



Virtual Investor & Analyst Event Series – Volume 6:

AOC 1001 MARINA™ Phase 1/2 Trial Preliminary Data Assessment



Exhibit 99.1

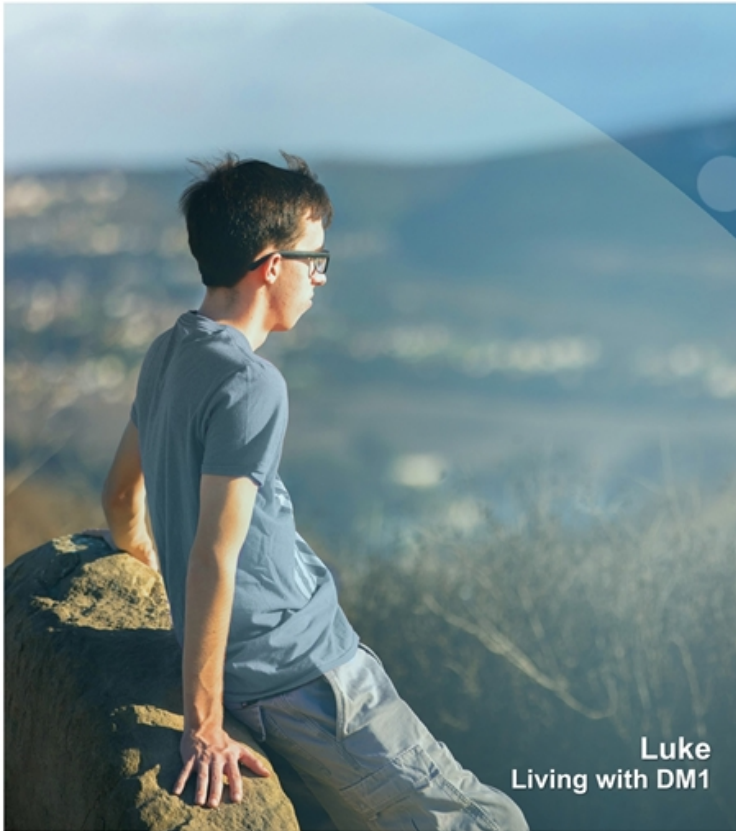


Forward Looking Statements

We caution the reader that this presentation contains forward-looking statements that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this presentation, including, but not limited to, statements regarding our future results of operations and financial position, business strategy, the anticipated timing, costs, design and conduct of our ongoing and planned preclinical studies and clinical trials, research and development plans, plans and projected timelines for AOC 1001, AOC 1020 and AOC 1044; timing and likelihood of success, prospective products, product approvals, plans and objectives of management for future operations, and future results of anticipated product development efforts, are forward-looking statements. 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, including, without limitation: we may not be able to resolve the partial clinical hold, and the analysis related to the underlying cause of the serious adverse event may result in delays in the MARINA study or an inability to complete the study; the Phase 1/2 MARINA trial results are based on a preliminary analysis of interim data available as of the data cutoffs, and the interim results do not predict the final results of the trial, and one or more of the safety or biomarker results may materially change following more comprehensive reviews of the data, as follow-up on the outcome of any particular patient continues, as and if additional patients enroll in the trial and as more patient data become available, any of which may materially alter the findings and conclusions from our preliminary analysis; 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 clinical holds, recalls or product liability claims; we are early in our development efforts and many of our development programs are in the preclinical or discovery stage; 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 success of our preclinical studies and clinical trials for our product candidates; 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; our dependence on third parties in connection with preclinical and clinical testing and product manufacturing; disruption to our operations from the COVID-19 pandemic; the war in Ukraine; 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; our ability to obtain and maintain intellectual property protection for our product candidates and proprietary technologies; we may use our capital resources sooner than we expect; and other risks described in our filings with the SEC, including under the heading "Risk Factors" in our Form 10-K for the year ending on December 31, 2021, filed with the SEC on March 1, 2022, and any 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, and 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.

Our Vision



Luke
Living with DM1



Our Vision To profoundly improve people's lives by revolutionizing the delivery of RNA therapeutics Luke Living with DM1

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

Delivering on Our Vision



DISRUPTIVE & BROAD PLATFORM

- Committed to delivering a new class of RNA therapies
- Advancing three AOCs in clinical development; two siRNAs and first PMO
- Broadening to other tissues & cell types through partnerships & internal discovery



ADVANCING & EXPANDING PIPELINE

- Progressing robust pipeline in muscle; 3 programs in clinical development in approx. a year
- AOC 1001* Phase 1/2 MARINA™ trial and MARINA-OLE™ ongoing
- AOC 1020 for FSHD in Phase 1/2 FORTITUDE™ trial
- AOC 1044 for DMD in Phase 1/2 EXPLORE44™ trial



AGILE & DIVERSE COMPANY

- Leveraging expertise in clinical and commercial execution
- Assembling an experienced team in rare & RNA therapies
- Building an integrated and diverse company in service of our patients

Delivering on 2022 Goals

Three programs in three distinct rare diseases in clinical development



DM1: AOC 1001* MARINA™

Successfully completed preliminary assessment

Top-line data and program updates planned for 2023



FSHD: AOC 1020 FORTITUDE™

IND cleared; trial initiation underway

Preliminary assessment in approximately half of participants in 1H 2024



DMD: AOC 1044 EXPLORE44™

IND cleared; trial initiation underway

Results from healthy volunteers in 2H 2023

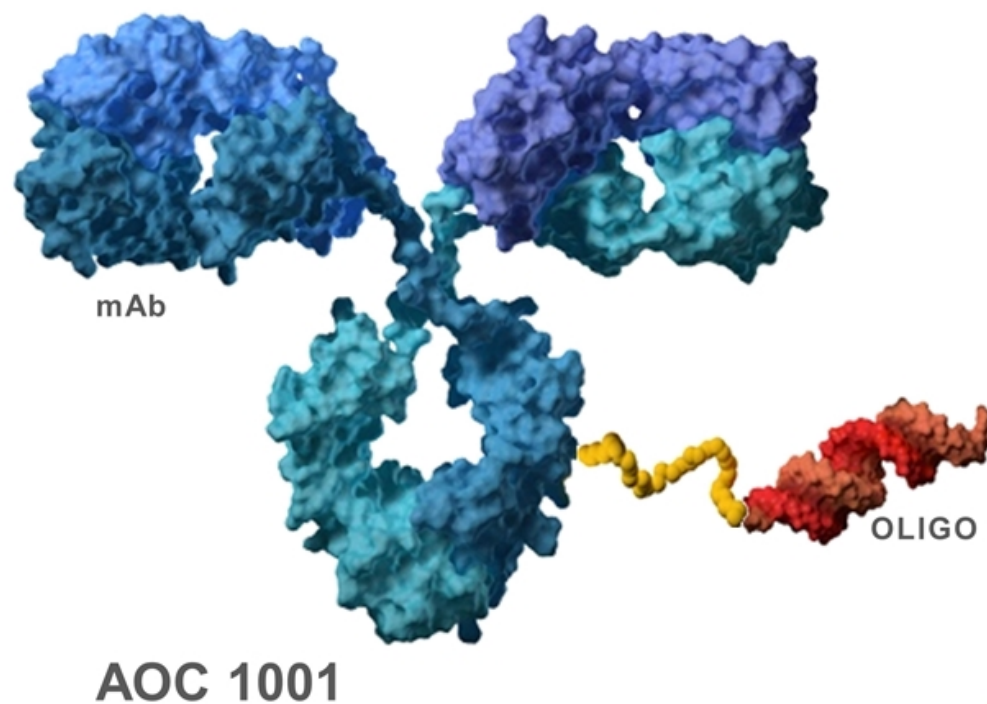
Overall program planned for potential Accelerated Approval



*Sept. 2022, FDA placed a partial clinical hold on new participant enrollment. All current participants may continue in their current dosing cohort. All participants in MARINA may roll over into the MARINA-OLE where they will receive AOC 1001 as planned. Avidity is working to resolve the partial clinical hold as quickly as possible.

Goals for the Day

- AOC 1001 Preliminary Data Assessment
- Living with DM1
- Disruptive and Broad AOC Platform
- Answer your questions



AOCs Deliver to Muscle – Revolutionary Advancement for the Field of RNA Therapeutics

Safety & Tolerability

MARINA Primary Endpoint; Phase 1/2 trial ongoing

Delivery to Muscle

First-ever successful targeted delivery of RNA to muscle – reinforces disruptive and broad potential of the AOC platform

DMPK Reduction

100% of treated participants had a DMPK reduction
45% mean DMPK reduction in treated participants

Impact on Disease Mechanism

16% splicing improvement across 22 gene panel
31% improvement in key set of muscle-specific genes

Early Signs of Clinical Activity

Myotonia improvement in early responders



Sarah Boyce
President and CEO

Steve Hughes, M.D.
Chief Medical Officer

Mike Flanagan, Ph.D.
Chief Technical Officer

Art Levin, Ph.D.
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**Nicholas E. Johnson, M.D.,
M.Sci., FAAN**

Avidity Management Team Members

**Virginia Commonwealth
University**

AOC 1001 MARINA™ Phase 1/2 Trial Preliminary Data Assessment



Agenda

- Welcome & Introduction
- **MARINA™: AOC 1001 Phase 1/2 Preliminary Data Assessment**
- Living with Myotonic Dystrophy Type 1
- Broad Utility & Power of the Platform
- Q&A Session
- Closing Remarks

Sarah Boyce, President & CEO

Steve Hughes, M.D., CMO
Mike Flanagan, Ph.D., CTO

Nicholas E. Johnson, M.D., M.Sci., FAAN
Virginia Commonwealth University

Art Levin, Ph.D., CSO

Avidity Management
Dr. Nicholas Johnson, VCU
Kath Gallagher, SVP, Communications & IR (Moderator)

Sarah Boyce, President & CEO





MARINA: A Phase 1/2 Clinical Trial to Evaluate AOC 1001 in Adult Patients with DM1

Steve Hughes, M.D., Chief Medical Officer

Myotonic Dystrophy Type 1 (DM1): Disease Overview

>40,000

PEOPLE WITH DM1 IN THE US

0

APPROVED THERAPIES

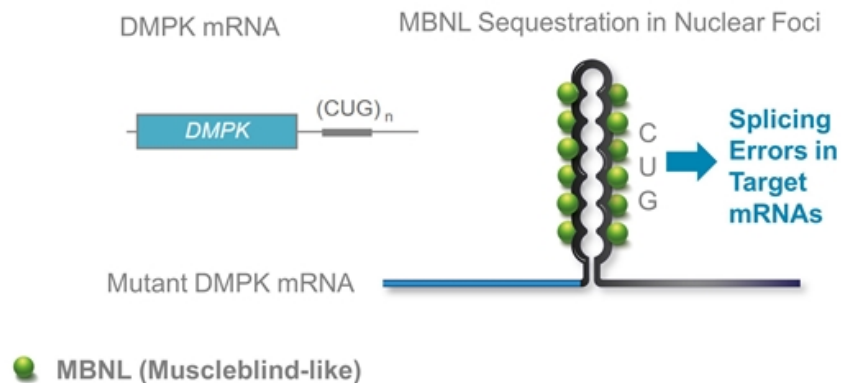
- DM1 is a complex disease with symptoms that present with high variability from patient to patient
- Monogenic, autosomal dominant, progressive disease that primarily affects muscle: skeletal, cardiac & smooth
- Increases in severity from generation to generation
- Significant impact on quality of life
- Shortened life-expectancy



