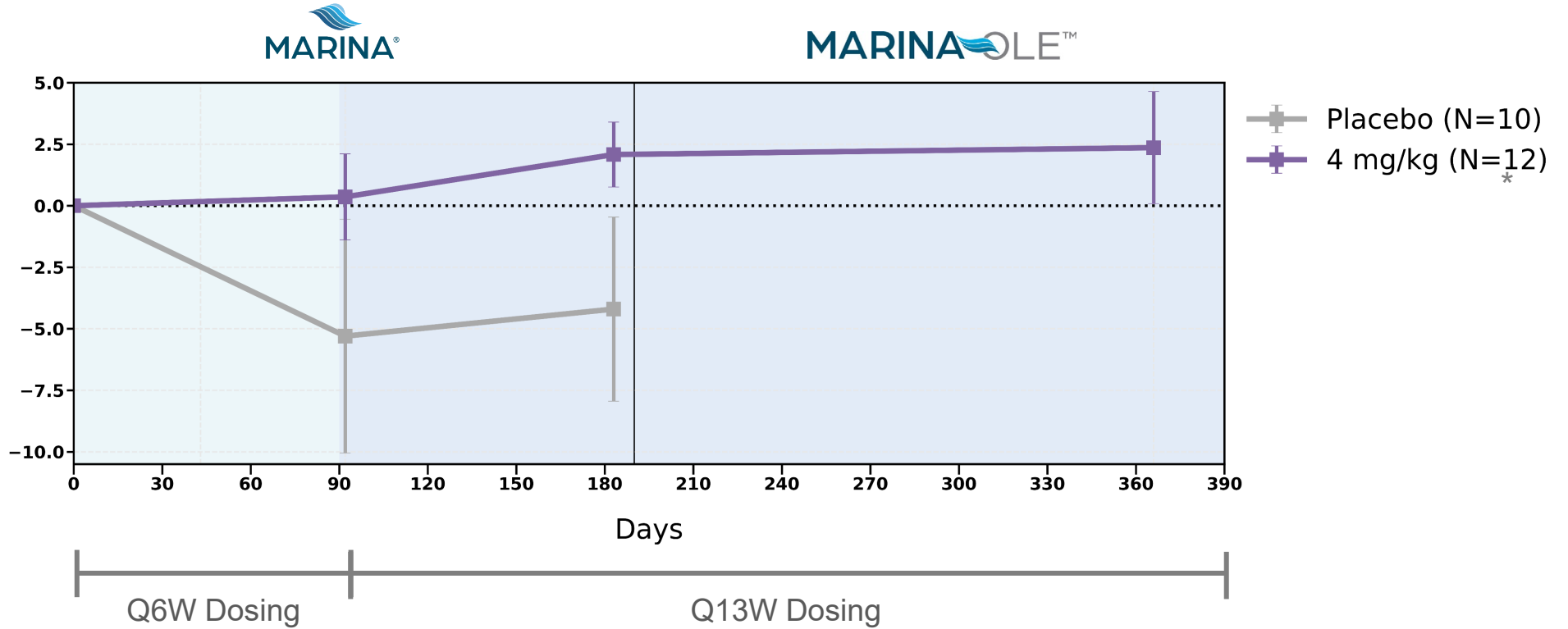
# Del-desiran: Long-term Improvement in Activities of Daily Living Measured by DM1-Activ Patient Reported Outcomes in MARINA<sup>®</sup> and MARINA-OLE<sup>™</sup>

DM1-Activ



Improvement

DM1-Activ Change from Baseline (CNTL)  
Mean (+/- SEM)

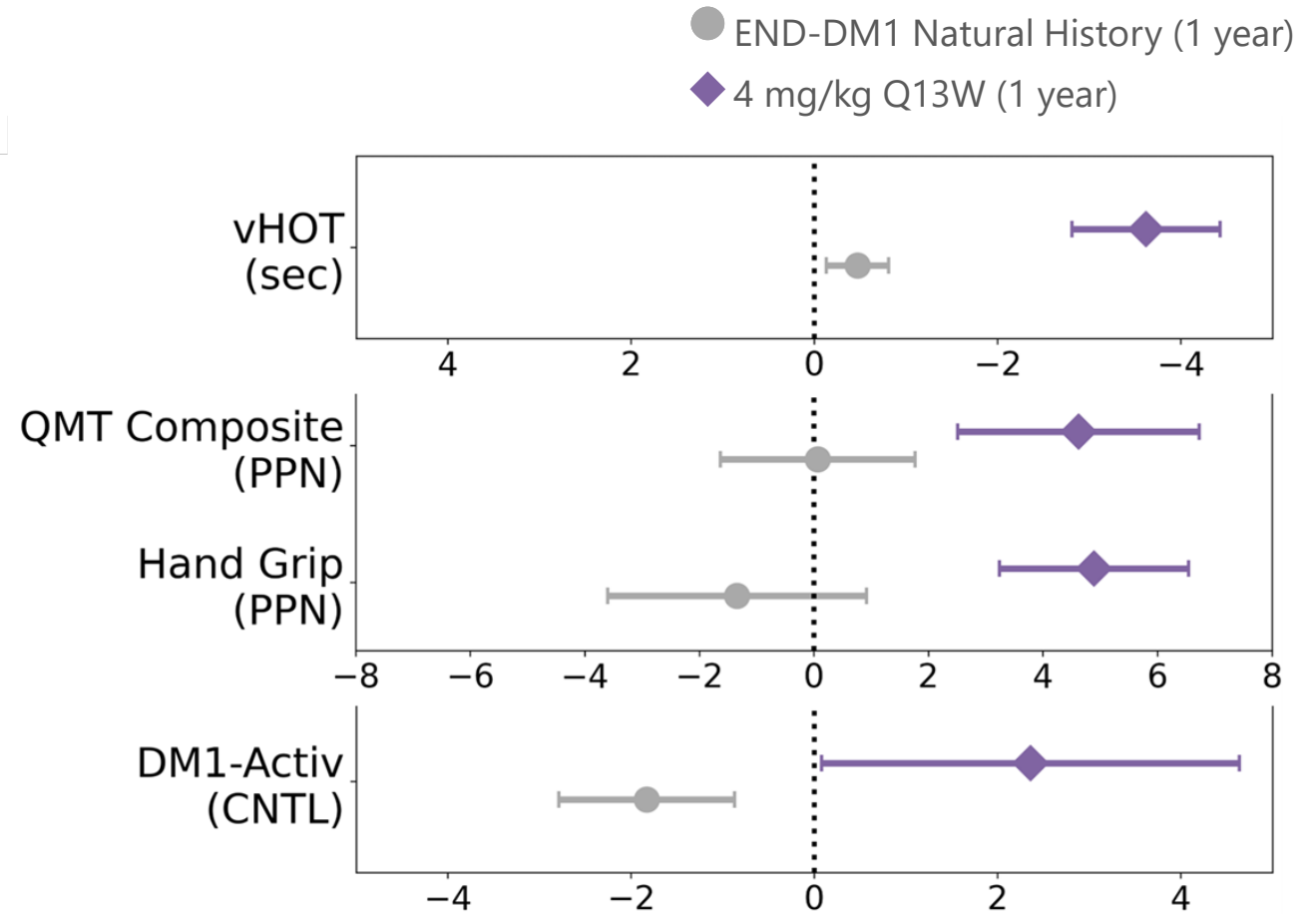


\*Day 360 excludes one participant who experienced an injury impairing their ability to perform mobility measures.  
CNTL= percentile  
SEM = standard error of the mean

# MARINA-OLE™ Data Summary

## Potential of *del-desiran* to be a transformational therapy for DM1 patients

- *Del-desiran* 4 mg/kg
  - Demonstrated favorable long-term safety and tolerability
  - Showed reversal of disease progression in MARINA® and MARINA-OLE™ compared to END-DM1 natural history data
  - Provided consistent and durable improvements in multiple clinical endpoints
- Global Phase 3 HARBOR™ trial initiated



# Patient Experiences: Impact of *del-desiran* on their life

“ I started this drug in June and like, two weeks after I took the first infusion, I went to open up a pop bottle, which I never would've been able to do. It **was a twist pop bottle...and it opened right up.**

My **strength was better, my outlook was better, my hands were working.**

I had more strength, and I could stretch them out. I could **open things and I could turn door knobs** and all these things that were harder.

Like, my **upper arm strength was better.** I could **walk better.**

I didn't need to wear my neck brace all the time and **everything just improved a lot.**”



“ Before the study I couldn't stand on my toes and since I've been **going back to working out, I can actually stand on my toes again.** So hopefully **building up some strength.**

The myotonia, if I would make a fist, I wouldn't be able to open my hand...I was able to squeeze my fist and **open my hand with no problems.**

My **tongue would cramp up when I would speak,** and I have not had any signs of that happening since the very first dose.”



## Patient Experience: Impact of *del-desiran* on their life MARINA<sup>OLE</sup>™

“ I've noticed a really big difference in the fact that I used to be a really active person before I got more symptomatic. After a few rounds of the infusion, I've actually been able to **get back to the gym and start working out**, working with a trainer. That's all because **my mobility has definitely increased**. My **range of motion has also increased**.

I think that it's amazing that when I was diagnosed, I was told there's no treatment, no cure. The study has **given me a lot of hope**. I would love for that to be able to be shared with other people in the community who have DM1. ”



# Delivering on DM1



- ✓ Initiation of global Phase 3 HARBOR trial - **Complete**
- ✓ FDA Breakthrough Therapy designation - **Complete**
- ✓ First look at MARINA-OLE long-term efficacy and safety data - **Complete**
- ✓ Demonstrated first-ever successful targeted delivery of RNA to muscle - **Complete**
- ✓ FDA & EMA Orphan Drug designation - **Complete**
- ✓ FDA Fast Track designation - **Complete**



## ***Del-brax (AOC 1020) Program for Facioscapulohumeral Muscular Dystrophy (FSHD)***

***“Living with FSHD feels like an  
imprisonment in your own body.”***

*— Amy, Living with FSHD*



# Facioscapulohumeral Muscular Dystrophy (FSHD)

Rare, hereditary disorder causing relentless loss of muscle function and progressive disability

~16,000 - 38,000

PEOPLE WITH FSHD IN THE US

0

APPROVED THERAPIES

- One of the most common forms of muscular dystrophy
- FSHD causes progressive muscle weakness, pain, fatigue and disability
- Onset typically occurs in teenage or early adult years
- Steady loss of independence and ability to care for oneself
  - 20% of patients become wheelchair dependent
- Autosomal dominant - multiple generations can be affected
  - 20-30% arise from spontaneous mutations
- **Del-brax**: designed to address root cause of FSHD by directly targeting double homeobox 4 (DUX4)

