Avidity Biosciences Announces New Positive AOC 1001 Data Demonstrating Improvement in Multiple Additional Functional Endpoints and Favorable Long-term Safety and Tolerability in People with Myotonic Dystrophy Type 1

New AOC 1001 data demonstrate improvement in additional functional measures including hand grip, muscle strength and patient reported outcomes, augmenting previously reported positive data showing improvements in myotonia, muscle strength and mobility

New long-term safety data of AOC 1001 continue to demonstrate favorable safety and tolerability with over 200 infusions totaling 46.2 patient-years of exposure

Data from 12 participants dose-escalated from 2 mg/kg to 4 mg/kg of AOC 1001 as part of the easement of the partial clinical hold showed no neurological events and no MRI changes following dosing

Company plans to share AOC 1001 data from MARINA-OLE study in first half of 2024 and is finalizing Phase 3 study design and global regulatory path for AOC 1001

SAN DIEGO, Oct. 7, 2023 /PRNewswire/ -- Avidity Biosciences, Inc. (Nasdaq: RNA), a biopharmaceutical company committed to delivering a new class of RNA therapeutics called Antibody Oligonucleotide Conjugates (AOCs™), today announced new positive AOC 1001 data demonstrating improvement in multiple additional functional endpoints and favorable long-term safety and tolerability in people living with myotonic dystrophy type 1 (DM1). AOC 1001, Avidity's lead clinical program utilizing its AOC platform, is designed to address the root cause of DM1, an underrecognized, progressive and often fatal neuromuscular disease with no approved therapies. The AOC 1001 data from the Phase 1/2 MARINA® trial and MARINA open-label extension (MARINA-OLE™) study will be highlighted in an oral presentation at the 28th Annual Congress of the World Muscle Society (WMS) in Charleston, South Carolina and can be found on Avidity's website on the Publications page.

"The new AOC 1001 data presented today demonstrating improvements in muscle strength and patient reported outcomes add to the previously reported positive topline data showing improvements in myotonia and mobility. The AOC 1001 data continues to be quite remarkable with consistent improvements across multiple functional endpoints," said Nicholas E. Johnson, M.D., M.Sci., FAAN, associate professor and vice chair of research in the Department of Neurology at Virginia Commonwealth University, lead investigator of the MARINA trial and study presenter. "The AOC 1001 functional data coupled with the long-term favorable tolerability and safety data provide us with hope that AOC 1001 has the potential to help patients with DM1, who are in desperate need of treatments."

The new AOC 1001 data demonstrate improvement in additional functional measures including hand grip, muscle strength and patient reported outcomes, augmenting previously reported positive data showing improvements in myotonia, muscle strength and mobility. With new long-term safety data from over 200 infusions totaling 46.2 patient-years of exposure, AOC 1001 continues to demonstrate favorable safety and tolerability with most adverse events (AEs) mild to moderate.

"Data from MARINA and MARINA-OLE reinforce our belief in the potential of AOC 1001 to become an effective treatment option for people living with DM1, a devastating rare disease for which there are no treatment options available. With this robust data package, we are finalizing the Phase 3 study design and global regulatory path for AOC 1001 and look forward to sharing a first look at efficacy data from the MARINA-OLE study in the first half of 2024," said Sarah Boyce, president and chief executive officer at Avidity. "In addition to our DM1 program, we continue to advance our DMD and FSHD clinical development programs and plan to report data from all three of our programs by mid-2024 while continuing to expand our discovery and development pipeline."

In May 2023, the U.S. Food and Drug Administration (FDA) eased the partial clinical hold on AOC 1001, allowing Avidity to double the number of participants in the MARINA-OLE study receiving 4 mg/kg of AOC 1001 from 12 to 24 participants. Data from the 12 participants dose-escalated from 2 mg/kg to 4 mg/kg of AOC 1001 as part of the easement of the partial clinical hold showed no neurological events and no MRI changes following dosing. The company continues to work as quickly as possible to resolve the partial clinical hold.

Data presented at World Muscle Society (WMS)
The Phase 1/2 MARINA trial was a randomized, double-blind, placebo-controlled study designed to evaluate the safety and tolerability of single and multiple ascending doses of AOC 1001 administered intravenously in adults

with DM1. Data were assessed from a 3:1 randomized study with 38 participants who were administered one dose of 1 mg/kg of AOC 1001, three doses of either 2 mg/kg of AOC 1001 or 4 mg/kg of AOC 1001 (reflected as siRNA dose), or placebo. The endpoints used in MARINA measure important aspects of the disease and correspond to those utilized in the ongoing END-DM1 natural history study. All 37 participants that completed the MARINA trial remain on AOC 1001 in the MARINA-OLE trial. Safety and tolerability data of AOC 1001 include data from MARINA and MARINA-OLE. There were 10 participants treated with placebo in MARINA that were newly treated with AOC 1001 in MARINA-OLE.