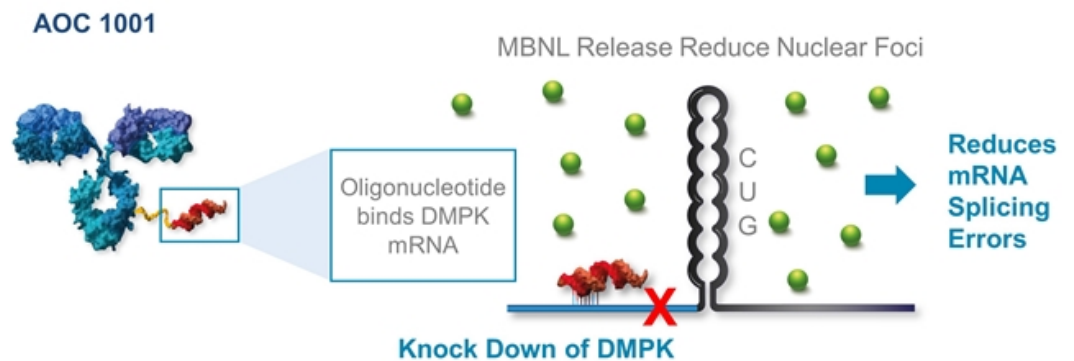
Loraine,
Kristl & Zen
Living with DM1

DM1 is Caused by a Toxic Gain-of-Function mRNA and is Well Suited to an siRNA Approach

Mechanism of Disease



Potential Therapeutic Approach



- Trinucleotide expansion in DMPK mRNA sequesters an RNA splicing protein MBNL (Muscleblind-like) in nuclear foci
- Sequestration of MBNL leads to RNA splicing errors in multiple muscle-related RNAs and induces DM1 disease manifestations
- Allows MBNL to be released to perform its natural function to aid in splicing key mRNAs in muscle
- Improves the splice patterns and muscle function. Splice patterns can serve as biomarkers

AOC 1001's Compelling Preclinical Package



Safety and Tolerability

Favorable toxicology profile in Non-Human Primates (NHPs)



Delivery to Muscle

Duration and delivery shown in wide range of muscles in multiple preclinical models



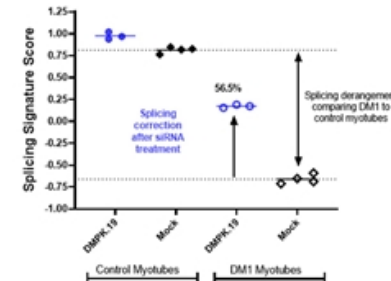
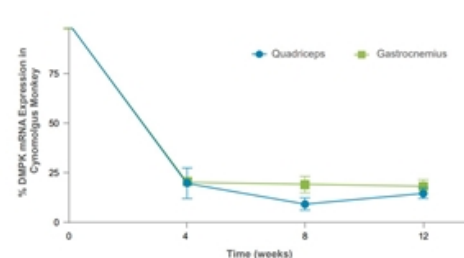
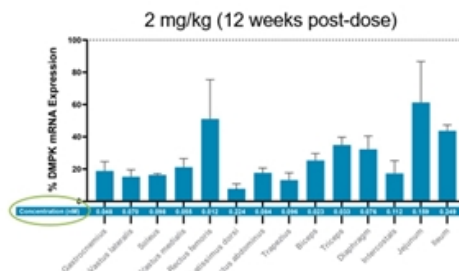
DMPK Reduction

75% reduction in NHPs



Impact on Disease Mechanism

Splicing Improvement in patient-derived muscle cells



MARINA™ and MARINA-OLE™ Allow for Both Short- and Long-term Data Collection to Support AOC 1001*


MARINA™

MARINA-OLE™

 Dose  Booster
Dose listed is siRNA



N = ~44 Ages 18-65 (3:1 randomization)
Part A receives single IV dose
Part B receives multi-ascending IV doses
 ➤ Quarterly doses - 1 booster after first 6 weeks
 6-month treatment and observation duration

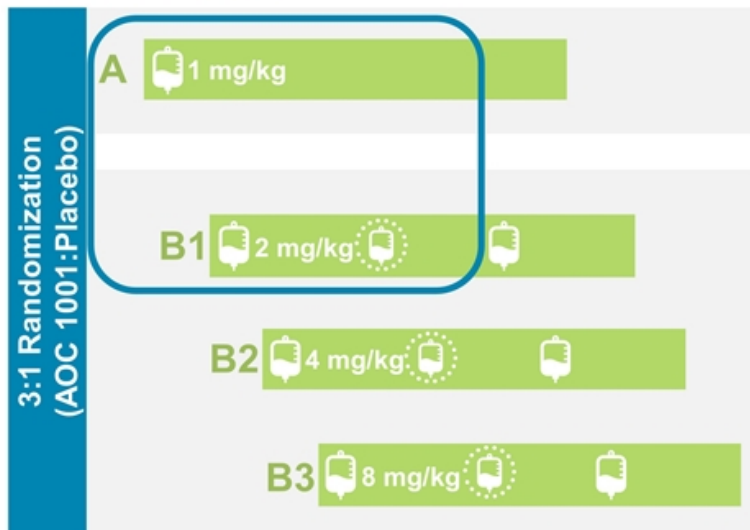
N = ~44 Ages 18-65
All participants receive AOC 1001
 Quarterly doses - 1 booster after first 6 weeks
 24-month treatment and 9-month observation duration



*Sept. 2022, FDA placed a partial clinical hold on new participant enrollment. All current participants may continue in their current dosing cohort. Avidity is working to resolve the partial clinical hold as quickly as possible.

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MARINA-OLE™

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 Dose listed is siRNA



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 24-month treatment and 9-month observation duration



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Early Data from MARINA Mid-Point at 6 weeks post 1 or 2 doses of AOC 1001

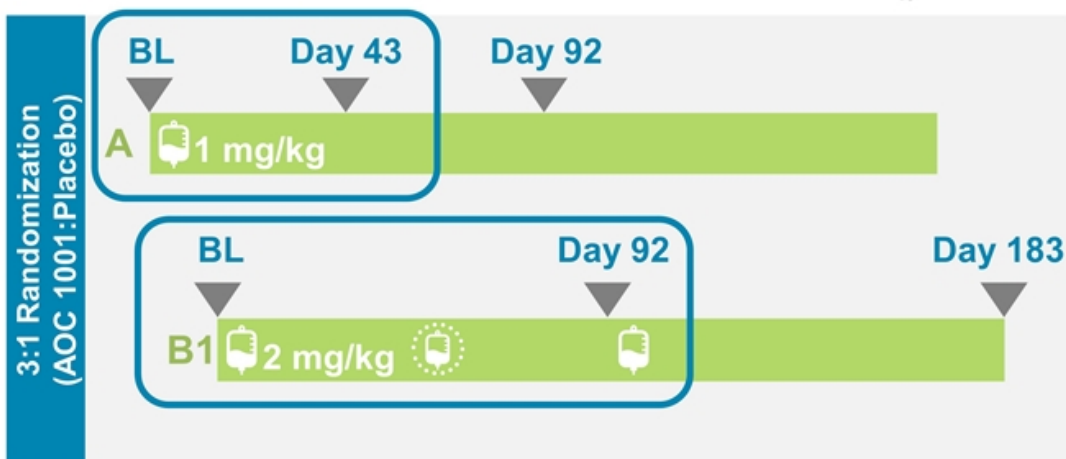


Dose listed is siRNA

▼ Biopsy

📅 Dose

📅 Booster



Safety includes all cohorts (including 4mg/kg) with a data cutoff of November 17th

NOTE: Day 92 biopsy in 2mg/kg cohort taken prior to third dose of AOC 1001

Biopsy	1 mg/kg (n=8 Participants)		2mg/kg (n=12 Participants)	
	Baseline	Day 43	Baseline	Day 92
DMPK	6 Active 2 Placebo	5* Active 2 Placebo	9 Active 3 Placebo	9 Active 3 Placebo
Splicing				8** Active 3 Placebo

Data at 3 Months: n=19 participants*

1mg/kg Cohort (n=5 active participants)

2mg/kg Cohort (n=9 active participants)

Pooled placebo (n=5 participants)

*One participant in the 1mg/kg cohort had insufficient tissue for analysis

**Due to timing, one splicing sample from the 2mg/kg cohort will be evaluated in the next batch analysis





MARINA™ MARINA-OLE™ Update*

- **MARINA™ is on a partial clinical hold for new participant enrollment**
 - The partial hold is in response to a serious adverse event (SAE) reported in a single participant in the 4mg/kg cohort.
 - No similar events observed in other participants in either MARINA or the MARINA-OLE
 - Avidity working to conclude the investigation of the SAE
- **Participants already in MARINA or the MARINA open label extension (MARINA-OLE™) continue to receive either AOC 1001 or placebo**
 - 38 participants enrolled in MARINA; to date, 100% of participants who completed MARINA have chosen to roll into the MARINA-OLE
- **Anticipate sharing an update on the partial hold by the end of the first quarter in 2023**
 - Plan to disclose more information on the SAE at that time
- **MARINA top-line data anticipated in 2023**

Baseline Demographics* Generally Well Matched Between Cohorts



Cohort A and B1 Enrolled Participants with Mild-Moderate Disease Severity

Mean (Range) or Number of subjects	Cohort A1 (1 mg/kg) N=8	Cohort B1 (2 mg/kg) N=12
Age	37.9 (21–64)	38.8 (18-60)
Sex	Male: 2 / Female: 6	Male: 1 / Female: 11
BMI	22.0 (16.1–29.2)	25.0 (17.5–32.0)
Mean CTG repeat length (range)	504 (150-725)	707 (150-1250)
Baseline Splicing (composite of 22 splicing events; higher number is more severe)	74 (38-96)	72 (39-105)

*Preliminary Results Based on Live, Unlocked Clinical Database – Numbers Subject to Change

Generally Favorable Safety and Tolerability



Subjects with ≥ 1 AE n (%)	Placebo n=10	1mg/kg n=6	2mg/kg n=9	4mg/kg n=13	Total AOC 1001 N=28
Any AE	8 (80%)	6 (100%)	9 (100%)	12 (92%)	27 (96%)
Related to study drug	2 (20%)	1 (17%)	3 (33%)	10 (77%)	14 (50%)
Serious AE (SAE)	0	0	1 (11%)	1 (8%)	2 (7%)
AE leading to study discontinuation	0	0	0	0	0
AE leading to death	0	0	0	0	0

17-Nov-2022 data cutoff. MARINA data only presented

Preliminary Results Based on Live, Unlocked Clinical Database – Numbers Subject to Change



Generally Favorable Safety and Tolerability



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17-Nov-2022 data cutoff. MARINA data only presented

Preliminary Results Based on Live, Unlocked Clinical Database – Numbers Subject to Change