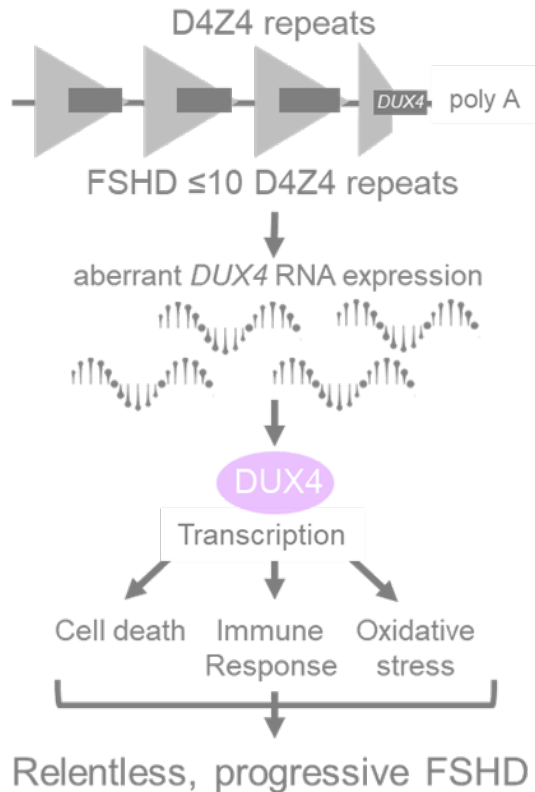


Russell  
Living with FSHD

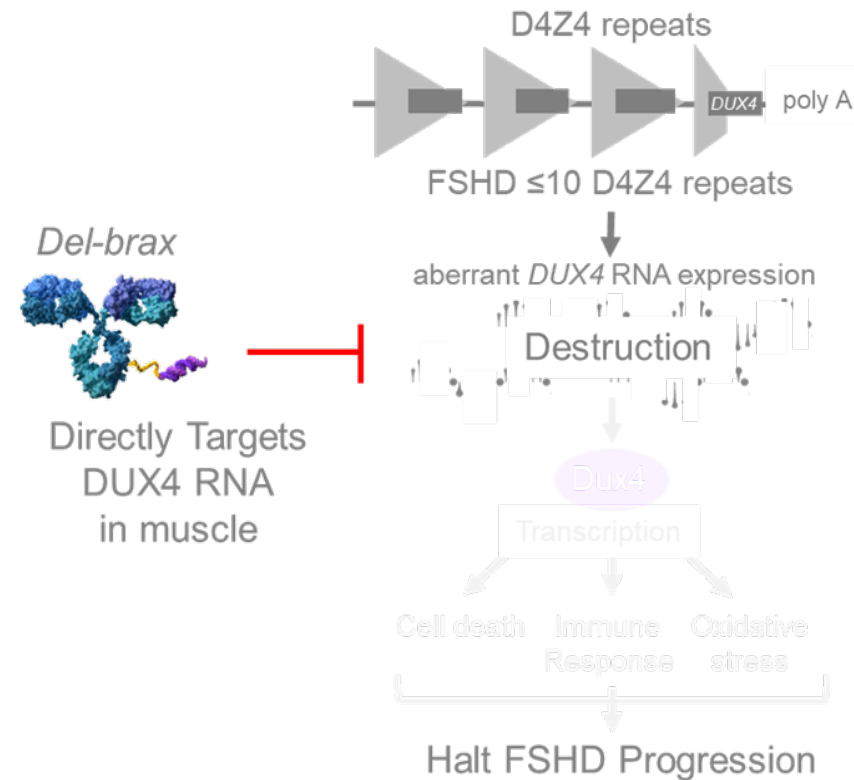
# Del-brax: Targets DUX4, the Root Cause of FSHD

Targets aberrant expression of DUX4 mRNA for destruction

## FSHD disease pathology<sup>1,2</sup>



## Del-brax Therapeutic Hypothesis





**Phase 1/2 FORTITUDE™ *del-brax* (AOC 1020) Data in  
People Living with FSHD Presented at the FSHD Society  
International Research Congress (IRC)**

June 2024

# Del-brax: Transforming the Treatment of FSHD

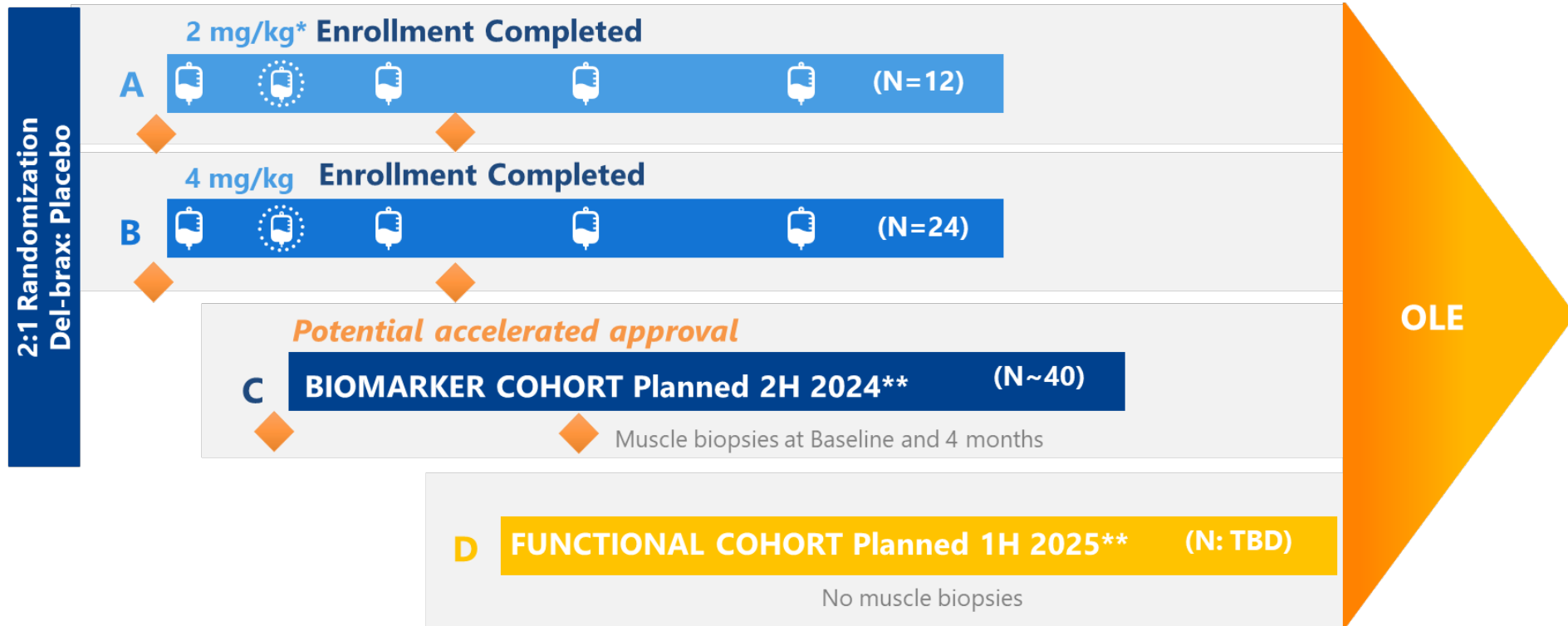
First-in-class and best-in-class: greater than 50% reduction in DUX4 regulated genes

Unprecedented & Consistent Reduction in DUX4 Regulated Genes	Signs of Functional Improvement and Reported Outcomes	Favorable Safety and Tolerability
<ul style="list-style-type: none"><li>• Greater than 50% reduction across multiple DUX4 gene panels</li><li>• All treated participants showed reductions greater than 20%</li><li>• Reduction of a newly-identified DUX4 circulating biomarker &amp; creatine kinase</li></ul>	<ul style="list-style-type: none"><li>• Improved muscle strength</li><li>• Increased reachable workspace compared to placebo and natural history study</li><li>• Positive patient and clinician reported outcomes</li></ul>	<ul style="list-style-type: none"><li>• All adverse events (AEs) were mild or moderate</li><li>• No serious AEs, No severe AEs</li><li>• No discontinuations</li></ul>

**Accelerating *Del-brax* Toward Approval**

# Accelerating *Del-brax* Registrational Plan

## Pulling forward registrational cohorts



Dose Booster Multidose quarterly with 1 booster after first 6 weeks; Dose listed is siRNA Muscle biopsies to be performed at Baseline and 4 months

\* Participants receive a first dose of 1mg/kg and then receive the 2mg/kg dose for the remainder of the study

\*\*Dose and schedule to be determined in Q3 2024

# Del-brax: Favorable Safety and Tolerability

Subjects with $\geq 1$ AE n (%)	Placebo N=13	2 mg/kg* N=8	4 mg/kg N=18
Any AE	11 (84.6%)	8 (100%)	17 (94.4%)
Related to study drug	3 (23.1%)	4 (50%)	9 (50%)
Severe AE	0	0	0
Serious AE (SAE)	0	0	0
AE leading to study discontinuation	0	0	0
AE leading to death	0	0	0

As of May 2024, data from FORTITUDE

## All 39 patients enrolled remain in study

- No serious adverse events (AE), no severe AE
- No discontinuations
- All AE were mild or moderate
- Most common related AE occurring in 2 or more participants:
  - Fatigue
  - Rash
  - Hemoglobin decreased/anemia
  - Chills

# Phase 1/2 FORTITUDE™ Trial Overview & Objectives

## Key Information

- Randomized, double blinded, placebo controlled
- Multiple dose
- N=39; Ages 18-65
- Follow-up of up to 12 months
- Biopsies in all cohorts

## Stages

### Phase 1/2

- Part A: 2 mg/kg single-cohort dose titration\*
- Part B: 4 mg/kg dose cohort\*\*

### Planned Phase 3 Cohorts

- Part C: Biomarker<sup>#</sup>
- Part D: Functional<sup>##</sup>

## Primary & Secondary Objectives

- Safety and tolerability of ascending doses of *del-brax* in participants with FSHD
- Pharmacokinetics

## Key Exploratory Objectives

- Pharmacodynamics
  - Biomarkers
- Measures of clinical activity
  - Muscle strength
  - Muscle function
  - Muscle composition (MRI)
- Patient and Clinician reported outcomes

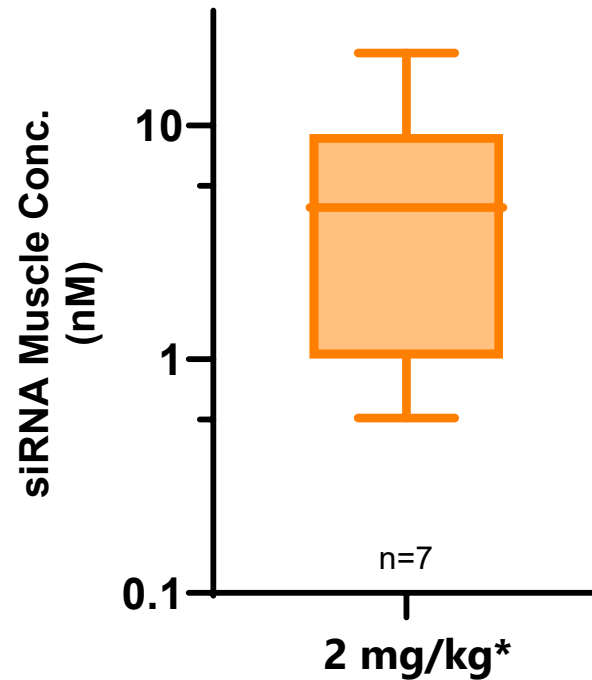
\*First dose at 1 mg/kg; all subsequent doses at 2 mg/kg – Enrollment Complete

