



Investor & Analyst Event Series – Volume 7

AOC 1001 MARINA™ Phase 1/2 Topline Data









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, including, but not limited to, statements regarding: the characterization and implications of the Phase 1/2 MARINA topline safety, biomarker and functional data; expectations related to Avidity's discussions with, and data to be provided to, the FDA and any change of status in the existing partial clinical hold related to the Phase 1/2 MARINA trial; the safety, tolerability and benefits of AOC 1001; the severity of adverse events related to AOC 1001; our future results of operations and financial position; our 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; the potential of the AOC platform; plans and objectives of management for future operations; and future results of anticipated product development efforts. 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 these items 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 of the underlying cause of the related serious adverse event may result in delays in the MARINA study or an inability to compete the study; the Phase 1/2 MARINA trial data as of the date hereof may differ materially from the final results of the trial; additional participant data related to AOC 1001 that continues to become available may be inconsistent with the data produced as of the date hereof and the conclusions drawn therefrom; 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; 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 AOC platform, 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 in our filings with the SEC, including under the heading "Risk Factors" in our Form 10-K for the year ending on December 31, 2022, filed with the SEC on February 28, 2023, 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. 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



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



Advancing a New Class of RNA Therapeutics

BROAD & DISRUPTIVE P L A T F O R M	 Committed to delivering a new class of RNA therapies Advancing three AOCs in clinical development; two siRNAs and first PMO Broadening beyond muscle to other indications like cardiology and immunology through internal discovery & partnerships 				
ADVANCING & EXPANDING PIPELINE	 Progressing robust pipeline in muscle; three programs in clinical development in approximately one year MARINA™ MARINA™LE™ explore 				
AGILE & DIVERSE COMPANY	 Leveraging expertise in rare diseases and RNA therapies to execute clinical programs and commercial operations Building an integrated and diverse company in service of our patients Strong financials with cash runway into mid-2025 				



*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.

AOC 1001 Topline Data: Disease Modification, Functional Improvement, and Dose Range Identified in DM1







Impact on Disease Mechanism

> Functional Improvement

Completed Successful MARINA Trial AOC 1001 demonstrates directional improvements in myotonia, strength and early signs of mobility in 6-month period

Functional improvements follow DMPK knockdown and splicing changes consistent with our understanding of the mechanism of disease

Identified Phase 3 dose range: 2-4mg/kg with 2mg/kg to be dosed more frequently

Favorable safety & tolerability profile*

Next step: align with health authorities on a path forward



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Goals for the Day

- Share AOC 1001 MARINA topline safety, functional and biomarker data
- Discuss Avidity's disruptive and broad AOC Platform
- Answer your questions







Sarah Boyce President & CEO

Steve Hughes, M.D. Chief Medical Officer



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



Art Levin, Ph.D. Distinguished Scientist & Strategic Leader



Mike MacLean Chief Financial & Business Officer





Kath Gallagher Elizabeth Ackermann SVP Corporate Communications SVP Clinical Development & Investor Relations

Avidity Management Team





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



AOC 1001 MARINA[™] Phase 1/2 Trial Topline Data Assessment

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

Steve Hughes, M.D., Chief Medical Officer

DM1 Burden and Significant Unmet Need

>40,000 PEOPLE WITH DM1 IN THE US



- 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
- Caused by triplet-repeat in DMPK gene, resulting in a toxic gain of function mRNA





Update on Clinical Trials



- Discussions with FDA on the AOC 1001 partial clinical hold for new participant enrollment remain ongoing
 - The partial hold is in response to a serious adverse event (SAE) reported in a single participant in the 4mg/kg cohort comprising of bilateral ischemia in the region of the lateral geniculate nuclei in the thalamus with subsequent hemorrhagic transformation. This was reported as thalamic hemorrhage
 - No plausible biological link to any component of AOC 1001, the AOC platform, the transferrin receptor delivery mechanism or reduction of DMPK was identified
 - Will share information on next steps once agreed plan is in place with FDA
- MARINA trial delivered solid data package to inform pivotal studies
 - MARINA trial concluded with 38 participants
 - Topline data was presented in oral presentation American Academy of Neurology (AAN) Annual Meeting
- First look at data from the MARINA-OLE study at the end of 2023



MARINA™ Trial Designed to Evaluate Safety and Tolerability of AOC 1001*



- With the 38 participants treated with AOC 1001 in MARINA and/or MARINA-OLE, we've administered 132 doses and accumulated ~27 total patient years of exposure[†]
- One participant receiving 4 mg/kg AOC 1001 discontinued treatment due to SAE
- As of April 20, 36 participants have enrolled in the MARINA-OLE



*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.