- **Majority of treatment emergent adverse events (AEs) were mild or moderate**

- The most common in the study were COVID-19 (16%) and headache (16%)
- Other AEs include:
 - Infusion related reactions
 - Reductions in hemoglobin
 - Elevations in ASTs or ALTs
 - No changes in bilirubin
 - No thrombocytopenia and no renal impairment reported


- **2 Serious Adverse Events (SAEs)**

- 1 SAE in the 4mg/kg cohort resulted in a partial clinical hold
- 1 unrelated SAE in reaction to opioid pain medication after an elective surgery

Summary



- **DM1 underrecognized, progressive and often fatal neuromuscular disease with a high unmet need and no approved therapies**
- **Data presented today is an early mid-point look at MARINA 6 weeks post 1 or 2 doses of AOC 1001**
 - Baseline demographics generally well matched between cohorts
 - Generally favorable safety and tolerability profile
- **Anticipate update on MARINA partial hold by the end of Q1 2023**
 - Plan to disclose more information on the SAE at that time
- **MARINA top-line data anticipated in 2023**

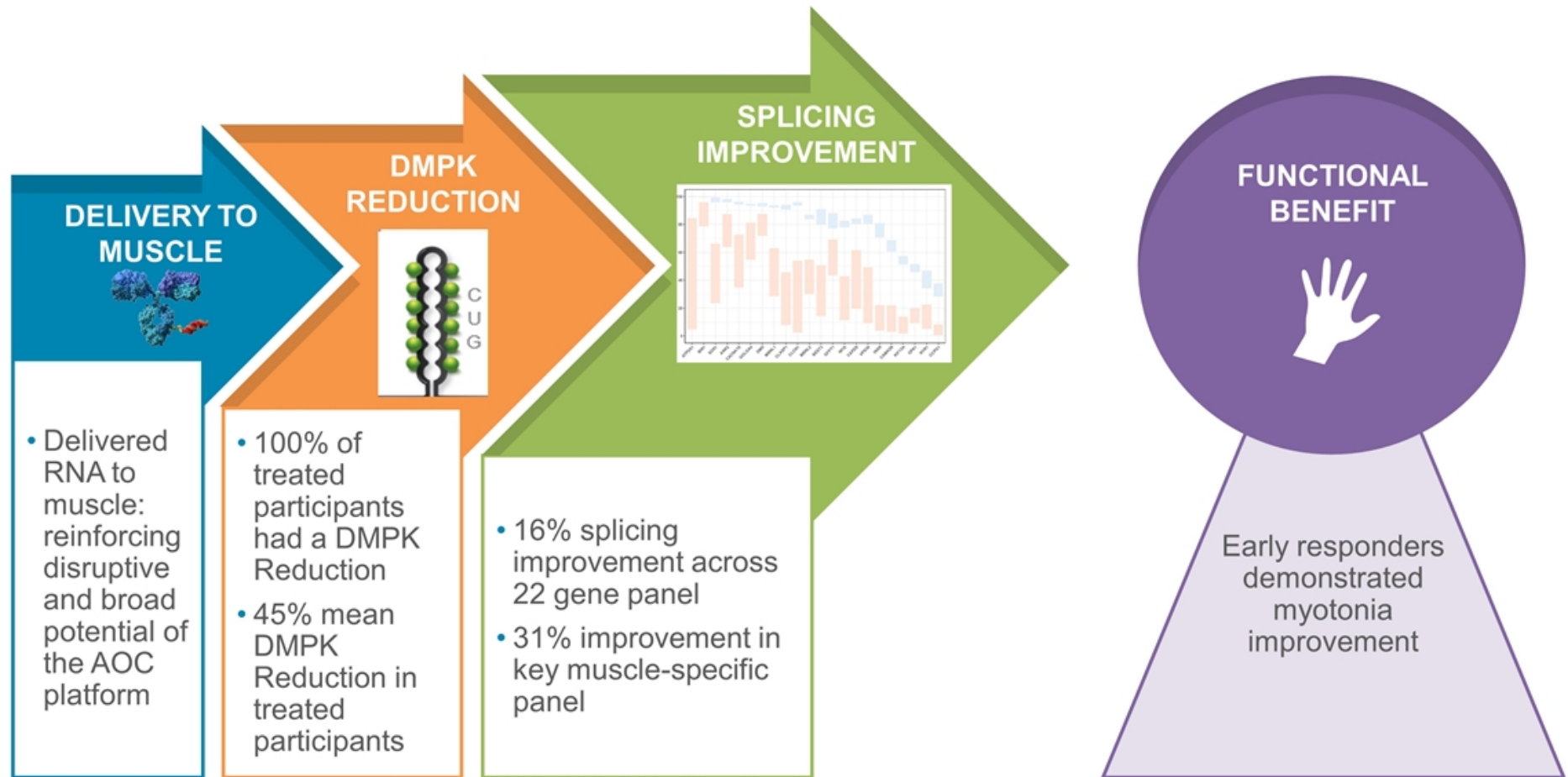


Delivering on the AOC Platform and Impacting the Underlying Disease Mechanism of DM1

W. Michael Flanagan, Ph.D., Chief Technical Officer



The DM1 Cascade to Functional Benefit

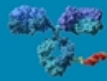


AOC 1001 Delivered siRNA to Muscle

Potential to Expand siRNA Therapeutics Beyond Liver



DELIVERY
TO MUSCLE



DMPK
REDUCTION



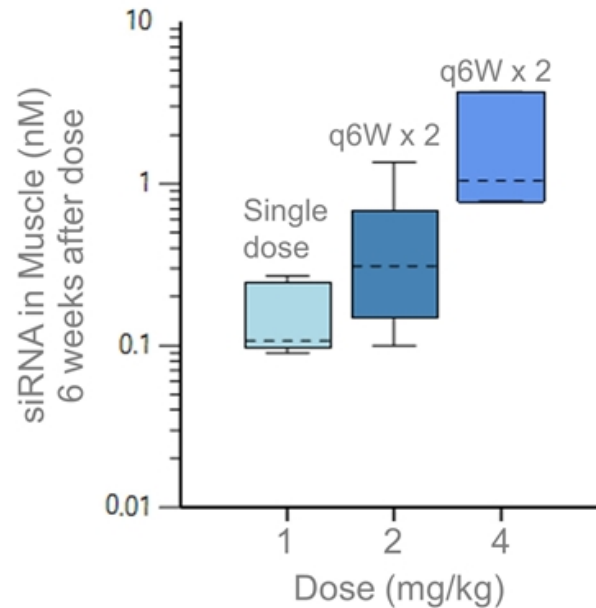
SPLICING
IMPROVEMENT



FUNCTIONAL
BENEFIT



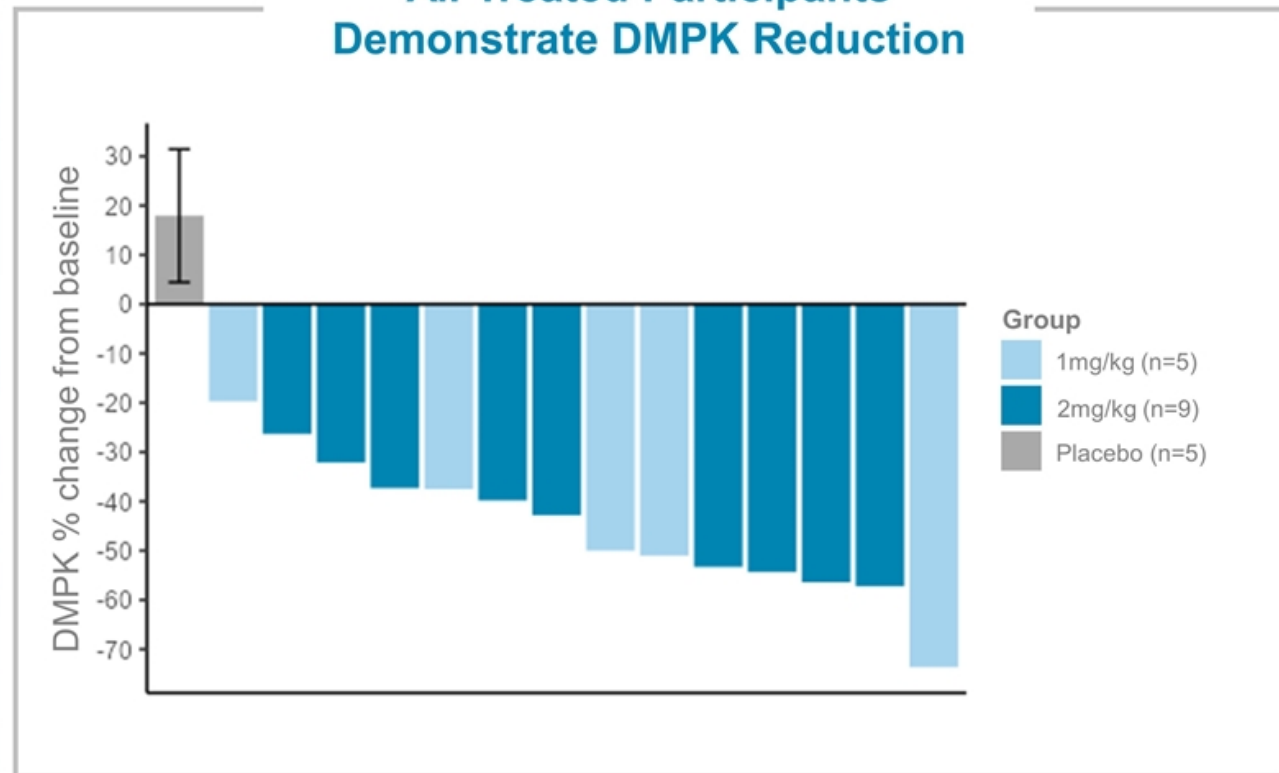
Dose Proportional Increase in Muscle siRNA Concentrations



Every Participant Treated with AOC1001 Showed DMPK Reduction*



All Treated Participants Demonstrate DMPK Reduction



- Placebo group combined from both cohorts and shown as standard error of mean
- Data represented as 6 weeks post last dose

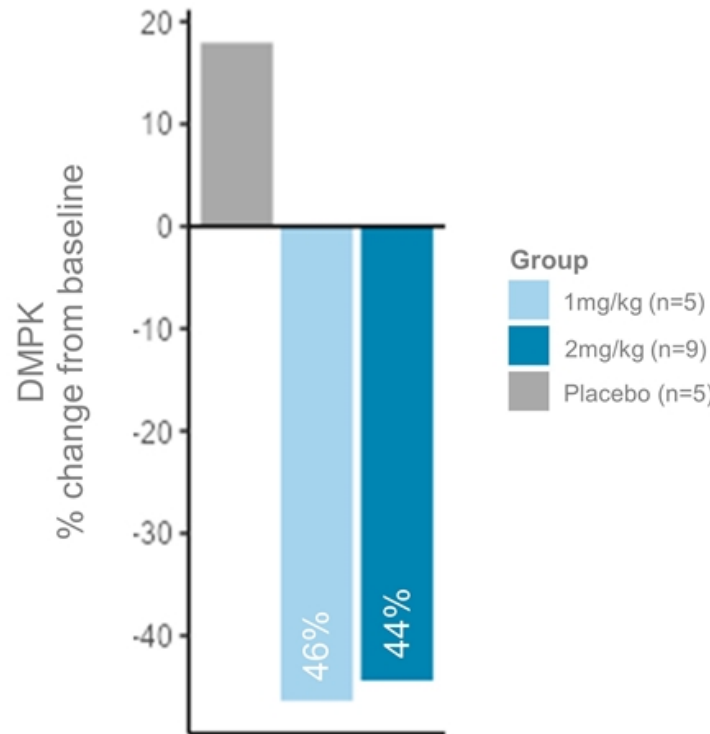
*One participant in the 1mg/kg cohort had insufficient tissue for analysis