New AOC 1001 data demonstrate improvement in additional functional measures augmenting previously reported positive data that demonstrated improvements in functional assessments of myotonia (video hand opening time, or vHOT), strength (Quantitative Muscle Testing total score, or QMT) and mobility (10-meter walk run test, or 10mWRT and the Timed Up and Go test, or TUG).

New positive AOC 1001 data presented at WMS include:

- Multiple additional measures of strength:
    - Hand grip
    - Manual Muscle Testing (MMT) composite score
    - Both upper and lower QMT composites
- DM1-Activ, a patient reported outcome (PRO) that measures activities of daily living (e.g., taking a shower, visiting family or friends, and walking up stairs).

New favorable long-term AOC 1001 safety and tolerability data include data from MARINA-OLE with over 200 infusions totaling 46.2 patient-years of exposure.

- The most common AEs in the MARINA-OLE were procedural pain (22%), pain in extremity (such as arm, leg or foot pain/soreness) and headache (both 16%).
- There was one resolved adverse event of mild increase in liver enzymes.
- There have been no reported AEs of anemia in the MARINA-OLE. In the MARINA clinical program, anemia has been asymptomatic except for one participant who did not require treatment.
- There have been no discontinuations in the MARINA-OLE study.

In addition to evaluating AOC 1001 in the MARINA-OLE trial in people living with DM1, Avidity is also advancing AOC 1044 in the Phase 1/2 EXPLORE44™ trial in people living with DMD44 and plans to report data from healthy volunteers in the EXPLORE44 trial in the fourth quarter of 2023. In addition, the company is evaluating AOC 1020 in the Phase 1/2 FORTITUDE™ trial in people living with FSHD. Data from a preliminary assessment in approximately half of the participants in the FORTITUDE trial is planned for the first half of 2024.

About the Phase 1/2 MARINA® Trial
The MARINA® trial is a randomized, double-blind, placebo-controlled, Phase 1/2 clinical trial that enrolled 38 adults with DM1. The primary objective of this study was to evaluate the safety and tolerability of single and multiple ascending doses of AOC 1001 administered intravenously. The MARINA trial assessed the activity of AOC 1001 across key biomarkers, including spliceopathy, an important biomarker for DM1, and knockdown of DMPK mRNA. Though the Phase 1/2 trial was not powered to assess functional benefit, it explored the clinical activity of AOC 1001 in multiple measures of muscle function including myotonia, muscle strength, measures of mobility as well as patient reported outcomes and quality of life measures. Patients had the option to enroll in MARINA-OLE, an open-label extension study, at the end of the post-treatment period. For more information on this study click here or visit http://www.clinicaltrials.gov and search for NCT05027269.

About the Phase 2 MARINA-OLE™ Study
MARINA-OLE™ is an open-label, multi-center trial designed to evaluate the long-term safety and tolerability of AOC 1001 in participants with DM1 who were previously enrolled in the MARINA Phase 1/2 trial. This trial will continue to evaluate the safety, tolerability, PK, PD, and efficacy of AOC 1001 in participants enrolled in the randomized, placebo-controlled, Phase 1/2 MARINA clinical trial. Participants enrolled in the MARINA-OLE study receive quarterly doses of AOC 1001 regardless of whether they received active treatment or placebo in the MARINA study. The total duration of active treatment with AOC 1001 in the MARINA-OLE study is approximately 24 months. Once patients have completed active treatment, there will be a nine-month safety follow-up period. Avidity may extend active treatment beyond 24 months at a future timepoint. For more information on this study click here or visit http://www.clinicaltrials.gov and search for NCT05479981.

About AOC 1001
AOC 1001, Avidity's lead product candidate utilizing its AOC platform, is designed to address the root cause of DM1 by reducing levels of a disease-related mRNA called DMPK. AOC 1001 consists of a proprietary monoclonal

antibody that binds to the transferrin receptor 1 (TfR1) conjugated with a siRNA targeting DMPK mRNA. In preclinical studies, AOC 1001 successfully delivered siRNAs to muscle cells, resulting in durable, dose-dependent reductions of DMPK RNA across a broad range of muscles including skeletal, cardiac, and smooth muscles. AOC 1001 is currently in Phase 1/2 development with the completed MARINA® trial and the ongoing MARINA-OLE™ trial in adults with DM1. The U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA) have granted Orphan Designation for AOC 1001 and the FDA has granted AOC 1001 Fast Track Designation.