**Upon entry into MARINA OLE, biopsies were only taken for participants in Cohort A. *Booster dose was only given to participants who were in Cohort A1 and placebo B1/B2 † As of early March 2023

Preliminary Assessment in December 2022: DM1 Cascade to Functional Benefit



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AOC 1001 Positive Topline Data Demonstrates Disease Modification, Functional Improvement and Identifies Pivotal Dose Range







MARINA Topline Functional Assessments



IMPROVEMENT IN MYOTONIA

Video Hand Opening Time (vHOT)



Independently adjudicated

IMPROVEMENT IN STRENGTH

Quantitative Muscle Testing (QMT) Total Score*



Elbow Flexion



Knee Ankle Extension Dorsiflexion & Knee Flexion

EARLY SIGNS OF IMPROVEMENT IN MOBILITY MEASURES

10 Meter Walk Run Test (10mWRT)



DITY

SCIENCES

Timed Up and Go (TUG)



Topline Data from the AOC 1001 MARINA Phase 1/2 Trial



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

Associate Professor & Vice Chair of Research, Department of Neurology, Virginia Commonwealth University

Dr. Johnson is an associate professor 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.



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Topline Data from the AOC 1001 MARINA Phase 1/2 Trial

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

Baseline Demographics and Disease Characteristics



Mean (SD) or n (%)	Placebo N=10	1mg/kg N=6	2 mg/kg N=9	4 mg/kg N=13
Age	46.5 (8.7)	37.0 (18.0)	37.6 (13.6)	44.0 (12.4)
Female	5 (50)	5 (83.3)	9 (100)	9 (69.2)
BMI	24.7 (3.5)	21.8 (5.2)	23.9 (5.0)	22.2 (4.5)
Spliceopathy score*	82.9 (11.8)	70.0 (20.2)	70.2 (20.8)	83.6 (20.2)
CTG Repeat Length, mean (SD)	616 (380)	463 (198)	675 (274)	585 (250)
Video Hand Opening Time (vHOT) (seconds) [◊]	10.1 (18.6)	6.8 (5.3)	8.0 (6.4)	10.2 (8.4)
10 Meter Walk Run test (10mWRT) (seconds)	6.8 (2.8)	5.2 (3.2)	6.7 (3.1)	7.7 (3.1)
Timed Up and Go (TUG) (seconds)	6.6 (2.6)	5.7 (2.0)	6.6 (1.5)	7.5 (2.2)
Quantitative Muscle Testing (QMT) [†] (% pred nl) [*]	51.5 (16.3)	56.3 (13.3)	50.1 (12.0)	41.6 (19.3)

* Composite of 22 splicing events; higher number is more severe; 1 participant in the placebo group and 3 participants in the 4mg/kg cohort had insufficient tissue for analysis ◊ As measured by the middle finger opening time

† QMT is a total composite score based on 6 muscle groups tested: hand grip, elbow extension, elbow flexion, ankle dorsiflexion, knee extension, knee flexion # % predicted normal



Generally Favorable Safety and Tolerability



Summary of Treatment emergent Adverse Events

Subjects with ≥ 1 AE n (%)	Placebo N=10	1 mg/kg N=6	2 mg/kg N=9	4 mg/kg N=13
Any AE	8 (80%)	6 (100%)	9 (100%)	13 (100%)
Related to study drug	2 (20%)	1 (17%)	3 (33%)	10 (77%)
Serious AE (SAE)*	0	0	1 (11%)	1 (8%)
AE leading to study discontinuation**	0	0	0	1 (8%)
AE leading to death	0	0	0	0

Most treatment emergent adverse events (AEs) were mild or moderate

- Most common AEs⁺
 - procedural pain (36%)
 - anemia (32%)
 - COVID-19 (23%)
 - headache (23%)
 - nausea (23%)
- 1 discontinuation due to an SAE
- Anemia events were monitorable and reversible
- Liver enzyme increases were observed (18%); interpretation is complicated by underlying disease & elevated baseline values (up to ~2.5x greater than upper limit of normal)
 - No impact on bilirubin



*1 SAE considered related to AOC 1001 4 mg/kg: resulted in a partial clinical hold; 1 SAE considered unrelated to treatment: reaction to opioid pain medication after an elective surgery

*Patient discontinued from the study due to the SAE

[†] Most common AEs are defined as those above 20% in combined 2 and 4 mg/kg treated participants

AOC 1001 Demonstrates Myotonia Reduction in Early Responder from 2mg/kg Cohort





Improvement visible 3 months following the third dose at 2 mg/kg



vHOT, video hand opening time.

Participants Treated with AOC 1001 Demonstrated Improvements in Myotonia, a Hallmark of DM1 at 2 mg/kg and 4 mg/kg

AOC 1001 achieved statistical significance at 4mg/kg in a post-hoc analysis at all time points





Participants Treated with AOC 1001 had Improvements in Total Muscle Strength at 2 mg/kg and 4 mg/kg

AOC 1001 achieved statistical significance at 4mg/kg in a post-hoc analysis at day 183





Placebo group combined from Cohort B1 (2mg/kg) and Cohort B2 (4mg/kg) Error bars = standard error of the mean (SEM) ⁺QMT Total Score is based on 6 muscle groups from both upper and lower body [‡] % predicted normal

AOC 1001 Showed Early Signs of Improvement in Mobility Measures







AOC 1001 Showed Early Signs of Improvement in Mobility Measures







AOC 1001 Demonstrates Myotonia Reduction in 4 mg/kg Cohort





Improvement visible 3 months following the third dose at 4 mg/kg



vHOT, video hand opening time.