Meaningful DMPK RNA Reduction Observed in Muscle

45% DMPK reduction after a single dose at 1 mg/kg or two doses at 2mg/kg



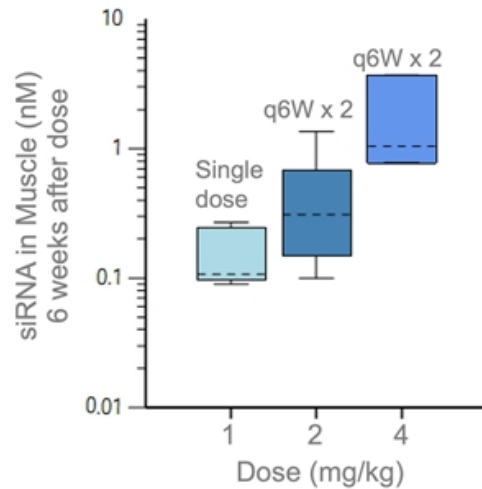
Mean % DMPK Reduction



- Data represented as 6 weeks post last dose

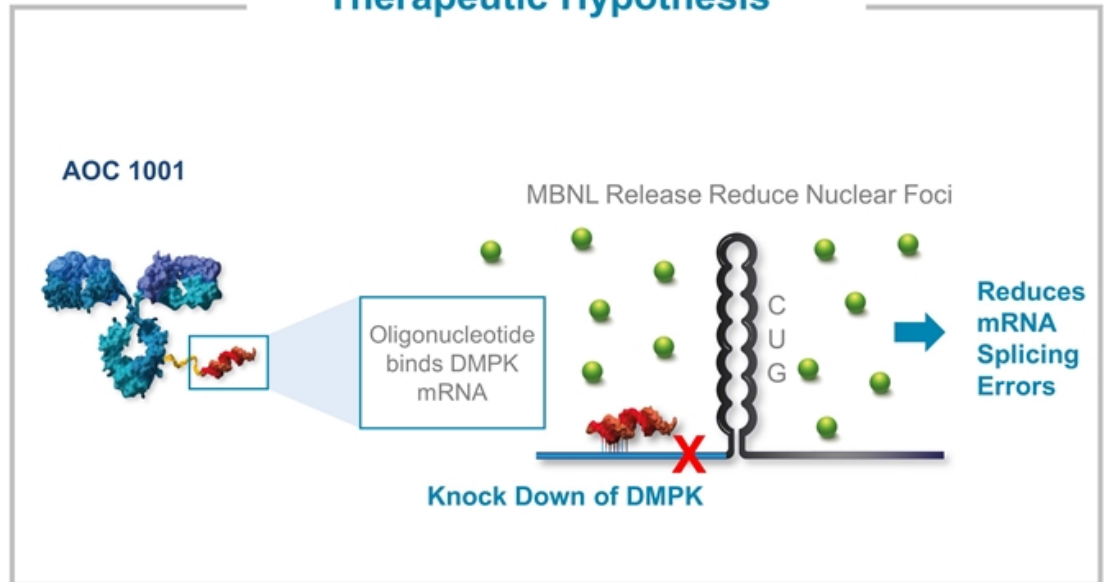
Why is DMPK inhibition similar between 1 and 2 mg/kg doses?

siRNA Concentrations



siRNA muscle tissue concentrations are overlapping between the 1 mg/kg and 2 mg/kg cohorts leading to similar DMPK inhibition

Therapeutic Hypothesis

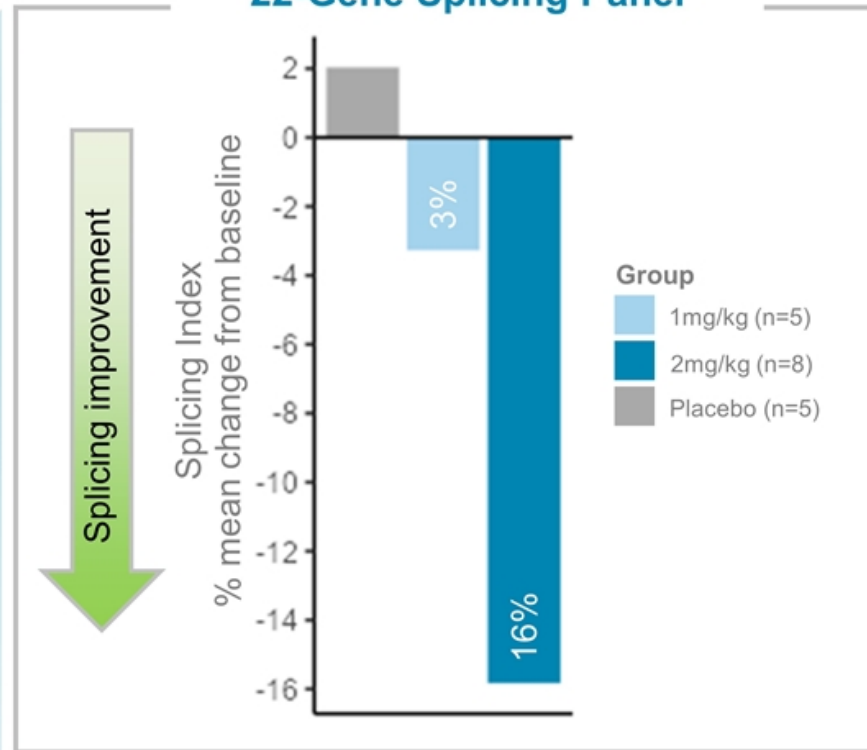


Dose and Time Dependence: Potential to observe dose-dependent DMPK inhibition with higher and longer dosing

Sustained DMPK Reduction Leads to Dose-Dependent Splicing Improvements



22-Gene Splicing Panel

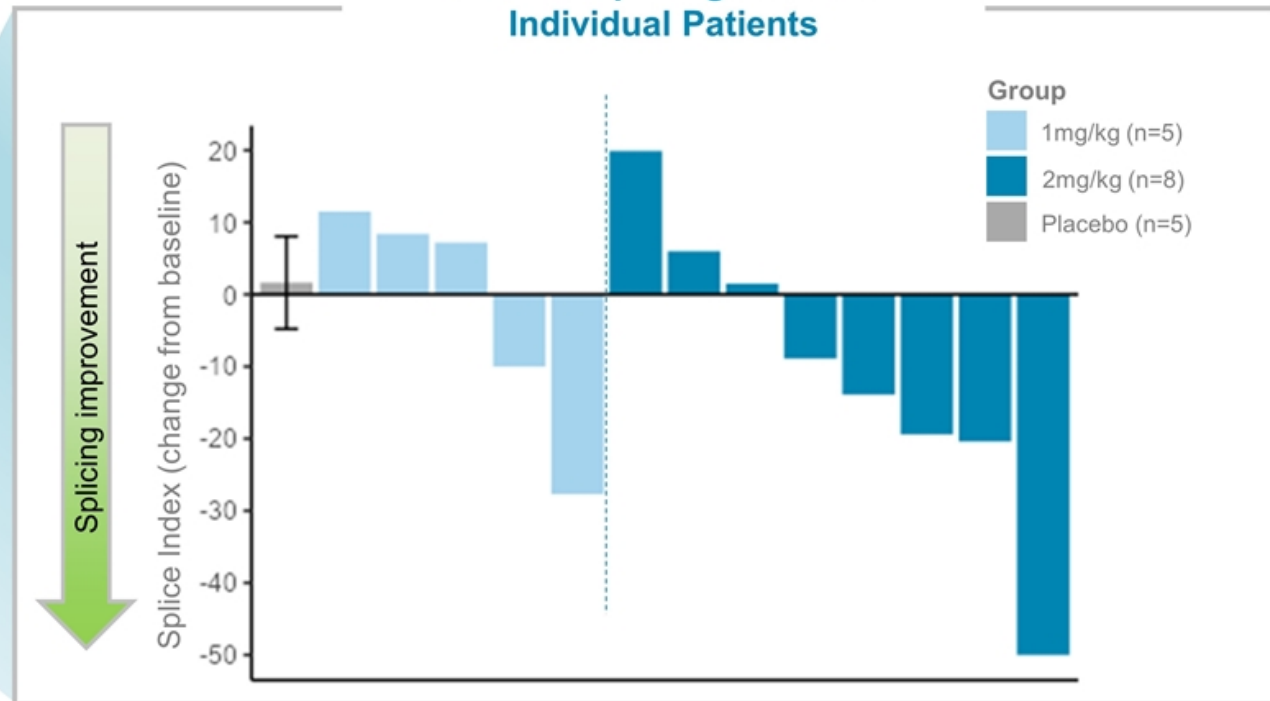


- Splicing measured by targeted RNA sequencing and calculated using published formula (Tanner et. al 2021)
- % mean change is calculated as mean change from baseline/mean baseline score across all matched samples in a cohort
- Data represented as 6 weeks post last dose

Splicing Improvements in Participants with DM1 Demonstrates AOC 1001 is Impacting Disease Mechanism