\*\*Enrollment Complete

<sup>#</sup>Planned 2H24

<sup>##</sup>Planned 1H25

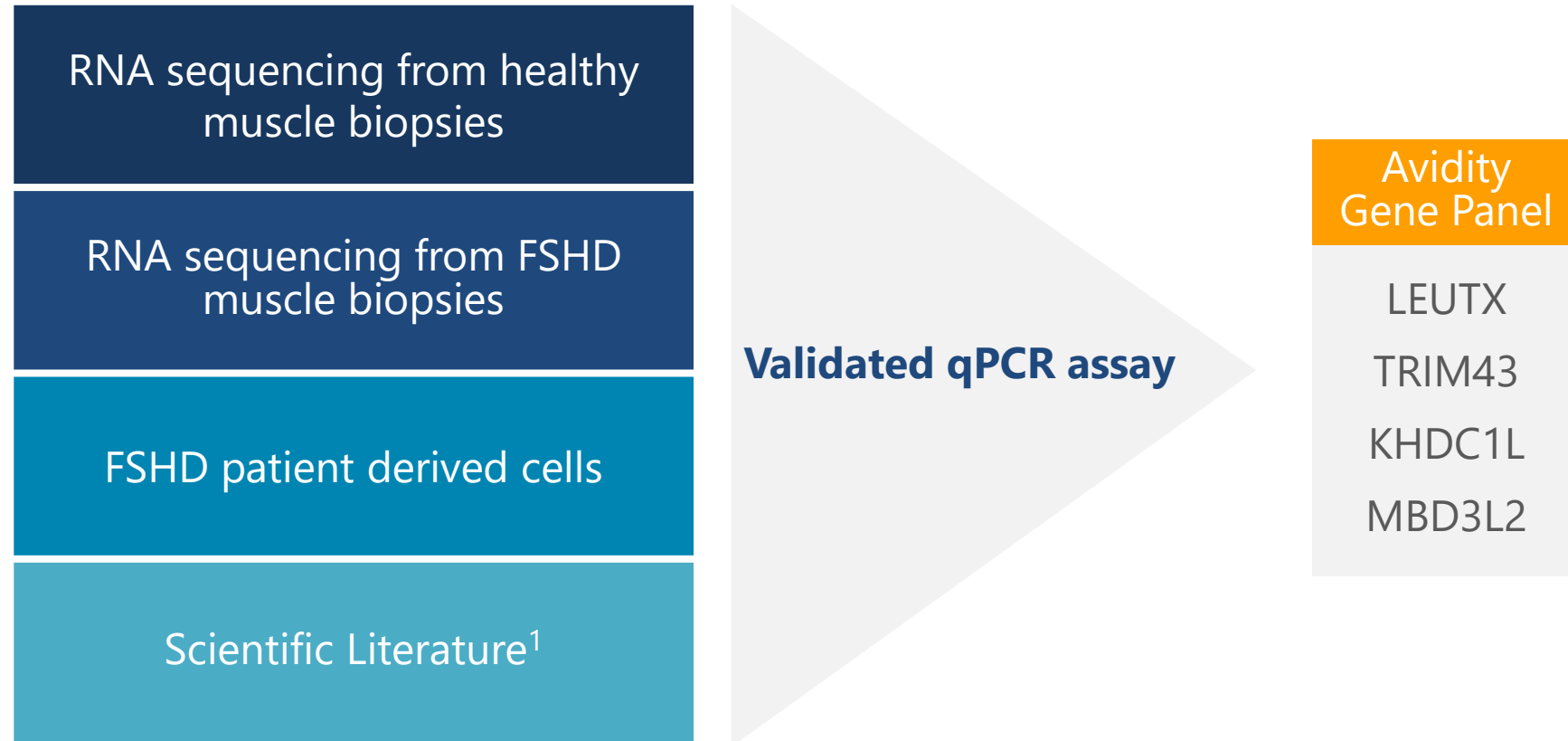
# Del-brax: Consistent and Effective Delivery of siRNA to Muscle





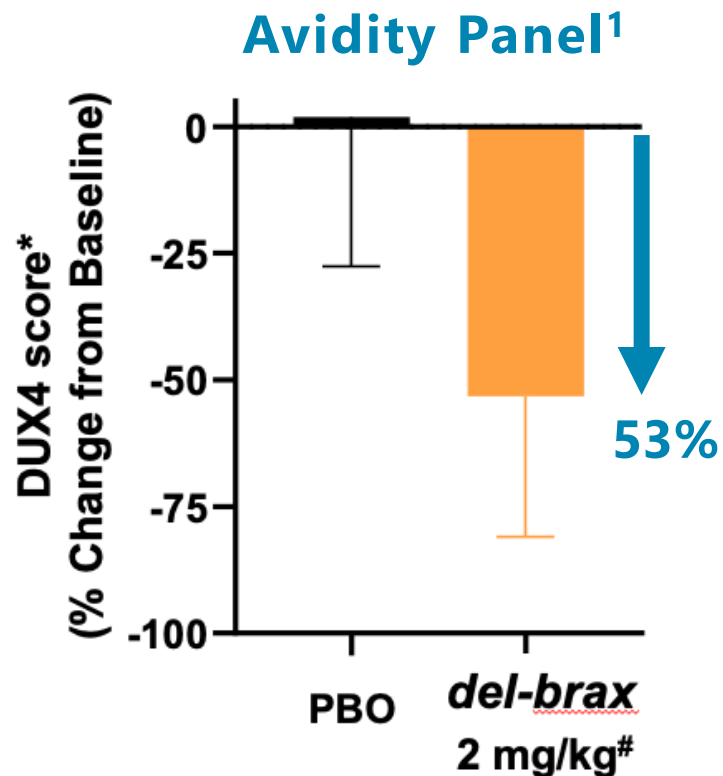
# DUX4-Regulated Genes Selected for Robustness and Reproducibility

Procured muscle biopsies, RNA sequencing, patient-derived cells informed the panel



# Del-brax Demonstrates Meaningful 53% Reduction in DUX4-regulated Genes

All *del-brax* treated participants showed reductions >20% in DUX4 regulated genes



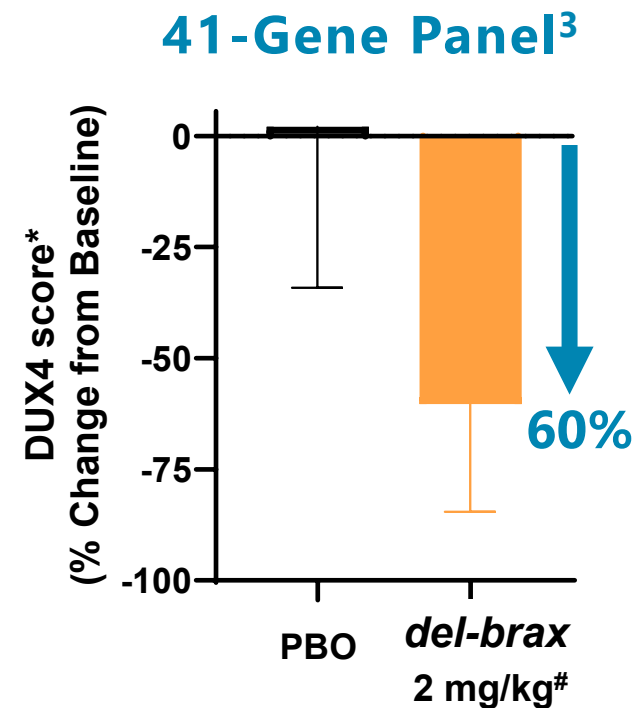
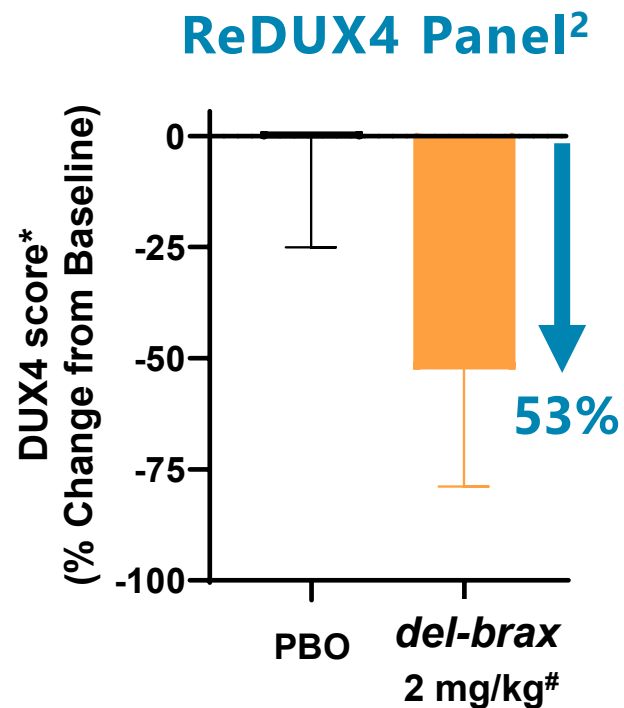
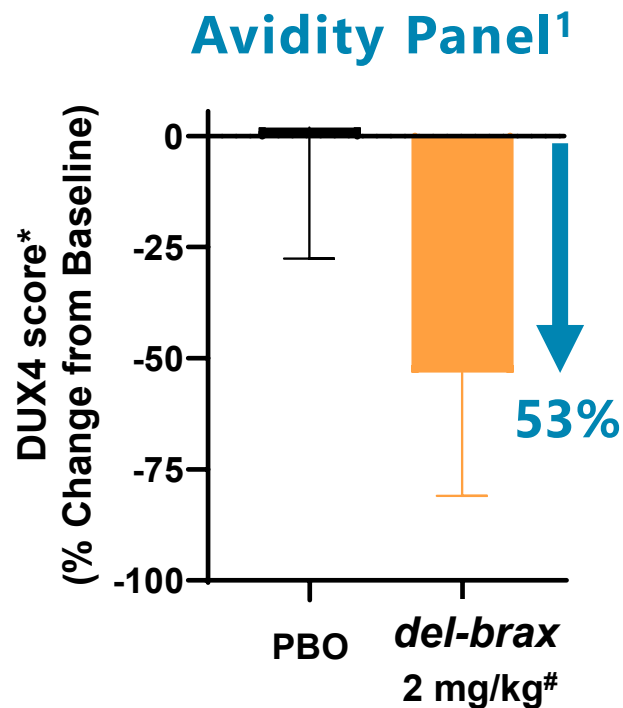
- All *del-brax* treated participants showed greater than 20% reduction in DUX4 regulated genes
- All muscle biopsies had evaluable DUX4 gene signatures at all timepoints
- MRI-informed muscle biopsies were successful

<sup>1</sup> Avidity 4-Gene panel (LEUTX, TRIM43, MBD3L2, KHDC1L, Reference genes: TBP, STATA5)

\* DUX4 score in MRI informed muscle biopsies were determined utilizing qPCR (Avidity panel). DUX4 score calculated as cumulative expression of each gene and data presented as change at 4M treatment relative to cohort normalized baseline. Mean +/- SEM, N=7 *del-brax*, N=4 PBO. One participant in treated group did not receive post-treatment biopsy.

