# Avidity Biosciences Announces FDA Eases Partial Clinical Hold on AOC 1001 Providing a Clear Path Forward to Finalize Pivotal Dose and Phase 3 Design in Adults with Myotonic Dystrophy Type 1

*Avidity plans to double the number of participants receiving 4 mg/kg of AOC 1001 in MARINA Open-Label Extension (MARINA-OLE™) study by dose escalating participants currently on 2 mg/kg of AOC 1001*

*FDA allows new participant enrollment for 2 mg/kg of AOC 1001*

*First look at data from the MARINA-OLE study planned for the end of 2023*

SAN DIEGO, May 17, 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 that the U.S. Food and Drug Administration (FDA) has eased the partial clinical hold on AOC 1001, allowing Avidity to double the number of participants in the MARINA Open-Label Extension (MARINA-OLE™) study receiving 4 mg/kg of AOC 1001. The FDA is also allowing new participant enrollment for AOC 1001 at 2 mg/kg. Data from the MARINA-OLE study will be used to finalize the AOC 1001 pivotal dose and Phase 3 study design for adults with myotonic dystrophy type 1 (DM1), an underrecognized, progressive and often fatal neuromuscular disease with no approved treatment options.

"This positive step forward in our discussions with FDA provides the opportunity to gather additional data on the 2-4 mg/kg dose range of AOC 1001 while, in parallel, finalizing our Phase 3 study design and aligning with health authorities on a global regulatory path for AOC 1001," said Sarah Boyce, president and chief executive officer at Avidity. "We recently announced positive topline data for AOC 1001 demonstrating functional improvement across multiple clinical outcome measures and look forward to sharing a first look at data from the MARINA-OLE study at the end of this year. We are focused on advancing AOC 1001 into a pivotal trial as quickly as possible as we know that the patient community is desperate for a treatment. We are extremely grateful to the DM1 community for their trust, support and ongoing partnership."

The easing of the partial clinical hold allows a number of current participants to be dose escalated to 4 mg/kg of AOC 1001 in the MARINA-OLE study and allows new participant enrollment at 2 mg/kg of AOC 1001. In September 2022, FDA placed a partial clinical hold on all new participant enrollment of AOC 1001 due to a rare serious adverse event reported in a single participant in the 4 mg/kg cohort of the Phase 1/2 MARINA™ trial.

Avidity announced positive topline AOC 1001 data from the Phase 1/2 MARINA trial demonstrating functional improvement in multiple clinical outcome measures, disease modification and a favorable safety and tolerability profile in adults with DM1 at the 75th American Academy of Neurology (AAN) Annual Meeting in April 2023.

Avidity concluded the MARINA trial with 38 participants enrolled and continues to dose 36 of those participants at both 2 mg/kg and 4 mg/kg of AOC 1001 in the MARINA-OLE study to evaluate the long-term safety and tolerability of AOC 1001 in adults with DM1. Avidity plans to double the number of participants receiving 4 mg/kg of AOC 1001 by dose escalating approximately 12 participants currently receiving AOC 1001 2 mg/kg in the MARINA-OLE study. All other participants will remain on their current dose of either 2 mg/kg or 4 mg/kg of AOC 1001. Avidity remains on track to share a first look at the data from the MARINA-OLE study at the end of 2023.

**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 who enroll in the MARINA-OLE study currently 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 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: Avidity's plans to escalate dosages of AOC 1001 administered to participants in the MARINA-OLE™ study, the levels of such dosages and the number of participants to be involved; Avidity's ability to advance AOC 1001 into a pivotal dose and trial, and the timing thereof; a Phase 3 study design related to AOC 1001 and adults with DM1; the characterization of the Phase 1/2 MARINA™ topline data; regulatory matters and Avidity's related plans; expectations related to enrollment of participants into the MARINA-OLE study at certain dosage levels; the timing and progression of the MARINA-OLE study and the dosage levels to be administered therein; any further changes to the status of the existing partial clinical hold; the safety, tolerability and benefits of AOC 1001; the timing of release of data from the MARINA-OLE study; the potential of Avidity's product candidates to treat rare diseases; the potential of the AOC platform and the potential of AOCs to target a range of different cells and tissues beyond muscle tissues, and to address diseases beyond those targeted by Avidity's current product candidates. 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 press release due to the risks and uncertainties inherent in our business, including, without limitation: Avidity may not be able to fully resolve the partial clinical hold and the analysis related to the underlying cause of the serious adverse event, which may result in delays in the clinical development of AOC 1001; additional participant data related to AOC 1001 that continues to become available, through dose escalation or otherwise, 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 Avidity's product candidates that may delay or limit their development, regulatory approval and/or commercialization, or may result in additional clinical holds, 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 MARINA-OLE study; the success of the MARINA-OLE study for AOC 1001; the results of the Phase 1/2 MARINA trial may not be predictive of results of the MARINA-OLE study; Avidity's dependence on third parties in connection with clinical testing and product manufacturing; regulatory developments in the United States and foreign countries, including acceptance of INDs and similar foreign regulatory filings and the proposed design of future clinical trials; Avidity could exhaust its available capital resources sooner than it currently expects and fail to raise additional needed capital; and other risks described in our Annual Report on Form 10-K for the 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.

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