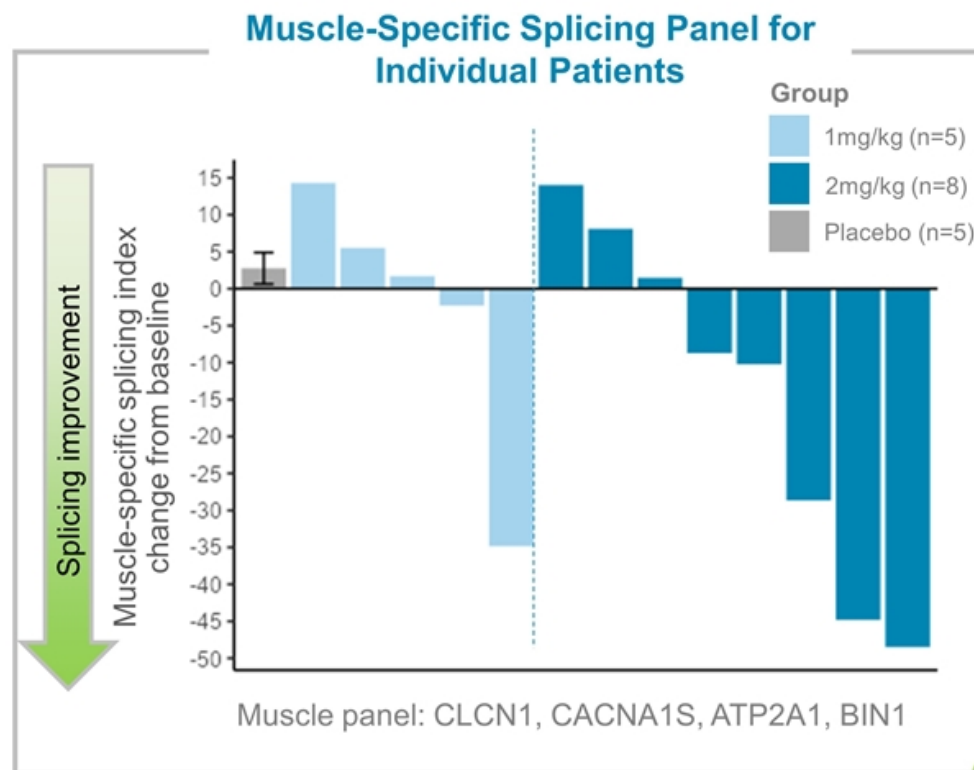
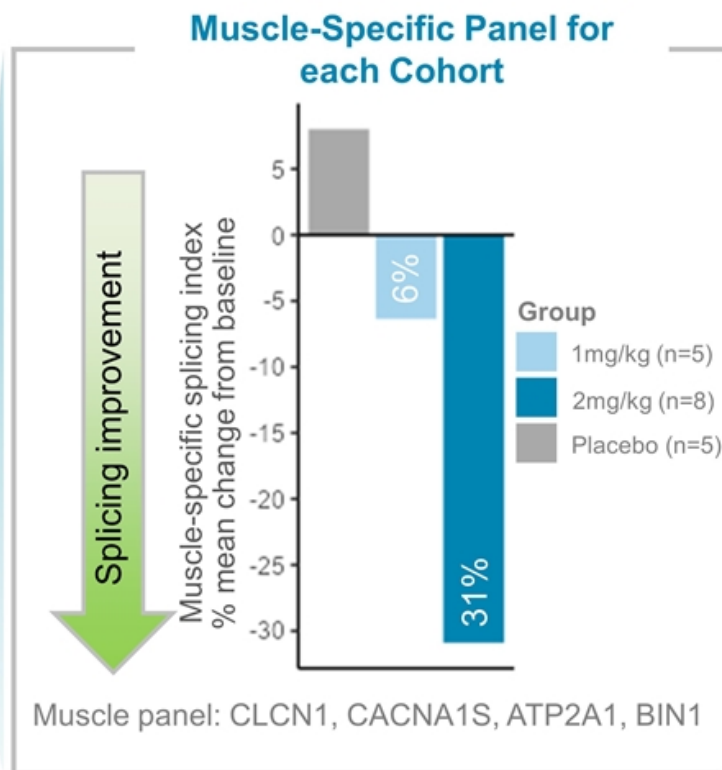
22-Gene Splicing Panel for Individual Patients



- Splicing measured by targeted RNA sequencing and calculated using published formula (Tanner et. al 2021)
- Splicing Index for each participant is calculated as absolute change from baseline (22-gene panel)
- Data represented as 6 weeks post last dose with placebo group combined from all cohorts (standard error of the mean)

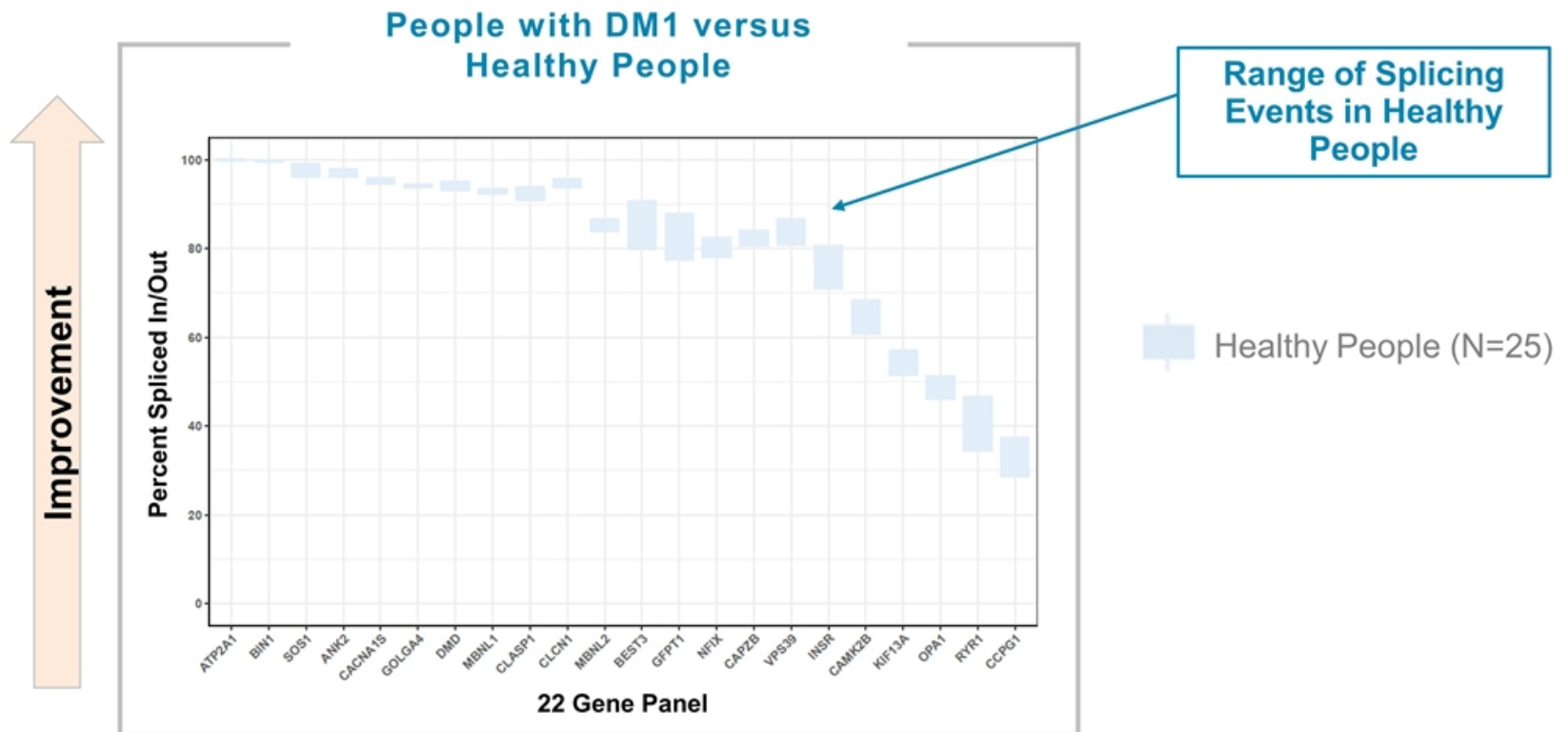
Muscle-Specific Biomarkers Shows 31% Splicing Improvement

Refining biomarker panel to guide future clinical development



- Splicing measured by targeted RNA sequencing and calculated using published formula (Tanner et. al 2021)
- Splicing Index for each participant is calculated as absolute change from baseline (4-gene panel)
- Data represented as 6 weeks post last dose with placebo group combined from all cohorts

Framework for Assessing Splicing Data Across 22 Genes in Healthy and DM1 Participants



Data from Charles Thornton, MD, University of Rochester Medical Center

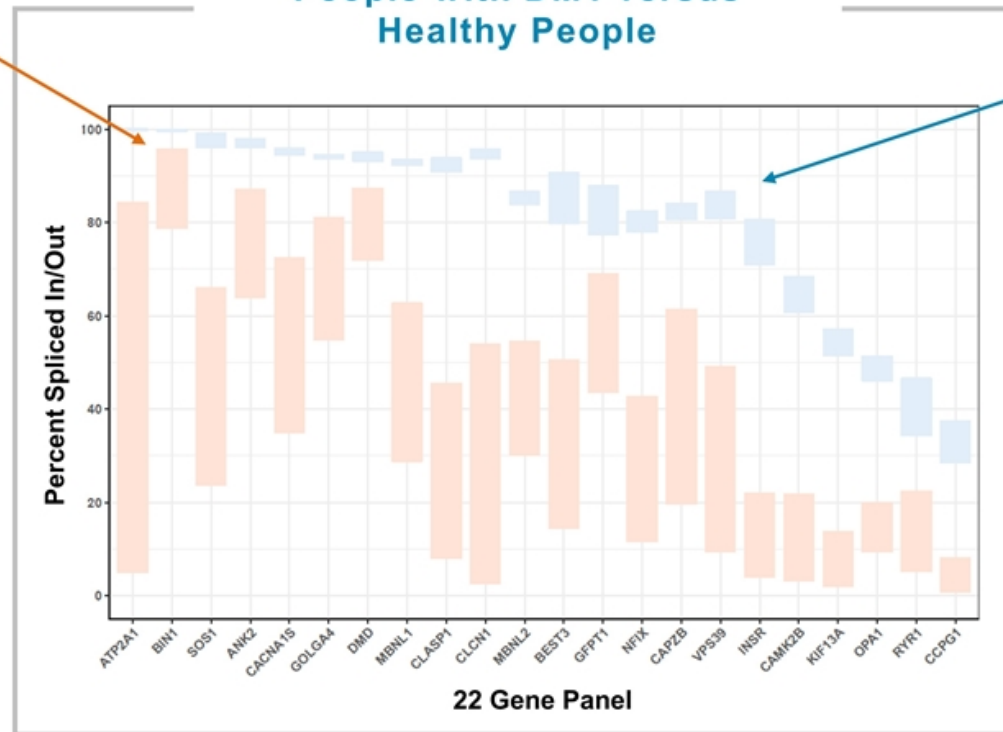
Framework for Assessing Splicing Data Across 22 Genes in Healthy and DM1 Participants

Range of Splicing Events in People with DM1

People with DM1 versus Healthy People

Range of Splicing Events in Healthy People

Improvement



Data from Charles Thornton, MD, University of Rochester Medical Center

Framework for Assessing Splicing Data Across 22 Genes in Healthy and DM1 Participants