# Doses were 1 mg/kg (D1), 2 mg/kg (D43 and D92) with biopsy 1 month after 3rd dose.

# Del-brax Shows Consistent >50% Reductions in DUX4-regulated Genes as Measured by Multiple Gene Panels



<sup>1</sup> Avidity 4-Gene panel (LEUTX, TRIM43, MBD3L2, KHDC1L; Reference genes: TBP, STATA5)

<sup>2</sup> ReDUX4 6-Gene panel (CCNA1, ZSCAN4, MBD3L2, KHDC1L, SLC34A2, PRAMEF6); Tawil, R. et al., *Lancet Neurol* **23**:477 (2024)

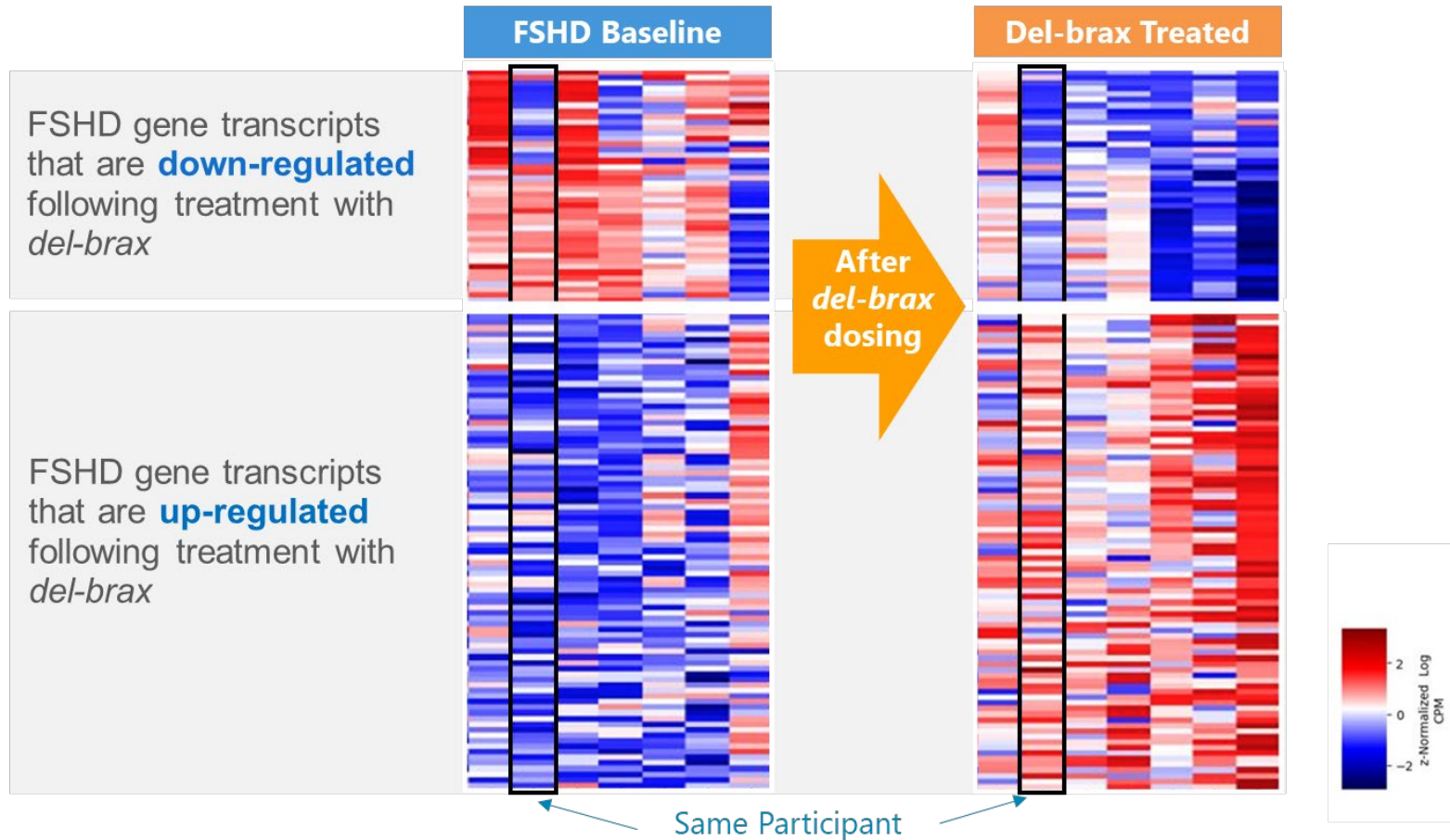
<sup>3</sup> Van den Heuvel, A. et al., *Scientific Reports* **12**:1426 (2022)

\* DUX4 score in MRI informed muscle biopsy were determined utilizing qPCR (Avidity panel) or RNASeq (ReDux and 41-Gene). DUX4 score calculated as cumulative expression of each gene and data presented as change at 4M treatment relative to cohort normalized baseline. Mean +/- SEM, N=7 del-brax, N=4 PBO. One participant in treated group did not receive post-treatment biopsy.

<sup>#</sup>Doses were 1 mg/kg (D1), 2 mg/kg (D43 and D92) with biopsy 1 month after 3rd dose.

# Del-brax Impacts Underlying FSHD Disease Biology

## Broad biological effects following *del-brax* treatment



Each column is a participant's disease signature at baseline compared to 1 month post 3<sup>rd</sup> dose

Differential gene expression (excluding DUX4 regulated genes) in muscle utilizing RNASeq.  
N=7 *del-brax* 1 mg/kg (D1), 2 mg/kg (D43 and D92). One participant missed post-dose biopsy.

# Circulating Biomarkers Provide Early Detection of Whole-Body Response to *Del-brax* Treatment

## Muscle Biopsy



- Sampling of single muscle
- Limited timepoints
- Invasive

## Circulating Biomarker



- Comprehensive assessment throughout body
- Continuous monitoring
- Patient friendly

# Novel DUX4-Regulated Circulating Biomarker

## Potential accelerated approval endpoint

### Multi-year Discovery Process



FSHD & Healthy Biopsies



Plasma from FSHD & Healthy Volunteers



Advisors & Disease Expertise

### Novel DUX4-Regulated Circulating Biomarker

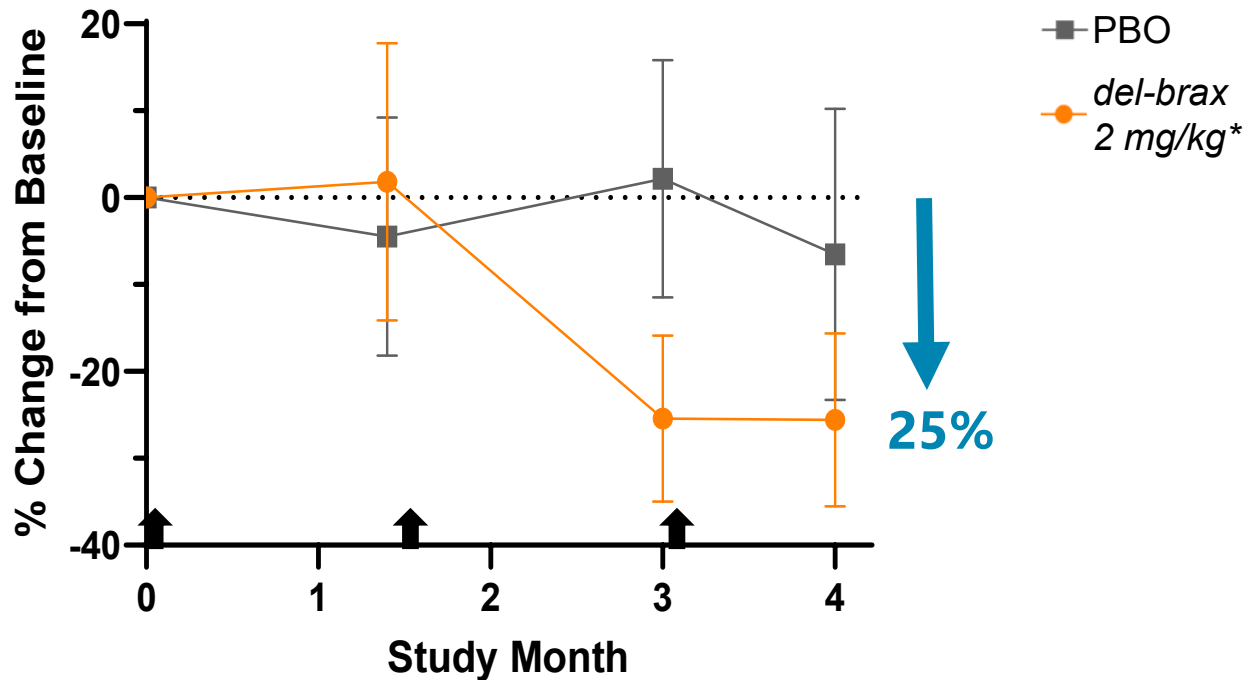
#### *Potential Accelerated Approval Endpoint*

- Significantly elevated in patients with FSHD as compared to healthy individuals
- Allows rapid and continuous monitoring of how participants are responding to *del-brax*
- Non-invasive, patient-friendly
- Guides selection of dose regimen

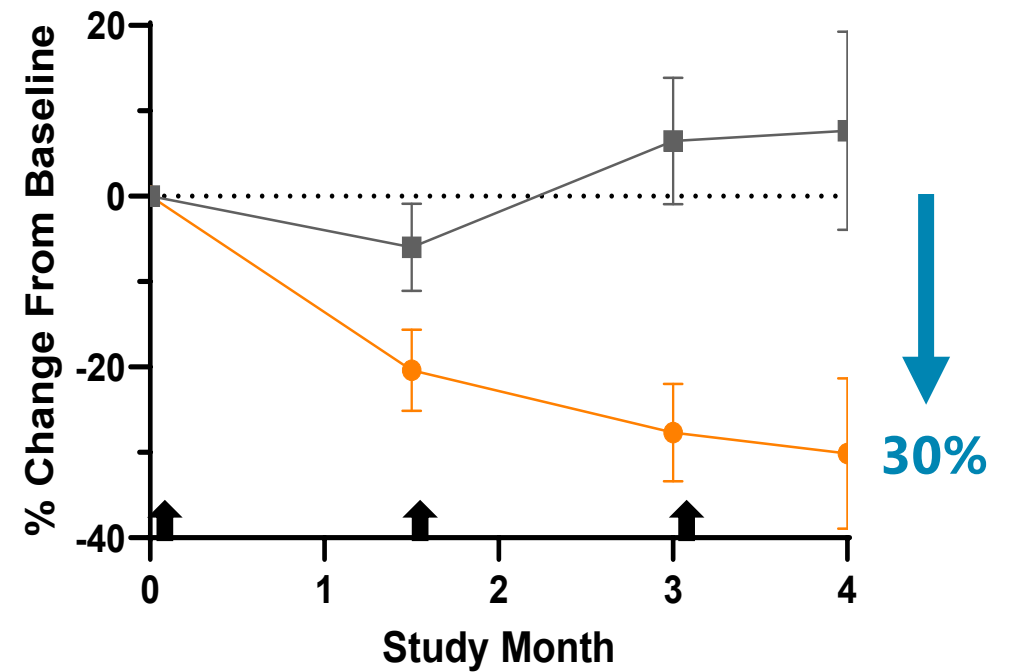
# Consistent and Confirmatory Decrease in Both Novel and Creatine Kinase Circulating Biomarkers

