Avidity Biosciences Announces Positive AOC 1001 Long-term Data Showing Reversal of Disease Progression in People Living with Myotonic Dystrophy Type 1 Across Multiple Endpoints; Same Key Endpoints Agreed for Phase 3 HARBOR™ Trial

Avidity accelerates global Phase 3 HARBOR™ study initiation to Q2 2024 following regulatory agreement on study design; primary endpoint is video hand opening time (vHOT) and secondary endpoints include muscle strength and activities of daily living

Delpacibart etedesiran (AOC 1001) demonstrated consistent and durable improvements in myotonia, muscle strength and activities of daily living in people with DM1 in long-term data from MARINA-OLE™

Delpacibart etedesiran (AOC 1001) 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

Avidity to host Volume 8 of investor and analyst event series via webcast March 4, 2024, at 8:00 a.m. ET

SAN DIEGO, March 4, 2024 /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 long-term AOC 1001 data from the MARINA open-label extension (MARINA-OLE™) trial showing reversal of disease progression in people living with myotonic dystrophy type 1 (DM1) across multiple endpoints including vHOT, muscle strength and activities of daily living when compared to END-DM1 natural history data. These endpoints are the same key endpoints that will be used in the global Phase 3 HARBOR™ trial for people living with DM1. The primary endpoint in the Phase 3 HARBOR trial is video hand opening time (vHOT), and key secondary endpoints include muscle strength as measured by hand grip strength and quantitative muscle testing (QMT) total score, and activities of daily living as measured by DM1-Activ. Avidity is accelerating the global Phase 3 HARBOR trial initiation to the second quarter of 2024.

Avidity also announced *delpacibart etedesiran* as the approved international nonproprietary name of AOC 1001, abbreviated as *del-desiran*. *Del-desiran* (AOC 1001) is an investigational treatment designed to address the root cause of DM1, an underrecognized, progressive and often fatal neuromuscular disease with no approved therapies.

"The long-term data from the MARINA-OLE study demonstrating that *del-desiran* improved measures of disease progression in DM1 patients compared to natural history data is remarkable," said John W. Day, MD, PhD, Professor of Neurology and Pediatrics, and Director, Division of Neuromuscular Medicine, Stanford University School of Medicine, an investigator of the MARINA® and MARINA-OLE trials. "The favorable long-term safety data and consistent, durable improvement in myotonia, muscle strength and patient-reported outcomes measures show the potential of *del-desiran* to make a meaningful difference in the lives of DM1 patients. I am very encouraged by the prospect of *del-desiran* as a potential treatment for DM1."

"Initiating our global pivotal study for *del-desiran* in the coming months is a significant step forward in bringing a much-needed treatment to people living with DM1 as quickly as possible. We are pleased that the agreed upon functional endpoints in the Phase 3 HARBOR study are the same endpoints in which *del-desiran* has demonstrated consistent and durable improvements in the MARINA studies," said Sarah Boyce, president and chief executive officer at Avidity. "Thank you to the DM1 community, in particular - the participants, their families, the investigators and their teams - for their support, dedication and commitment to the MARINA program. The depth and breadth of *del-desiran* data that we have gathered from these studies offer hope for people living with DM1, a devastating rare disease for which there are no treatment options available."

Data Presented at 2024 Muscular Dystrophy Association (MDA) Clinical & Scientific Conference, March 3-6
MARINA-OLE™ is an open-label, multi-center trial to evaluate the safety, tolerability, PK, PD, and efficacy of *del-desiran* (AOC 1001) in participants that were enrolled in the randomized, placebo-controlled, Phase 1/2 MARINA® clinical trial. Participants enrolled in the MARINA-OLE study receive quarterly doses of *del-desiran* (AOC 1001) regardless of whether they received active treatment or placebo in the MARINA study. All 37 participants that completed the MARINA trial remain on *del-desiran* (AOC 1001) in the MARINA-OLE trial.

Long-term efficacy data presented were assessed from 12 participants on 4 mg/kg *del-desiran* (AOC 1001) in the MARINA-OLE study. The endpoints used in the MARINA-OLE measure important aspects of the disease and correspond to those utilized in the ongoing END-DM1 natural history study.