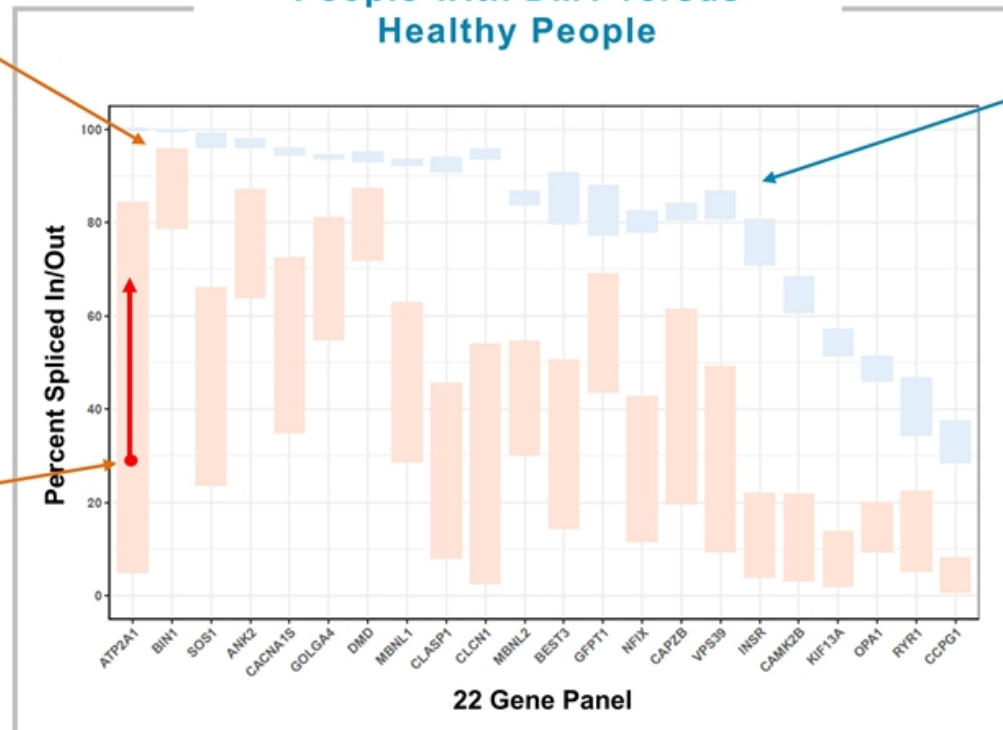
Range of Splicing Events in People with DM1

People with DM1 versus Healthy People

Range of Splicing Events in Healthy People

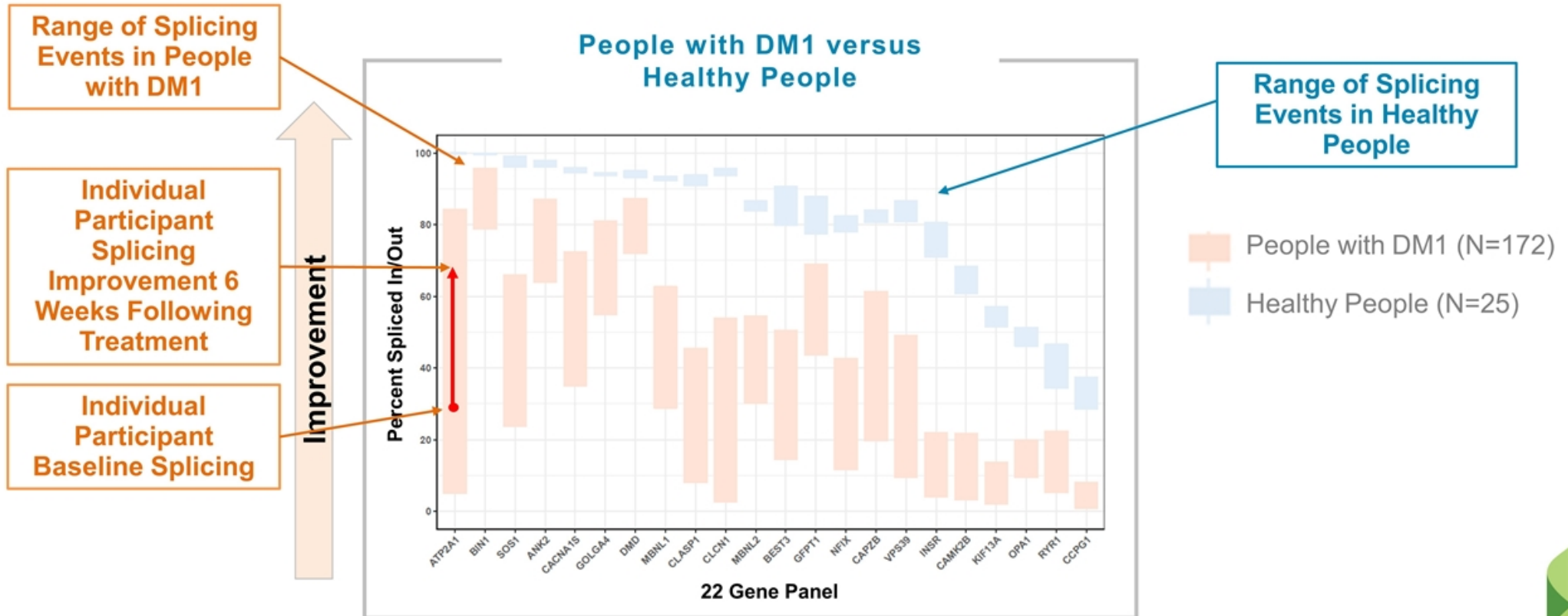
Individual Participant Baseline Splicing

Improvement



Data from Charles Thornton, MD, University of Rochester Medical Center

Framework for Assessing Splicing Data Across 22 Genes in Healthy and DM1 Participants

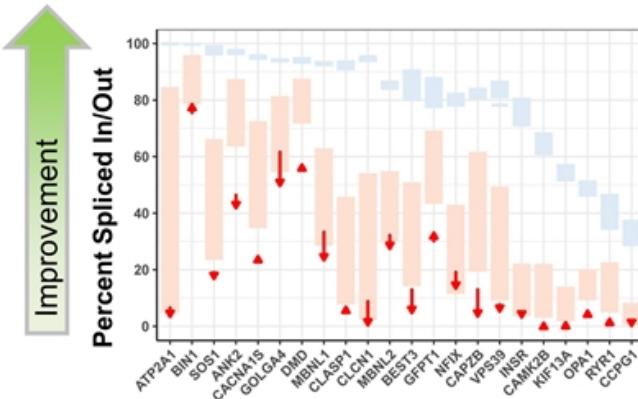


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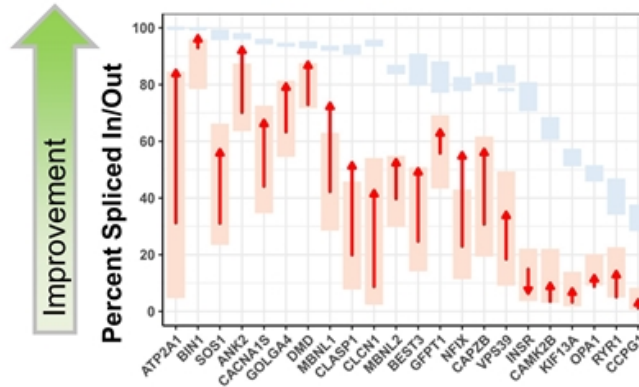
Improved Splicing Observed Across 22-gene Panel in Two Early Responders Following Treatment



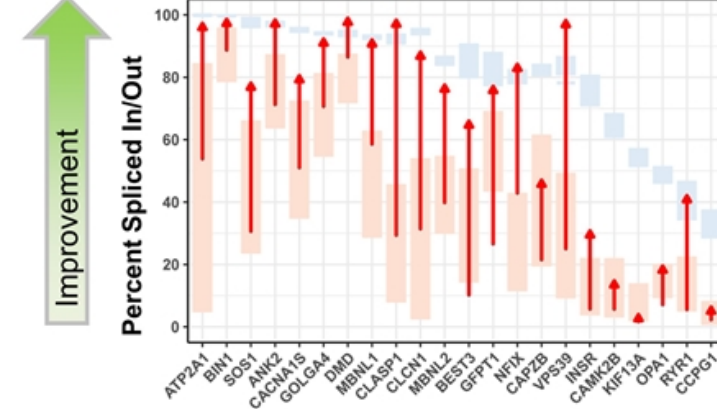
Representative Placebo Participant



Early Responder
1 mg/kg, single dose



Early Responder
2mg/kg, two doses



- People with DM1 (N=172)
- Healthy People (N=25)
- Splicing change – study participant

Splicing improvements demonstrate AOC 1001 activity in the nucleus



Population data from Charles Thornton, MD, University of Rochester Medical Center

AOC 1001 Shows Early Signs of Myotonia Benefit

Early responder from Cohort A (1mg/kg) shows improvement weeks after first dose

Participant from
1mg/kg Single Dose

Baseline vHOT



Day 43 vHOT
6 weeks after single dose



Day 92 vHOT
12 weeks after single dose



Day 183 vHOT
24 weeks after single dose



Improvement visible at Day 43 but myotonia benefit wanes by 6 months following a single dose at 1 mg/kg



vHOT = video hand opening time

AOC 1001 Shows Early Signs of Myotonia Benefit

Early responder from Cohort B1 (2mg/kg) shows improvement weeks after first dose

Participant from
2mg/kg Multidose

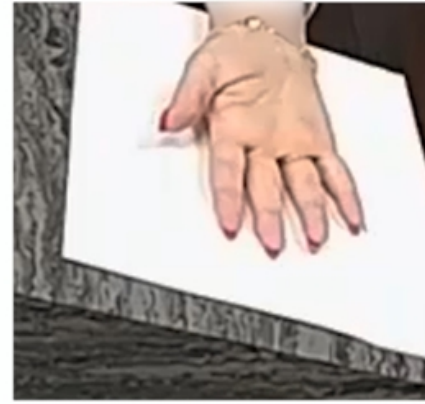
Baseline vHOT



Day 43 vHOT
6 weeks after first dose



Day 92 vHOT
6 weeks after second dose



Day 183 vHOT
12 weeks after third dose



Improvement visible at Day 43 that is sustained for at least 12 weeks following the third dose at 2 mg/kg



vHOT = video hand opening time

AOC 1001 Shows Early Signs of Myotonia Benefit

Early responder from Cohort B1 (2mg/kg) shows improvement

Participant from
2mg/kg Multidose

Baseline vHOT



Day 183 vHOT
12 weeks after third dose



Improvement visible at Day 43 that is sustained for at least 12 weeks following the third dose at 2 mg/kg

vHOT = video hand opening time

Delivering on the Platform and Impacting Disease Mechanism



Platform Achievements:

- AOC technology delivered siRNA to muscle – a first for the RNA field
- AOC 1001 achieved a meaningful DMPK reduction in 100% of treated participants
- 45% mean DMPK Reduction in treated participants

DM1 Advancements:

- AOC 1001 showed early signs of myotonia improvement just weeks after dosing with the two lowest doses in the trial
- Splicing improvements demonstrated AOC 1001 activity in the nucleus
 - 16% splicing improvement across 22 gene panel
 - 31% improvement in key muscle-specific panel

Next Steps:

- Continuing batch analyses of 2mg/kg and 4mg/kg samples from participants in MARINA & MARINA-OLE
- Refining biomarker panel to be utilized in pivotal trials



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Art Levin, Ph.D., CSO

Avidity Management
Dr. Nicholas Johnson, VCU
Kath Gallagher, SVP, Communications & IR (Moderator)

Sarah Boyce, President & CEO



Clinical Impact of Myotonic Dystrophy Type 1



Nicholas E. Johnson, M.D., M.Sci., FAAN

Vice Chair for Research, Department of Neurology, Virginia Commonwealth University

Dr. Johnson is an associate professor, division chief of neuromuscular, and vice chair of research in the department of neurology at Virginia Commonwealth University with a focus in inherited neuromuscular disorders. He received his undergraduate degree in molecular and cellular biology and psychology at the University of Arizona. He then obtained his medical degree at the University of Arizona. He completed his neurology residency and combined fellowship in neuromuscular medicine and experimental therapeutics at the University of Rochester. His laboratory is focused on identifying the pathogenesis of myotonic dystrophy, the limb girdle muscular dystrophies, and facioscapulohumeral muscular dystrophy and identifying appropriate clinical endpoints for these conditions. Dr. Johnson conducts therapeutic trials in many other inherited nerve and muscle disorders.