Decreases in creatine kinase, an indicator of muscle damage

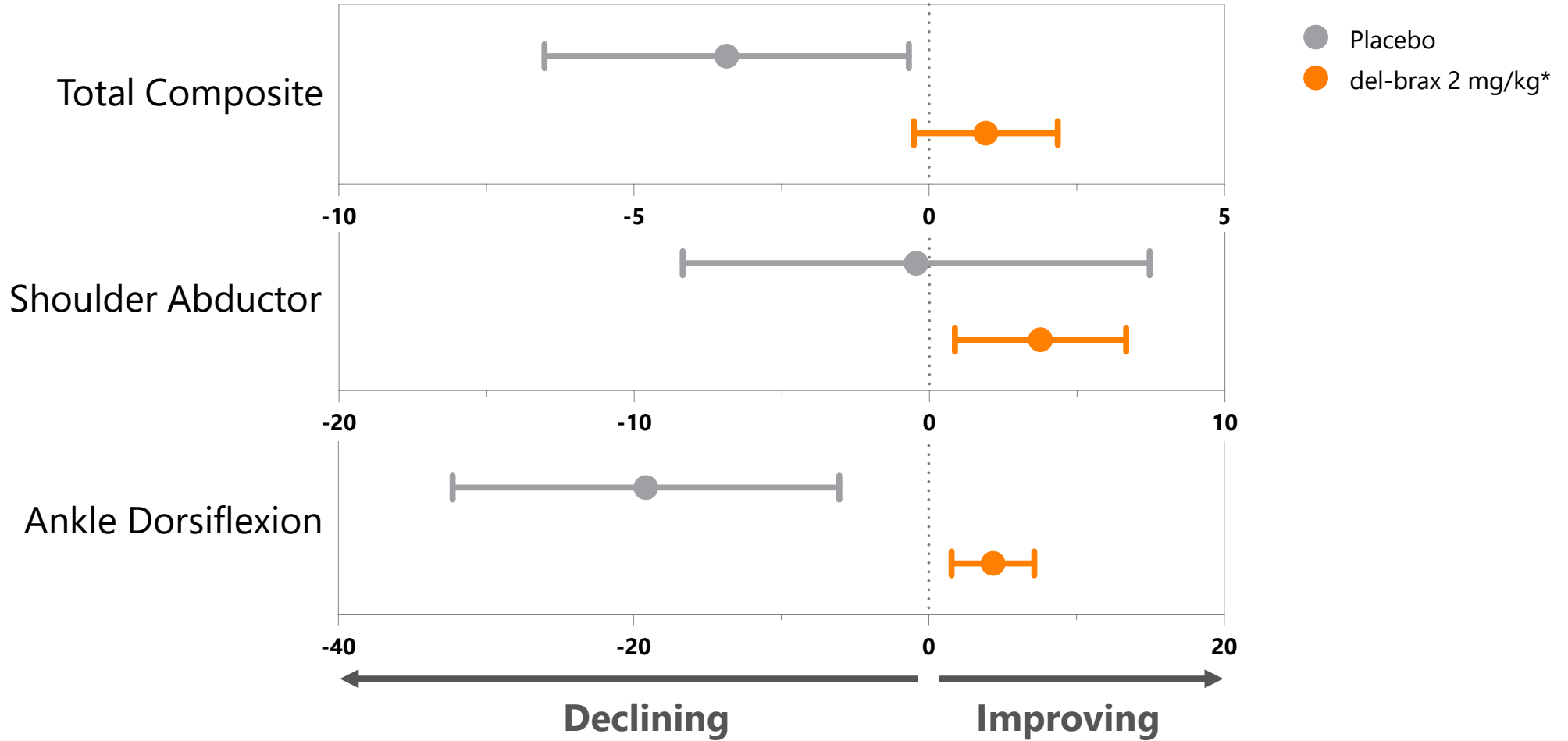
## Novel DUX4-regulated biomarker



## Creatine kinase biomarker



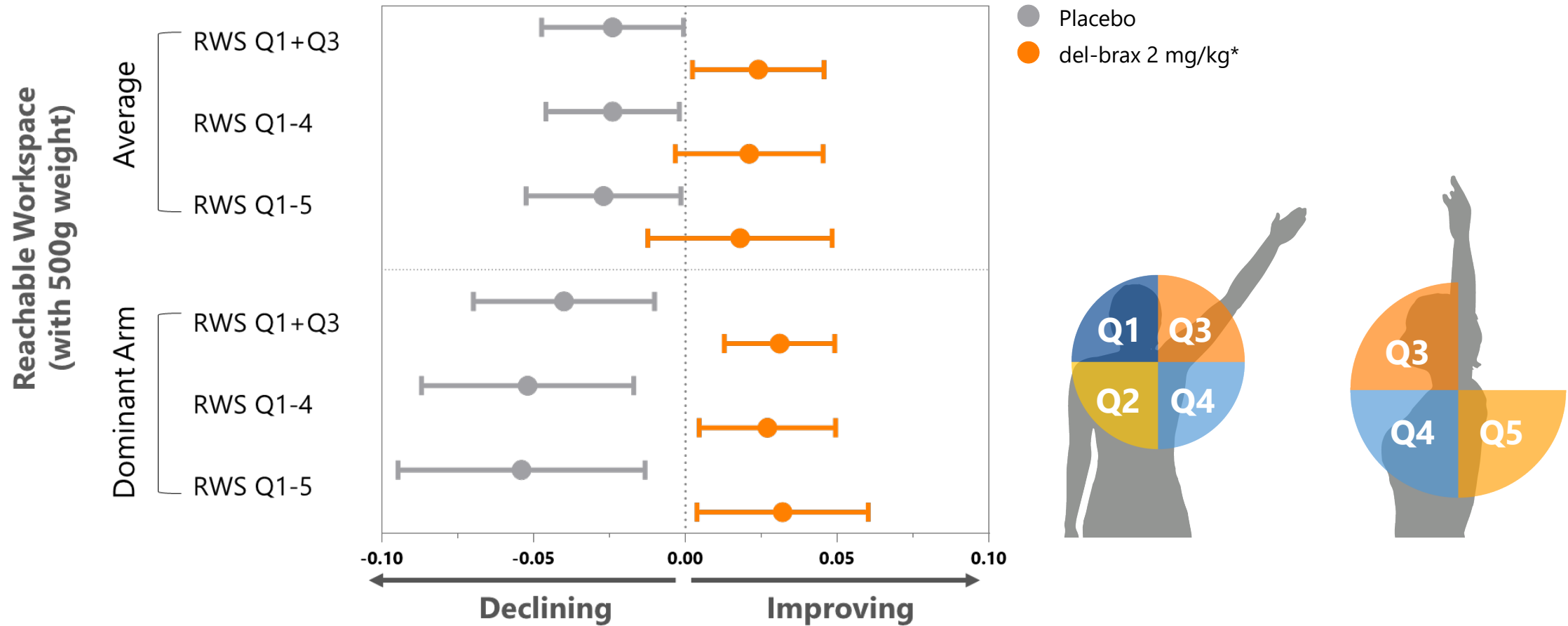
# Del-brax Improved Muscle Strength in Both Upper and Lower Limb





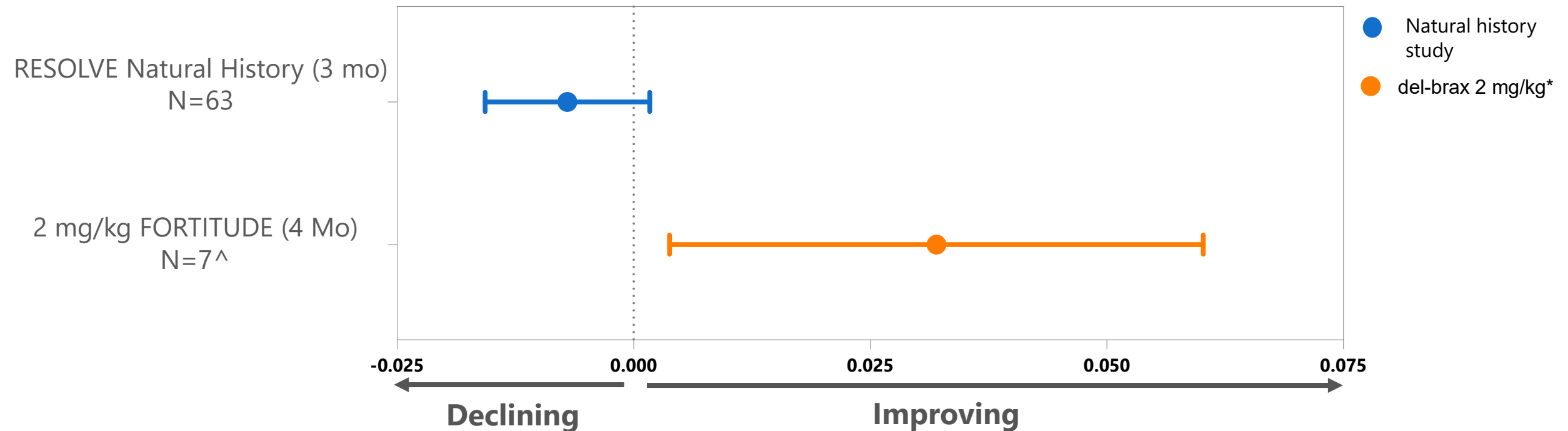
# Del-brax Improved Reachable Workspace Compared to Placebo