The long-term data from the MARINA-OLE trial are being presented in a poster session at the 2024 Muscular Dystrophy Association (MDA) Clinical & Scientific Conference being held March 3-6, 2024, in Orlando, Florida and can also be found on Avidity's website on the Publications page.

MARINA-OLE data compared to END-DM1 natural history data

For the first time new data were reported from END-DM1, a natural history study to establish biomarkers and clinical endpoints in DM1 by understanding the progression of myotonic dystrophy. Long-term *del-desiran* (AOC 1001) data from the MARINA-OLE study show reversal of disease progression in people living with DM1 across multiple endpoints including myotonia, muscle strength and patient reported activities of daily living compared to a matched END-DM1 natural history study population over one year.

Avidity is grateful to the END-DM1 team for their partnership over the years and for their approval and permission to share this analysis from the study.

Del-desiran long-term efficacy data from MARINA-OLE

In the MARINA-OLE study, *del-desiran* (AOC 1001) 4 mg/kg provided consistent and durable improvements in the following:

- Myotonia (video hand opening time, or vHOT)
- Multiple measures of strength:
    - Hand grip
    - Quantitative Muscle Testing (QMT) total score which includes hand grip; elbow extension and elbow flexion; knee extension and knee flexion, and ankle dorsiflexion
- 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)

Del-desiran safety and tolerability data from MARINA-OLE

With over 265 infusions totaling 61.1 patient-years of exposure,*del-desiran* (AOC 1001) continues to demonstrate favorable safety and tolerability. In the MARINA-OLE study of *del-desiran* (AOC 1001):

- All related adverse events (AE) were mild or moderate
- The most common related AEs reported in 2 or more participants in the MARINA-OLE were nausea and headache
- There were no study drug related SAEs
- There have been no discontinuations in the MARINA-OLE study

Video Webcast Information

The company is hosting Volume 8 of its investor and analyst event series on March 4, 2024, beginning at 8:00 a.m. ET to discuss new positive long-term *del-desiran* (AOC 1001) data from the MARINA-OLE™ trial in people living with DM1. The virtual event will be available via a live video webcast and can be accessed here or from the "Events and Presentations" page in the "Investors" section of Avidity's website. A replay of the webcast will be archived on Avidity's website following the event.

About the Phase 1/2 MARINA® Trial

The MARINA® trial was 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 *del-desiran* (AOC 1001) administered intravenously. The MARINA trial assessed the activity of *del-desiran* (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 *del-desiran* (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 *del-desiran* (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 *del-desiran* (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 *del-desiran* (AOC 1001) regardless of whether they received active treatment or placebo in the MARINA study. The total duration of active treatment with *del-desiran* (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 *Del-desiran* (AOC 1001)

Del-desiran (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. *Del-desiran* (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, *del-desiran* (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. *Del-desiran* (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 *del-desiran (AOC 1001)* and the FDA has granted *del-desiran (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 long-term efficacy data associated with *delpacibart etedesiran (del-desiran, or* AOC 1001) from the MARINA-OLE™ study; the impact of such data on the advancement of *del-desiran*; a global pivotal Phase 3 trial for *del-desiran*, the timing of its initiation and key endpoints to be used therein; regulatory agreement regarding a Phase 3 trial for *del-desiran*; expectations related to the MARINA-OLE study and *del-desiran*; timelines for active treatment and safety follow-up in MARINA-OLE; data from the END-DM1 study and its importance to the assessment of *del-desiran*; 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. This press release also contains estimates and other statistical data made by independent parties and by us. This data involves a number of assumptions and limitations, and the reader is cautioned not to give undue weight to such estimates.

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 *del-desiran*; additional participant data related to *del-desiran* 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; Avidity's dependence on third parties in connection with preclinical and clinical testing and product manufacturing; regulatory developments in the United States and foreign countries; and other risks described in Avidity's Annual Report on Form 10-K for the fiscal year ended December 31, 2023, filed with the Securities and Exchange Commission (SEC) onFebruary 28, 2024, 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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