Clinical Impact of Myotonic Dystrophy Type 1

Nicholas Johnson, MD, Msci, FAAN

Vice Chair of Research, Associate Professor

Director, Muscular Dystrophy Translational Program

Departments of Neurology, Human Molecular Genetics

Virginia Commonwealth University



VCU

Myotonic Dystrophy Type 1

- Autosomal Dominant
- Core features in skeletal muscle
 - Weakness/wasting
 - Preferentially affects distal, cranial, and respiratory muscles
 - Myotonia
 - Preferentially affects hand/forearm muscles
- Multi-systemic
- Mean age of death is age 55

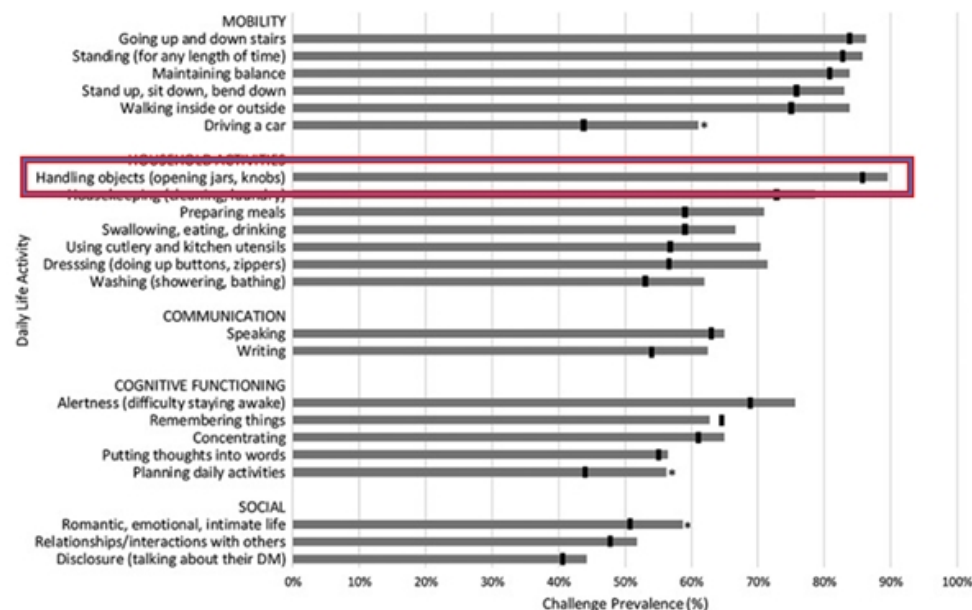
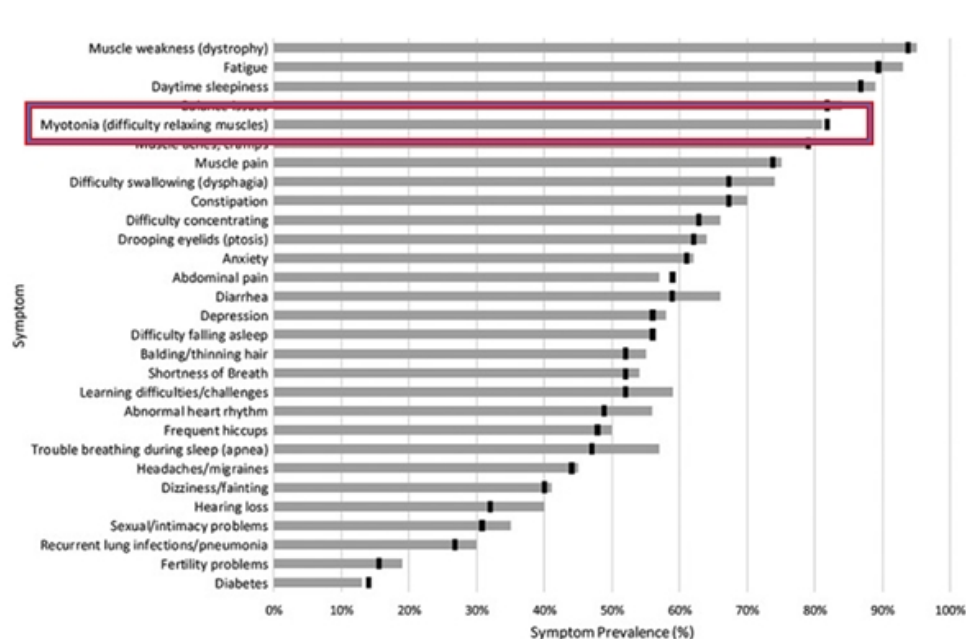
Example of grip myotonia



Other Systems

- Respiratory
 - Respiratory failure is most common cause of death
- Cardiac
 - Bradycardia, heart block, sudden death
- Ocular
 - Cataracts
- Gastrointestinal
 - Smooth muscle is affected
- Endocrine
 - insulin resistance
- CNS
 - Sleep regulation
 - A range of behavioral & cognitive changes may occur
- Increased risk of neoplasms

Myotonia is a prevalent cause of disability



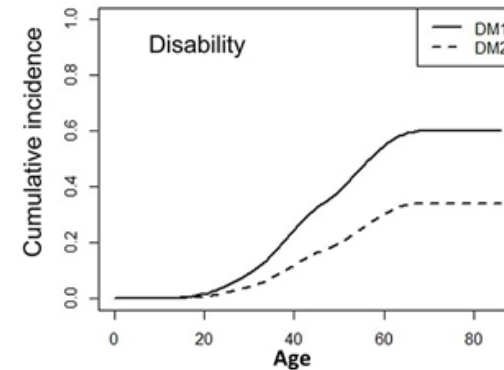
Survey of 1,180 Individuals with myotonic dystrophy (457 DM1 participants)

Hagerman, et al. 2019

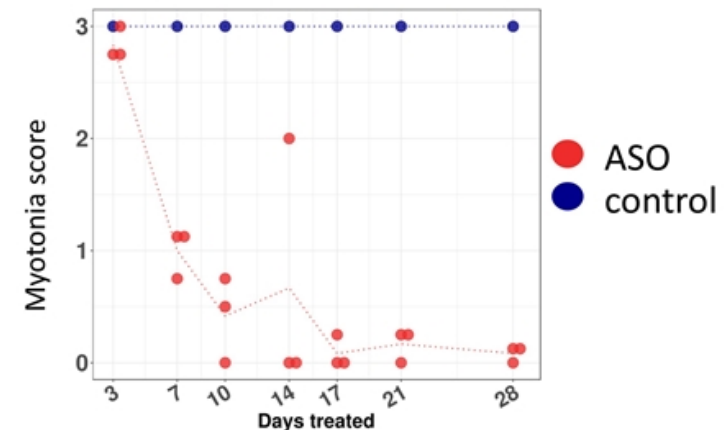
Myotonia in DM1 relates to ion channelopathies

- Chloride channel mis-splicing causes myotonia
- Calcium channel mis-splicing aggravates myotonia
- Together they may also cause inexcitability / weakness
- Hands are selectively affected

Hand impairment leads to disability



Twice weekly SQ injection transgenic mice

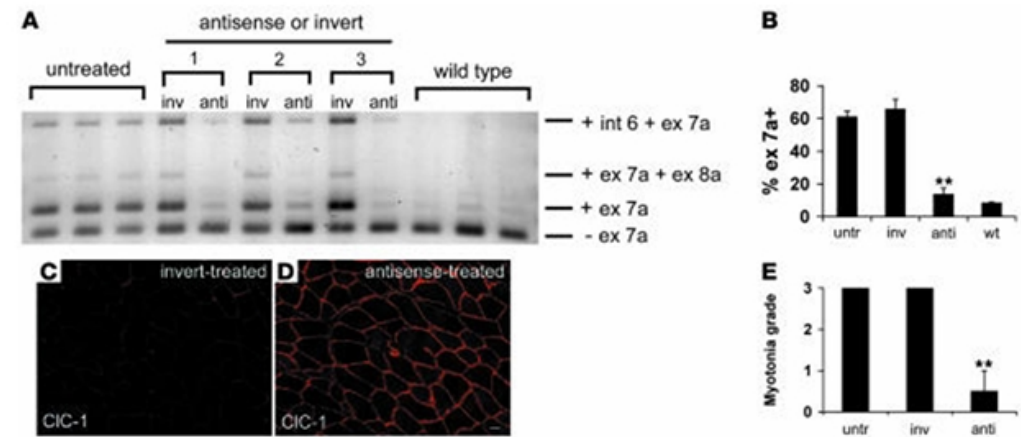


Correction of chloride channel splicing improves myotonia

Mouse model of myotonic dystrophy (HSA^{LR})

Use ASO to correct chloride channel splicing associated with DM1

Correction of chloride channel improves myotonia



Wheeler, et al., 2007

The Importance of Myotonia

- Prevalent cause of disability
- Directly tied to repeat expansion
- Channel dysfunction (e.g., myotonia) may change faster than strength

The International END-DM1 Study will Help Establish Biomarkers and Clinical Endpoints Needed to Support DM1 Clinical Trial Design



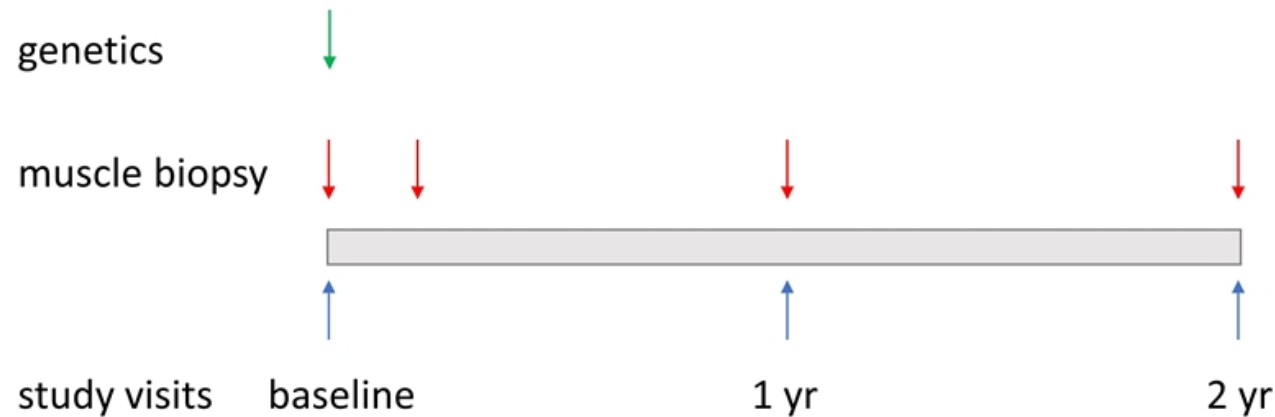
END-DM1, Establishing Biomarkers and Clinical Endpoints in Myotonic Dystrophy Type 1. ClinicalTrials.gov. NCT03981575 (END-DM1). [Last accessed March 2022].