About Myotonic Dystrophy Type 1
Myotonic dystrophy type 1 (DM1) is an underrecognized, progressive and often fatal disease caused by a triplet-repeat in the DMPK gene, resulting in a toxic gain of function mRNA. The disease is highly variable with respect to severity, presentation and age of onset, however all forms of DM1 are associated with high levels of disease burden and may cause premature mortality. DM1 primarily affects skeletal and cardiac muscle, however patients can suffer from a constellation of manifestations including myotonia and muscle weakness, respiratory problems, fatigue, hypersomnia, cardiac abnormalities, severe gastrointestinal complications, and cognitive and behavioral impairment. Currently, there are no approved treatments for people living with DM1.

About Avidity
Avidity Biosciences, Inc.'s mission is to profoundly improve people's lives by delivering a new class of RNA therapeutics - Antibody Oligonucleotide Conjugates (AOCs™). Avidity is revolutionizing the field of RNA with its proprietary AOCs, which are designed to combine the specificity of monoclonal antibodies with the precision of oligonucleotide therapies to address targets and diseases previously unreachable with existing RNA therapies. Utilizing its proprietary AOC platform, Avidity demonstrated the first-ever successful targeted delivery of RNA into muscle and is leading the field with clinical development programs for three rare muscle diseases: myotonic dystrophy type 1 (DM1), Duchenne muscular dystrophy (DMD) and facioscapulohumeral muscular dystrophy (FSHD). Avidity is broadening the reach of AOCs with its advancing and expanding pipeline including programs in cardiology and immunology through internal discovery efforts and key partnerships. Avidity is headquartered in San Diego, CA. For more information about our AOC platform, clinical development pipeline and people, please visit www.aviditybiosciences.com and engage with us on LinkedIn and X (formerly Twitter).

Forward-Looking Statements
Avidity cautions readers that statements contained in this press release regarding matters that are not historical facts are forward-looking statements. These statements are based on the company's current beliefs and expectations. Such forward-looking statements include, but are not limited to, statements regarding: the characterization of safety, tolerability and functional data associated with AOC 1001; the impact of such data on the advancement of AOC 1001; expectations related to the MARINA-OLE study and AOC 1001; the anticipated timing of release of data from the MARINA-OLE™, EXPLORE44™ and FORTITUDE™ trials; plans for a Phase 3 study and global regulatory path for AOC 1001; plans for the progression of clinical programs for AOC 1001, AOC 1044 and AOC 1020 and the timing thereof; the potential of Avidity's product candidates to treat rare diseases and Avidity's efforts to bring them to people suffering from applicable diseases; the potential of AOCs to target a range of different cells and tissues beyond the liver, and to treat cardiac and immunological diseases; and Avidity's plans to expand its AOC platform and to invest in its pipeline programs.

The inclusion of forward-looking statements should not be regarded as a representation by Avidity that any of these plans will be achieved. Actual results may differ from those set forth in this press release due to the risks and uncertainties inherent in Avidity's business, including, without limitation: Avidity may not be able to resolve the partial clinical hold related to the serious adverse event which occurred in the Phase 1/2 MARINA trial, which may result in delays in the clinical development of AOC 1001; 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 further analysis of existing data and analysis of new data may lead to conclusions different from those established as of the date hereof; unexpected adverse side effects to, or inadequate efficacy of, Avidity's product candidates that may delay or limit their development, regulatory approval and/or commercialization, or may result in additional clinical holds which may not be timely lifted, recalls or product liability claims; Avidity is early in its development efforts; Avidity's approach to the discovery and development of product candidates based on its AOC platform is unproven, and the company does not know whether it will be able to develop any products of commercial value; potential delays in the commencement, enrollment, data readouts and completion of preclinical studies or clinical trials; the success of its preclinical studies and clinical trials for the company's product candidates; Avidity's dependence on third parties in connection with preclinical and clinical testing and product manufacturing; Avidity may not realize the expected benefits of its collaborations; regulatory developments in the United States and foreign countries; Avidity could exhaust its available capital resources sooner than it currently expects and fail to raise additional needed funds; and other risks described in Avidity's Annual Report on Form 10-K for the fiscal year ended December 31, 2022, filed with the Securities and Exchange Commission (SEC) on February 28, 2023, and in subsequent filings with the SEC. Avidity cautions readers not to place undue reliance on these forward-looking statements, which speak only as of the date

hereof, and the company undertakes no obligation to update such statements to reflect events that occur or circumstances that arise after the date hereof. 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.

Investor Contact:
Geoffrey Grande, CFA
(619) 837-5014
investors@avidity bio.com

Media Contact:
Navjot Rai
(619) 837-5016
media@avidity bio.com

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