Improved range of motion and function; similar trends observed without weight



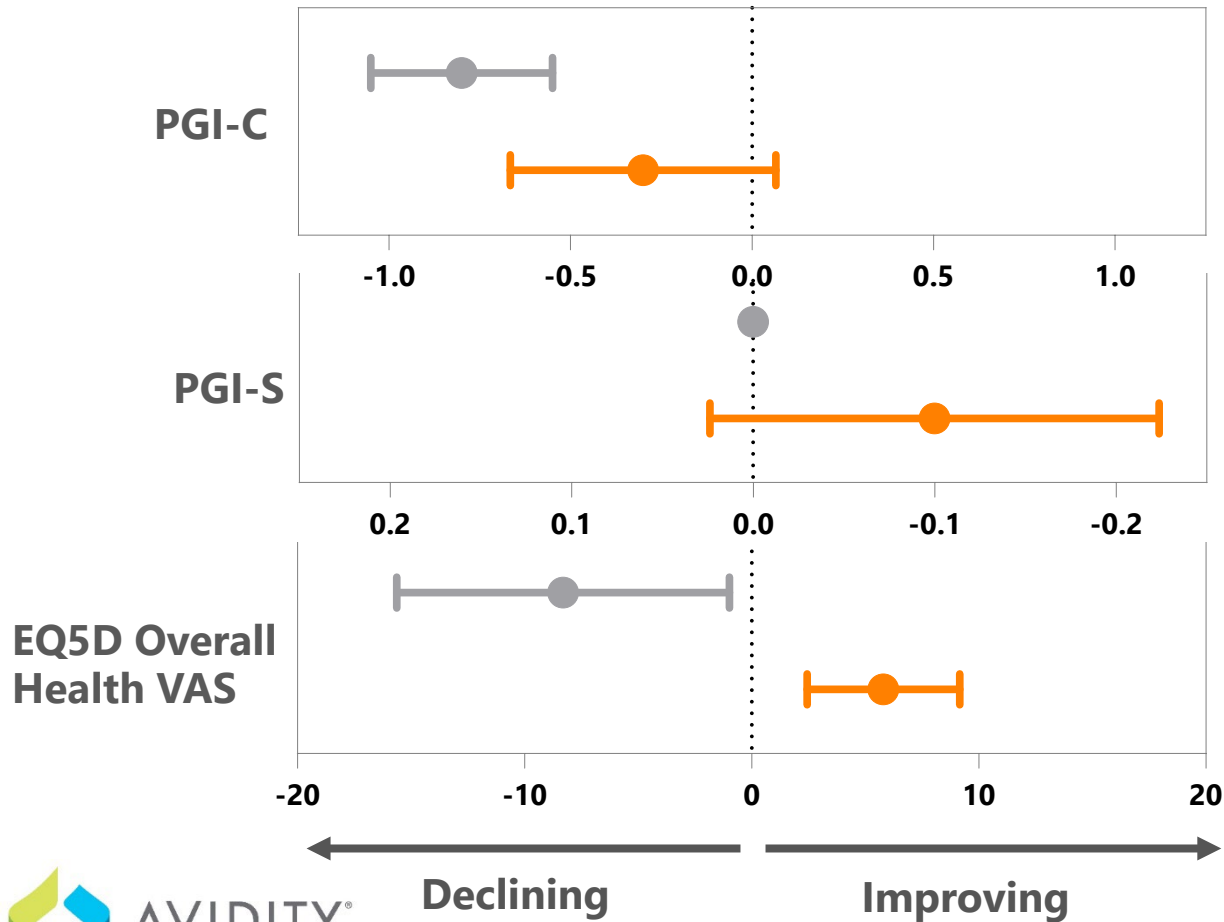
# Del-brax Improved Reachable Workspace Compared to Matched Natural History Data

## Reachable Workspace Q1-5; Dominant Arm; Weight: 500 g

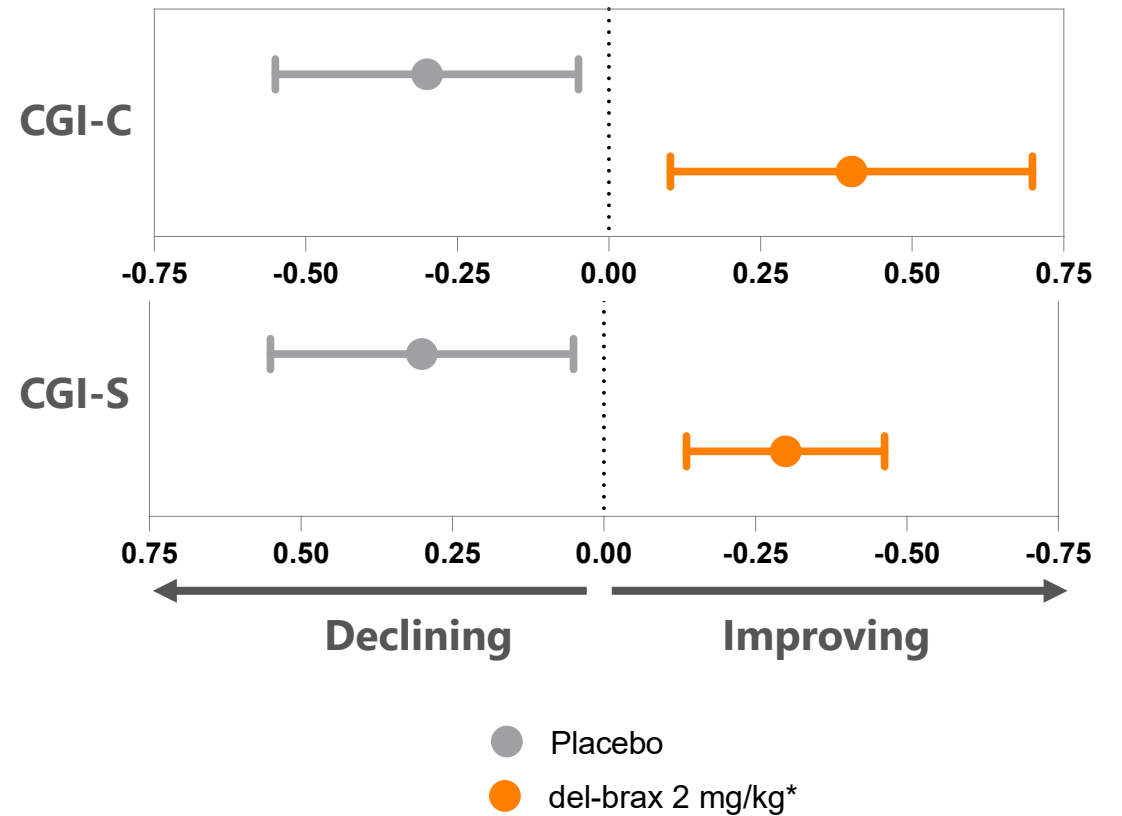


# Del-brax: Positive Trends Toward Improvement in Both Patient and Clinician Reported Outcome Measures

**Patient Reported Outcome Measures**  
Change from Baseline at Month 4 (SEM)



**Clinician Reported Outcome Measures**  
Change from Baseline at Month 4 (SEM)



# Collaboration with FSHD Community to Advance New Treatment Options



## Patients and their families are at the heart of everything we do

- Actively working with and supporting FSHD advocacy groups
- Investing in gaining a deep understanding of patient and caregiver perspectives and journey with FSHD
- Continually seeking community input throughout the drug development process to best meet patient needs
- Collaborating with community leaders to address gaps in support services and resources
- Supporting natural history studies with FSHD Clinical Trial Research Network (**ReSolve**, **MOVE-FSHD** and **MOVE+** studies)

# Delivering on FSHD



- ❑ Initiation of Phase 3 Functional Cohort (1H 2025)
- ❑ Initiation of Phase 3 Biomarker Cohort (2H 2024)
- ✓ FORTITUDE initial data in participants living with FSHD – **Complete**
- ✓ Completion of enrollment for Cohorts A & B in FORTITUDE trial - **Complete**
- ✓ FDA & EMA Orphan Drug designation - **Complete**
- ✓ FDA Fast Track Designation - **Complete**

**Nathan,  
Living with DMD, and  
his father, Brad**

## ***Del-zota (AOC1044) Program for Duchenne Muscular Dystrophy (DMD)***

*“My advice to any other family dealing with this is to take it day by day, do as much research as possible, and connect with others. I hope that someday there will be a cure for DMD, and no other family will have to go through this”*

*— Brad, Nathan’s Father, DMD Advocate*

# DMD: Hereditary Disorder Causing Progressive, Debilitating Muscle Damage and Significantly Reduced Life Expectancy

~10,000 - 15,000

PEOPLE WITH DMD IN THE US  
SIMILAR PREVALENCE IN EUROPE

~900

PEOPLE WITH DMD44 IN THE US

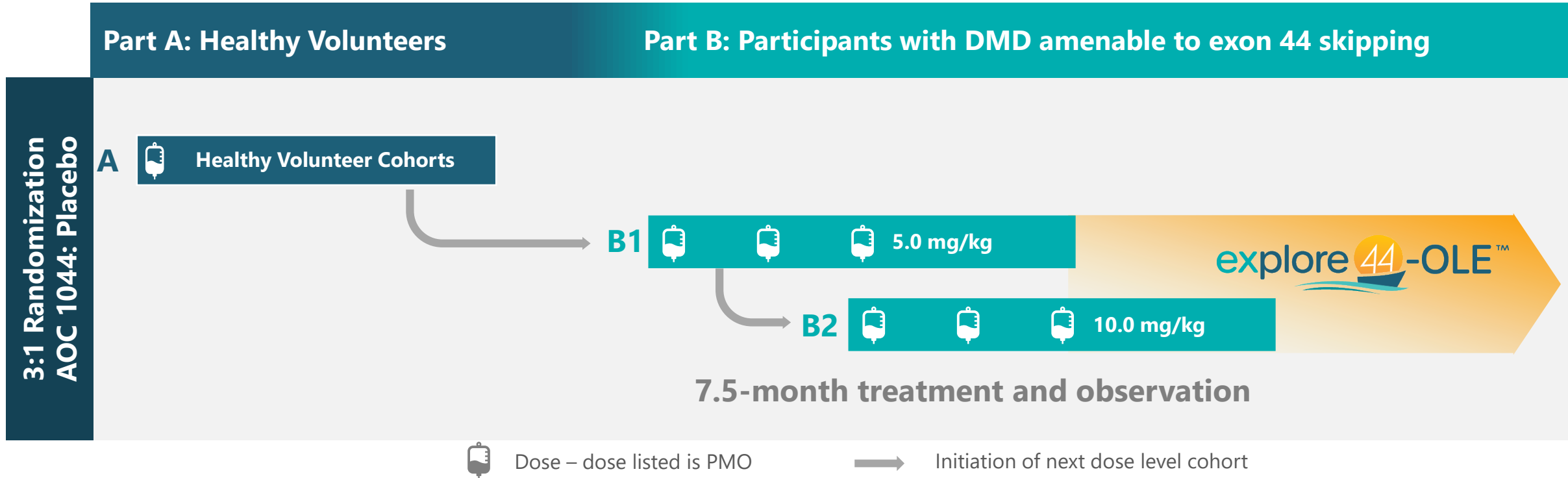
- Monogenic, X-linked, recessive condition characterized by progressive muscle damage and weakness
- Primarily affects males, loss of ambulation by teenage years
- Significantly reduces life expectancy
- Caused by mutations in the DMD gene, which encodes for the dystrophin protein
  - ~7% of DMD skip-amenable patients have mutations amenable to exon 44 skipping (DMD44)
  - ~900 patients with DMD44 in US
- *Del-zota*: designed to specifically skip exon 44 of dystrophin gene to enable dystrophin production

DMD Advocates

Lee, living with DMD, and Ginne, his mother



# Expediting *Del-zota* Registrational Plan



3:1 Randomization  
AOC 1044: Placebo

- EXPLORE44™ enrollment complete; dose-escalation to 20 mg/kg not necessary
- Plan to enroll additional patients in the EXPLORE44™ Open-Label Extension study
- Regulatory interactions to discuss the most expeditious path to accelerated approval





**Phase 1/2 EXPLORE44™ *Del-zota* (AOC 1044) Data in  
People Living with DMD44**

**August 2024**

# EXPLORE44 Phase 1/2 DMD44 Cohorts: Overview & Objectives

## Key Information

- Multiple dose
- N=24; Ages 7-27
- Ambulatory and non-ambulatory
- Biopsies in all cohorts
- Participants eligible to roll-over into extension