- Current natural history study for the Myotonic Dystrophy Clinical Research Network (DMCRN)
- Enrolling 700 participants
- Observation period: 24 months
- Characterizing endpoints, patient-reported outcomes, and patient populations to support design and recruitment of interventional trials

Specific goals of END-DM1 study

- Characterize DM1 severity and disease progression over two years in a large cohort (n = 700)
 - Determine basal levels of impairment using standardized measures motor function and muscle strength and a patient-reported outcome (PRO)
 - Test for patient characteristics at baseline that predict subsequent progression
- Complete the development of muscle RNA alternative splice events as biomarkers of DM1 severity.
 - Optimize sample collection (smaller needles, less invasive)
 - Test-retest reliability

Scheme of END-DM1 study



- 700 patients (320 enrolled)
- International network
- Supported by FDA. Now also buttressed by Myotonic Dystrophy Foundation and industry* (expansion to EU/NZ/CA)

* Avidity Biosciences, Dyne Therapeutics, Entrada Therapeutics, Vertex Pharmaceuticals

Clinical outcomes in END-DM1 study

Mobility (leg function)

- 10 m walk/run
- 6-minute walk
- Timed up and go
- 4 stair climb

Respiratory function

- vital capacity sitting and supine

Hand function

- 9-hole peg
- Grip strength
- Pinch strength

Myotonia

- Video-recorded hand opening time (vHOT)

General muscle function

- Quantitative myometry (maximal isometric strength of limb muscles)
- tongue and lip muscle strength (IOPI)

Cardiac

- ECG

Patient reported outcomes

- DM Activ
- MDHI
- Anchoring questions for MCID

CNS

- Cogstate

Summary

- DM1 is a prevalent disease with significant morbidity and mortality
- The DMCRN natural history studies inform therapeutic trial design including:
 - COAs
 - Biomarkers
- This support will be provided to the Avidity program



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- Welcome & Introduction
- MARINA™: AOC 1001 Phase 1/2 Preliminary Data Assessment
- Living with Myotonic Dystrophy Type 1
- Broad Utility & Power of the Platform
- Q&A Session
- Closing Remarks

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Delivering on the RNA Revolution

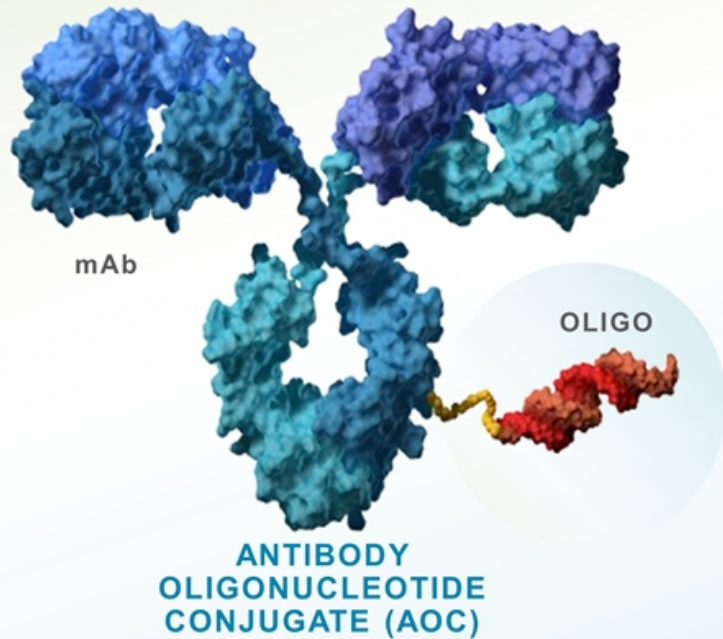
Art Levin, Ph.D., Chief Scientific Officer

The DM1 Cascade to Functional Benefit



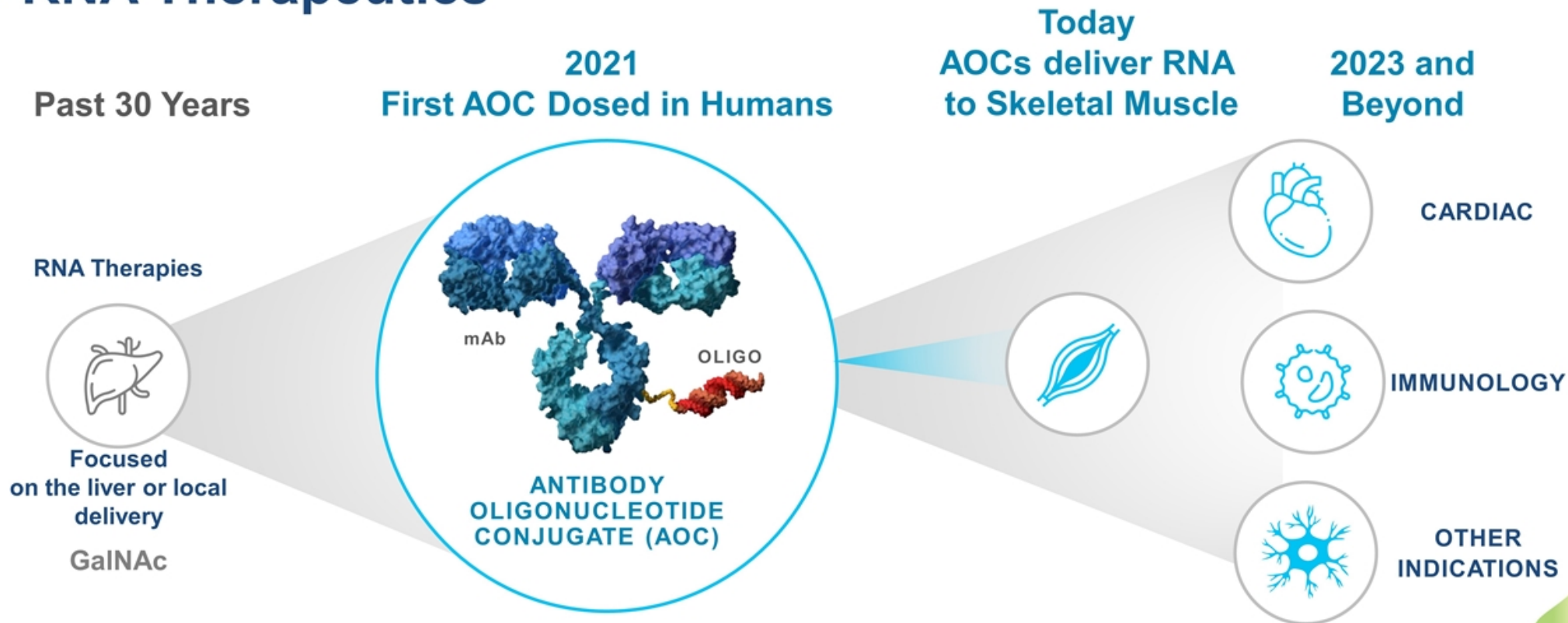
Splicing improvements leading to early signs of clinical activity with improvement in myotonia

Avidity Followed the Data to Engineer AOCs - A Powerful Potential New Class of Drugs



- Designed to combine the proven and safe technologies of approved monoclonal antibodies and oligonucleotides
 - ✓ Specificity of targeting with mAbs
 - ✓ Potency & precision of oligonucleotides
 - ✓ Targets tissues with durable agents
- Designed to deliver to tissues previously untreatable with RNA therapeutics
- Focused first on muscle, broadening to other tissues (i.e. cardiac) and cell types (i.e. B Cells)
- Readily scalable with many experienced manufacturers

AOCs Deliver to Muscle Starting A Breakthrough for RNA Therapeutics





Delivering on the RNA Revolution

- **Broad and disruptive AOC platform - new class of RNA therapeutics**
 - Followed the data to design and engineer AOCs
 - Delivered siRNA to muscle for the first time ever with AOC 1001 - a breakthrough for the field of RNA therapeutics
 - AOC platform expands ability to address targets and diseases previously unreachable with existing RNA therapies
- **Avidity AOC clinical and development programs**
 - AOC 1001 data reads through to the AOC platform
 - Advancing our three AOC clinical programs for the treatment of muscle diseases
 - Continue to expand our pipeline and programs in cardiology, immunology and other diseases

Delivering on the RNA Revolution



DM1

**MARINA™ / MARINA-OLE™ ongoing
MARINA Top-Line Data anticipated
in 2023**



DMD

**Cleared to initiate EXPLORE44™
Results from Healthy Volunteers
anticipated in 2H 2023**



FSHD

**Cleared to initiate FORTITUDE™
Preliminary Assessment anticipated
in 1H 2024**



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AOCs Deliver to Muscle – Revolutionary Advancement for the Field of RNA Therapeutics

Safety & Tolerability

MARINA Primary Endpoint; Phase 1/2 trial ongoing

Delivery to Muscle

First-ever successful targeted delivery of RNA to muscle – reinforces disruptive and broad potential of the AOC platform

DMPK Reduction

100% of treated participants had a DMPK reduction
45% mean DMPK reduction in treated participants

Impact on Disease Mechanism

16% splicing improvement across 22 gene panel
31% improvement in key set of muscle-specific genes

Early Signs of Clinical Activity

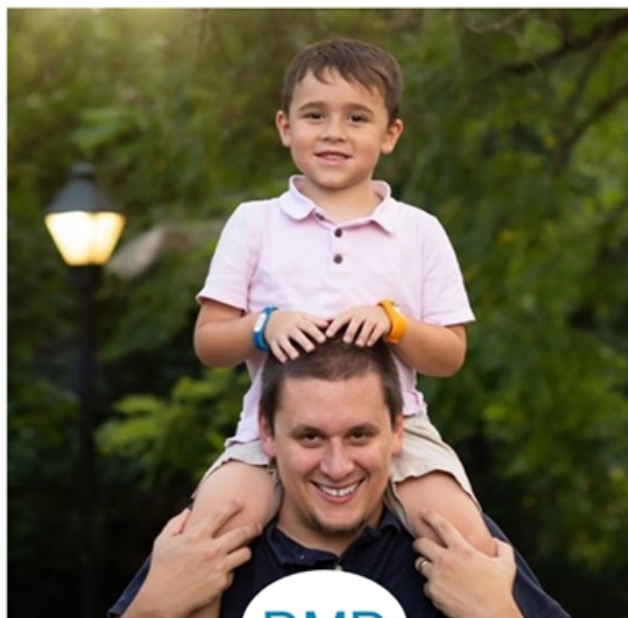
Myotonia improvement in early responders

Delivering on the RNA Revolution



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DELIVERING NEXT

**Pursuing preclinical proof of concept in
additional skeletal muscle and other tissues**



Delivering on the RNA Revolution Pursuing preclinical proof of concept in additional skeletal muscle and other tissues DELIVERING NEXT



Virtual Investor & Analyst Event Series – Volume 6: AOC 1001 MARINA™ Phase 1/2 Trial Preliminary Data Assessment

