Avidity Biosciences Provides Regulatory Update on AOC 1001 for Myotonic Dystrophy Type 1 and Plans to Present Top-line Data from Phase 1/2 MARINA™ Trial at AAN Annual Meeting

Discussions with the FDA ongoing as Avidity submits emerging AOC 1001 data from the MARINA trial

AOC 1001 continues to be generally well tolerated; Avidity provides more information on the rare serious adverse event in a single participant that led to the partial clinical hold

AOC 1001 top-line safety and functional data to be presented at the American Academy of Neurology (AAN) Annual Meeting on April 27, 2023

Avidity to hold a webcast/conference call today at 8:00 a.m. ET/5:00 a.m. PT

SAN DIEGO, March 30, 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 provided an update on the Phase 1/2 MARINA™ trial of AOC 1001 in adults with myotonic dystrophy type 1 (DM1), an underrecognized, progressive and often fatal neuromuscular disease with no approved treatment options. Discussions are ongoing with the U.S. Food and Drug Administration (FDA) regarding the partial clinical hold on new participant enrollment as Avidity continues to provide new AOC 1001 data as it emerges from the MARINA trial. AOC 1001 consists of a proprietary monoclonal antibody that binds to the transferrin receptor 1 (TfR1) conjugated with a siRNA targeting DMPK mRNA.

In September 2022, the FDA placed a partial clinical hold on new participant enrollment in the Phase 1/2 MARINA clinical trial after reviewing information provided by Avidity related to a serious adverse event reported in a single participant in the 4 mg/kg cohort of the MARINA study. As previously disclosed, the event was classified by the investigator as drug related. Avidity conducted a thorough analysis with the help of multiple independent experts and concluded that the participant most likely experienced an extremely rare neurological event comprising of bilateral ischemia in the region of the lateral geniculate nuclei in the thalamus with subsequent hemorrhagic transformation. The location in the lateral geniculate nuclei and the bilateral nature of the event is what makes this event extremely rare. After this extensive investigation, Avidity cannot identify a plausible biological link to any component of AOC 1001, the AOC platform, the transferrin receptor delivery mechanism or reduction of DMPK. It is important to note that AOC 1001 does not cross the blood brain barrier.

In December 2022, the company announced positive data from a preliminary assessment of the Phase 1/2 MARINA study of AOC 1001 demonstrating the first-ever successful targeted delivery of RNA to skeletal muscle, DMPK reduction and splicing improvements, with early signs of clinical activity with improvement in myotonia after just one or two doses of AOC 1001. The top-line data from MARINA will be presented in an oral presentation on April 27, 2023 at the 75th American Academy of Neurology (AAN) Annual Meeting in Boston, Mass.

"The safety of patients is our top priority. We are grateful to the participants in our clinical trials and their families, as well as the broader DM1 community, for their ongoing trust and collaboration. We share the urgency for a treatment for people living with this devastating disease with no approved therapies. Our team is focused on resolving the partial clinical hold and advancing AOC 1001 to a pivotal trial as quickly as possible," said Sarah Boyce, president and chief executive officer at Avidity. "We are continuing to work diligently with the FDA and remain very confident in AOC 1001 and its benefit/risk profile. We will continue to share emerging data with the FDA as we conclude the MARINA trial. We look forward to reporting safety and functional top-line data from the MARINA trial at AAN next month."

Data from the preliminary assessment of AOC 1001 supports that the targeted dose range is between 2 mg/kg and 4 mg/kg. Therefore, Avidity is concluding the MARINA trial with the 38 participants enrolled at 1mg/kg, 2mg/kg and 4mg/kg of AOC 1001 and will not move forward with the 8 mg/kg dose of AOC 1001.

Avidity will continue to dose the participants at both 2 mg/kg and 4 mg/kg of AOC 1001 in the MARINA open-label extension study (MARINA-OLE™) 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. Avidity remains on track to share a first look at the data from the MARINA-OLE study at the end of 2023.

Avidity is advancing its three distinct rare disease Phase 1/2 programs in the clinic: AOC 1001 for DM1, AOC 1020 for the treatment of facioscapulohumeral muscular dystrophy (FSHD) and AOC 1044 for the treatment of Duchenne muscular dystrophy (DMD) mutations amenable to exon 44 skipping (DMD44).

Today's Webcast Information
Avidity's management team will host a webcast and conference call at 8:00 a.m. ET / 5:00 a.m. PT today, March 30, 2023. The live call can be accessed by dialing 833-816-1372 (US) and 1-412-317-0467 (International) and requesting Avidity Biosciences. A live webcast will also be available on 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 is a randomized, double-blind, placebo-controlled, Phase 1/2 clinical trial initially expected to enroll approximately 44 adults with DM1. The primary objective of this study is to evaluate the safety and tolerability of single and multiple ascending doses of AOC 1001 administered intravenously. The MARINA trial will begin to assess 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 is not powered to assess functional benefit, it will explore the clinical activity of AOC 1001 including measures of mobility and muscle strength as well as patient reported outcomes and quality of life measures. Patients have 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 myotonic dystrophy type 1 (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 that enrolled in the randomized, placebo-controlled, Phase 1/2 MARINA clinical trial. Participants who enroll in the MARINA-OLE study will 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 is approximately 24 months. Once patients have completed active treatment, there will be a 9-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 ongoing MARINA™ trial in adults with DM1. Patients in the MARINA study are eligible to enroll in the MARINA-OLE™ study. 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's proprietary AOCs are designed to combine the specificity of monoclonal antibodies with the precision of oligonucleotide therapies to target the root cause of diseases previously untreatable with RNA therapeutics. Avidity's advancing and expanding pipeline has three programs in clinical development. AOC 1001 is designed to treat people with myotonic dystrophy type 1 (DM1) and is currently in Phase 1/2 development with the ongoing MARINA™ and MARINA-OLE™ trials. AOC 1020 is designed to treat people living with facioscapulohumeral muscular dystrophy (FSHD) and is currently in Phase 1/2 development with the FORTITUDE™ trial. AOC 1044 is designed for people with Duchenne muscular dystrophy (DMD) mutations amenable to exon 44 skipping and is currently in Phase 1/2 development with the EXPLORE44™ trial. AOC 1044 is the first of multiple AOCs the company is developing for DMD. Avidity is also broadening the reach of AOCs beyond muscle tissues through both internal discovery efforts and key partnerships as the company continues to deliver on the RNA revolution. Avidity is headquartered in San Diego, CA. For more information about our science, 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: expectations related to new patient enrollment and the continuation of existing participants in the MARINA trial and enrollment of participants into the MARINA-OLE™ trial; the timing and progression of such clinical programs and the dosage levels to be administered therein; 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; the safety and benefits of AOC 1001; the timing of release of preliminary data from the MARINA-OLE trial; top-line data from the MARINA trial and the announcement thereof; the potential of Avidity's product candidates to treat rare diseases; and the potential of AOCs to target a range of different cells and tissues beyond muscle tissues. 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: further changes, if any, to the status of the existing partial clinical hold related to the MARINA trial; 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 commencement, enrollment and completion of preclinical studies or clinical trials; the success of its preclinical studies and clinical trials for the company's product candidates; the results of preclinical studies and early clinical trials are not necessarily predictive of future results; 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, 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 prior press releases and 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. 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:
Kathleen Gallagher
(858) 401-7900 x550
investors@aviditybio.com

Media Contact:
Navjot Rai
(858) 401-7900 x550
media@aviditybio.com

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