## Primary Objective

- Safety and tolerability of multiple doses in DMD patients amenable to exon 44 skipping

## Secondary Objectives

- Pharmacokinetics
- Pharmacodynamics
- Exon 44 skipping
- Dystrophin protein levels

## Key Exploratory Objectives

- Measures of muscle function
- Patient-reported outcomes (PRO)
- Quality of life

# Del-zota: Favorable Safety and Tolerability in DMD44 Patients

Subjects with $\geq 1$ TEAE n (%)	Placebo N=7	5.0 mg/kg N=9	10 mg/kg N=9
Any AE	4 (57%)	8 (89%)	4 (44%)
Related to study drug	0	2 (22%)	1 (11%)
Serious AE (SAE)	0	1 (11%)	0
AE leading to study discontinuation	0	2 (22%)	0
AE leading to death	0	0	0

**Most treatment emergent adverse events (TEAEs) were mild or moderate**

- No related AE occurred in >1 patient
- 1 participant discontinued due to serious AE of anaphylaxis
- 1 participant discontinued due to moderate infusion related reaction
- No symptomatic hemoglobin changes, hypomagnesemia or renal events

Data from EXPLORE44™ as of 25 July 2024

# Del-zota: First of Multiple AOCs in DMD Franchise

Data support expediting advancement of additional exon-skipping candidates

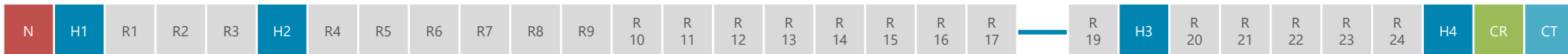
✓ Unsurpassed Delivery to Muscle	✓ Statistically Significant Robust Exon Skipping	✓ Statistically Significant Dystrophin Production	✓ Profound Decrease in Creatine Kinase Biomarker
<ul style="list-style-type: none"><li>• Consistent delivery of PMO of 200 nM in skeletal muscle</li><li>• Once again, reinforcing the disruptive and broad potential of our AOC platform</li></ul>	<ul style="list-style-type: none"><li>• 37% increase in exon 44 skipping</li><li>• Up to 66% increase in exon 44 skipping</li></ul>	<ul style="list-style-type: none"><li>• Increase of 25% of normal in dystrophin production</li><li>• Restored total dystrophin up to 54% of normal</li></ul>	<ul style="list-style-type: none"><li>• Creatine kinase levels reduced to near normal with greater than 80% reduction compared to baseline</li></ul>

# Del-zota Produces Near Full-Length Dystrophin

## Naturally occurring dystrophin



## Representative dystrophin produced by *del-zota*

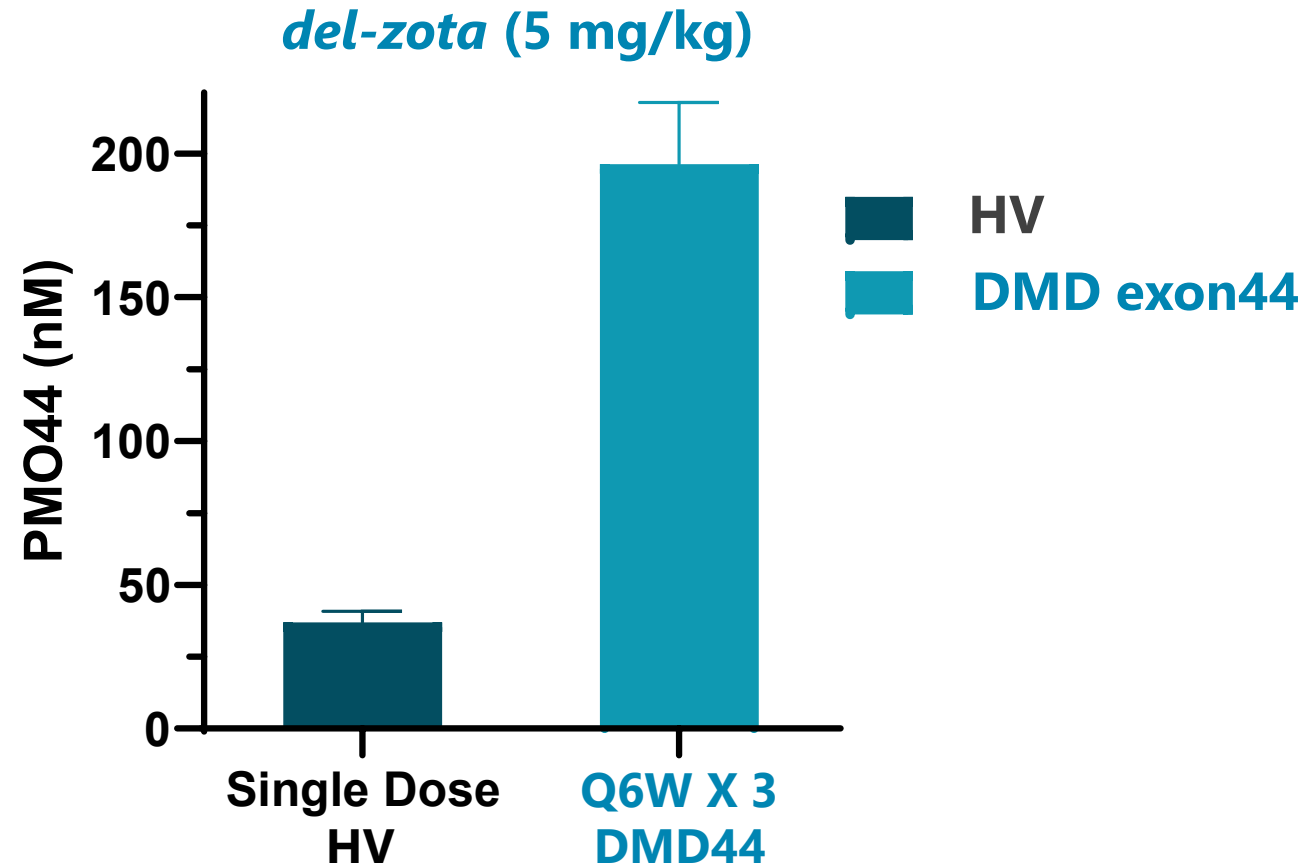


## Micro-dystrophin produced by gene therapies



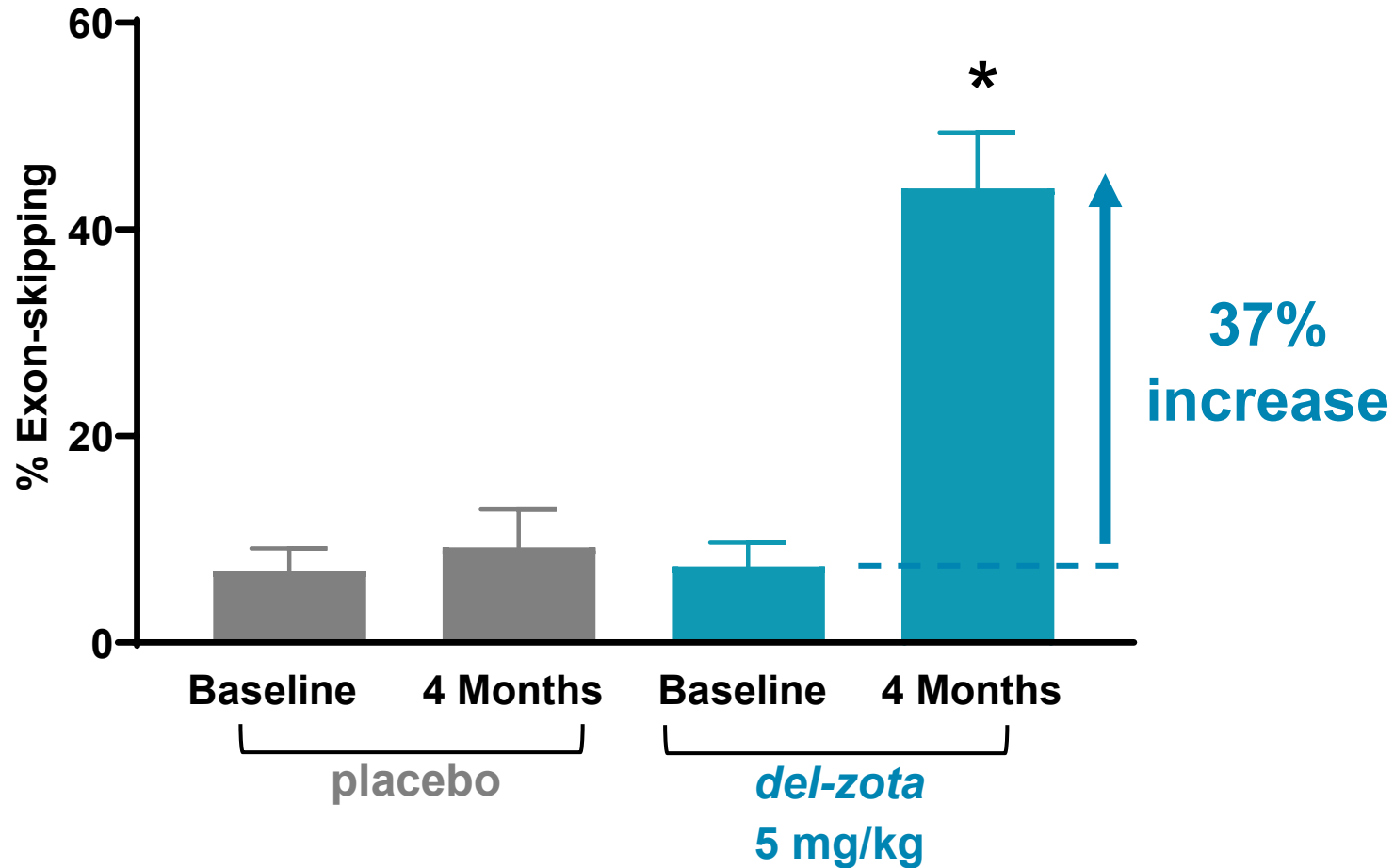
# Del-zota: Unsurpassed Delivery to Muscle in DMD Participants