MARINA Phase 1/2 Trial Demonstrates AOC 1001 Impacts Disease Mechanism and Achieves Functional Improvement MARINATM

- DM1 is an underrecognized, progressive, and often fatal neuromuscular disease with a high unmet need and no approved therapies
- AOC 1001 is an investigational antibody oligonucleotide conjugate that successfully delivered siRNA to muscle resulting in DMPK reductions and splicing improvements leading to functional improvements
- Top line data from MARINA demonstrate directional improvement in multiple clinical endpoints in the dose range of 2-4mg/kg of AOC 1001 including:
 - o Improvements in myotonia (vHOT) as early as 6 weeks after dosing with a sustained effect at month 6
 - Improvement in QMT total strength measure observed at month 6
 - Early signs of mobility improvements in the 10mWRT and the TUG
- AOC 1001 had a generally favorable safety and tolerability profile
- Data support advancement of AOC 1001 into Phase 3 study



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AOC 1001: Impact on Disease Mechanism

W. Michael Flanagan Chief Scientific and Technical Officer

AOC 1001 Positive Topline Data Demonstrates Disease Modification, Functional Improvement and Identifies Pivotal Dose Range







MARINA™ Topline Data at 6 Weeks Post-Dose



NOTE: Day 92 biopsy in 2mg/kg & 4mg/kg cohorts taken prior to third dose of AOC 1001

Cohort	Number of Participants Enrolled	Number of Biopsies Available for PK/PD Analysis	
		PK	PD
Placebo	10	N/A	9
1mg/kg	6	6	5
2mg/kg	9	8	9
4mg/kg	13	10	9

- 1 participant in 2 mg/kg group had a muscle biopsy soon after the third dose and was removed from the PK analysis
- 1 participant in the placebo group, 1 from the 1mg/kg and 3 participants in the 4mg/kg cohort had insufficient tissue for analysis
- The participant who experienced the SAE only received a baseline biopsy



MARINA[™]

AOC 1001 Delivered siRNA to Muscle Expanding siRNA Therapeutics Beyond Liver





OUCIENCES

AOC 1001 Produced 42% mean DMPK Knockdown **Demonstrating Target Engagement**





Splicing Improvements in 22 Gene Panel Demonstrates AOC 1001 is Impacting DM1 Disease Mechanism



Data shown at 6 weeks post a single dose of the 1mg/kg and 6 weeks post two doses of 2mg/kg or 4 mg/kg

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) Placebo group combined from all cohorts (standard error of the mean) mean absolute change from baseline score across all matched samples in a cohort

RANGE

DITY

MARINA[™]

Muscle-Specific Biomarkers Show Splicing Improvement



Placebo group combined from all cohorts (standard error of the mean) Mean change from baseline is the mean absolute change from baseline score across all matched samples in a cohort

OUCIENCES

MARINATM

AOC 1001 (2 mg/kg) Broadly Impacts DM1 Disease Mechanism in Over 1,000 Splicing Events

\VIDITY





Each column represents 1 participant's splicing at baseline compared to 6 weeks post dose



Delivering on the AOC Platform and Impacting Disease Mechanism

Platform Achievements:

PROOF OF

AOC PLATFORM

IPACT ON

DISEASE MECHANISM

INCTIONAL

MPROVEMENT

DENTIFIED

PIVOTAL

DOSE RANGE

DITY

- AOC technology delivered siRNA to muscle a first for the RNA field
- AOC 1001 achieved DMPK knockdown demonstrating target engagement
- 42% mean DMPK reduction in treated participants

DM1 Advancements:

- Demonstrated splicing improvement leading to functional benefit
- Broad splicing changes in over a thousand genes confirm activity in the nucleus

Next Steps:

- Analyze & interpret additional biomarker data from MARINA including:
 - Analysis of third biopsies in MARINA
 - Continue to analyze RNA sequencing data from all cohorts
- Analyze day 183 biopsies from MARINA and MARINA-OLE

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Delivering on the AOC Platform -Broad Utility & Power of the Platform

Art Levin, Avidity Board Member and Distinguished Scientist & Strategic Leader

AOC[™] Platform: Building on the Power of Oligonucleotides



AOC platform advantages include:

- ✓ 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



Diverse and Expanding AOC Pipeline

PROGRAM / INDICATION	TARGET	LEAD OPTIMIZATION	IND ENABLING	PHASE 1/2	PHASE 3
AOC 1001 Myotonic Dystrophy Type 1 (DM1)	DMPK			MARIN	I A™ MARINA≪ DLE™
AOC 1044 Duchenne Muscular Dystrophy (DMD)	Exon 44			explore	
AOC 1020 Facioscapulohumeral Muscular Dystrophy (FSHD)	DUX4			FORTI	TUDE™
Additional DMD Programs	Exon 45 & Undisclosed				
Rare Skeletal Muscle Program	Undisclosed				
Rare Cardiac Program	Undisclosed				



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A New Paradigm of RNA Therapeutics with AOCs Targeting muscle and other tissues beyond the liver



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



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Q&A Session