PMO tissue concentration of 200 nM after 3 doses



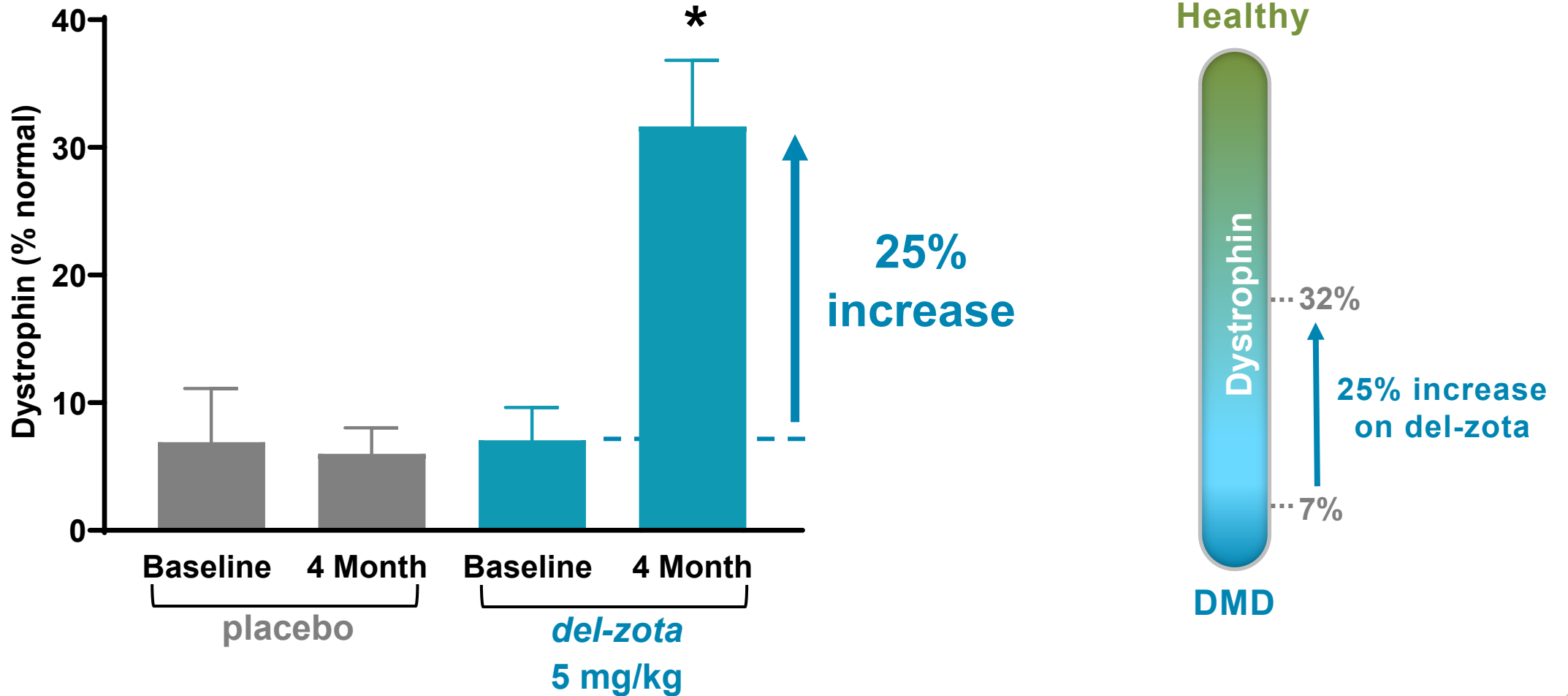
# Del-zota: Increase of 37% in Exon 44 Skipping

Statistically significant increase in exon 44 skipping of up to 66%



# Del-zota: Increase of 25% of Normal in Dystrophin Production

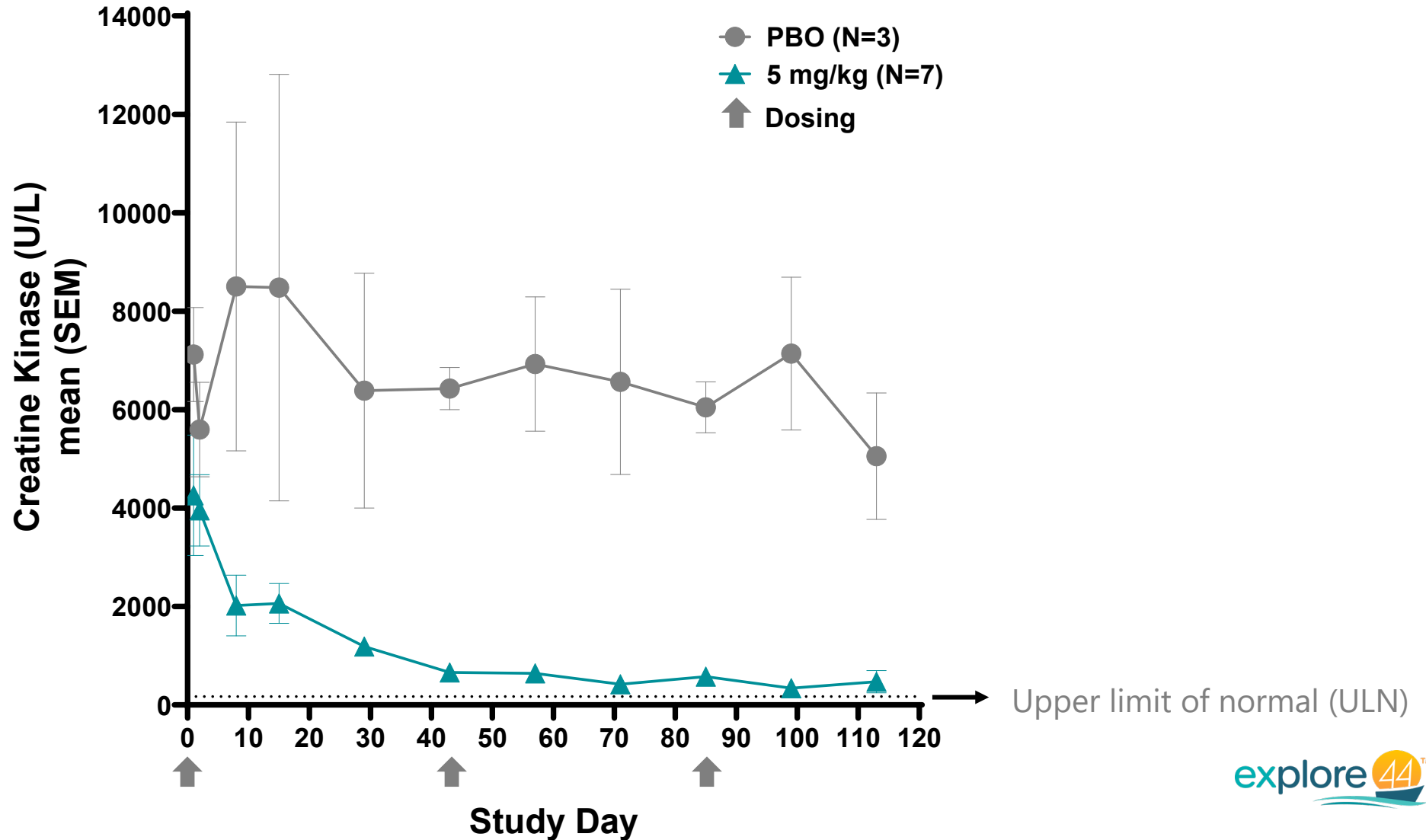
Significantly restored total dystrophin up to 54% of normal





# Del-zota: Creatine Kinase Levels Decrease to Near Normal

Creatine kinase reduced by greater than 80% compared to baseline



# Phase 1/2 Del-zota 5 mg/kg Patient Data



- In Q3 2024, shared positive 5 mg/kg cohort data from the Phase 1/2 EXPLORE44™ trial of people living with DMD44.
- *Del-zota* demonstrated:
  - Unsurpassed delivery of PMO of 200 nM in skeletal muscle
  - Statistically significant 37% increase in exon 44 skipping and up to 66% exon 44 skipping
  - Statistically significant increase of 25% of normal in dystrophin production and restored total dystrophin up to 54% of normal
  - Reduction in creatine kinase levels to near normal with greater than 80% reduction compared to baseline
  - Favorable safety and tolerability with most treatment emergent adverse events (AEs) mild or moderate in participants with DMD44.

# Avidity is Committed to Partnering with the DMD Community to Efficiently Advance Treatment Options

We understand the responsibility to get treatments to patients as quickly as possible



- FDA has granted *del-zota* Orphan Drug, Fast Track and Rare Pediatric Disease designations. EMA has granted *del-zota* Orphan designation
- EXPLORE44™ enrollment complete; plan to enroll additional patients in the EXPLORE44™ open-label extension study
- Looking forward to regulatory interactions to discuss the most expeditious path to accelerated approval

# Delivering on DMD



Lee,  
Living with DMD,  
and his family

- ❑ Preclinical development of additional DMD programs - **Ongoing**
- ✓ Reported EXPLORE44 5mg/kg patient data – **Complete**
- ✓ Reported EXPLORE44 healthy volunteer data - **Complete**
- ✓ Initiated enrollment of participants with DMD44 in EXPLORE44 - **Complete**
- ✓ FDA Rare Pediatric Disease Designation - **Complete**
- ✓ FDA & EMA Orphan Drug designation - **Complete**
- ✓ FDA Fast Track designation - **Complete**

# Expanding Use of AOCs Beyond Skeletal Muscle

Industry-leading partners validate broad potential of AOC platform; including precision cardiology and immunology

## PRECISION CARDIOLOGY

### Bristol Myers Squibb

Global licensing & research collaboration focused on up to five cardiovascular indications

Expansion of our Bristol Myers Squibb/MyoKardia single target research arrangement

**\$100M up-front plus potential for ~\$2.2B**

\$60M upfront payment

\$40M equity investment at a 40% premium

Up to ~\$1.35B in R&D milestone payments, up to ~\$825 million in commercial milestone payments and tiered royalties on net sales

## IMMUNOLOGY

### *Lilly*

Global licensing & research collaboration focused on immunology and other select indications

**Up to \$405M**

Potential milestone payments per target, plus mid-single to low double-digit tiered royalties

# The Experience to Deliver a New Class of RNA Therapeutics

## AVIDITY MANAGEMENT TEAM



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President & CEO



**Art Levin, PhD**  
Distinguished Scientist & Strategic Leader



**Steve Hughes, MD**  
Chief Medical Officer



**W. Michael Flanagan, PhD**  
Chief Scientific & Technical Officer



**Michael MacLean**  
Chief Financial & Business Officer



**Teresa McCarthy**  
Chief Human Resources Officer



**Eric Mosbrooker**  
Chief Strategy Officer



**John B. Moriarty, Jr., J.D.**  
Chief Legal Officer & Company Secretary



**Kath Gallagher**  
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Strategic Leader,  
Avidity Biosciences



# Solid Cash Position – Funded into mid 2027

## Q2 2024 financial results

In millions	Q224	Q124	Q223	Q224 vs Q124	Q224 vs Q223
Collaboration revenue	\$2.0	\$3.5	\$2.3	(\$1.5)	(\$0.3)
R&D expenses	63.9	66.8	42.6	(2.9)	21.3
G&A expenses	20.7	13.9	12.3	6.8	8.4
Total operating expenses	84.6	80.7	54.9	3.9	29.7
Loss from operations	(82.6)	(77.2)	(52.6)	(5.4)	(30.0)
Other income/expenses, net	11.8	8.3	5.6	3.5	6.2
Net loss	(\$70.8)	(\$68.9)	(\$47.0)	(\$1.9)	(\$23.8)

In millions	Q224	Q124
Cash, cash equivalents and marketable securities	\$1,299.0	\$915.9

**Solid cash position with ~\$1.6 billion providing funding into mid 2027\***  
**Advancing three clinical development programs for *del-desiran*, *del-brax* and *del-zota* into pivotal studies and expanding our DMD franchise and AOC platform, including precision cardiology programs**