Avidity Announces Positive AOC 1001 Phase 1/2 MARINA™ Data Demonstrating First-Ever Successful Targeted Delivery of RNA to Muscle - Revolutionary Advancement for the Field of RNA Therapeutics

AOC 1001 delivered siRNA to skeletal muscle and produced meaningful DMPK reduction in 100% of participants with a 45% mean reduction in DMPK after a single dose of 1 mg/kg or two doses of 2 mg/kg

AOC 1001 produced splicing improvement of 31% in a key set of muscle-specific genes in people with DM1, with a splicing improvement of 16% across a broad 22-gene panel

Early signs of clinical activity, with improvement in myotonia demonstrated in adults with DM1 treated with AOC 1001

Avidity continues to work to resolve partial clinical hold on new participant enrollment

Volume 6 of virtual investor and analyst series today, Wednesday, December 14 at 8:00 a.m. ET

SAN DIEGO, Dec. 14, 2022 /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 positive AOC 1001 data from the preliminary assessment of the Phase 1/2 MARINA™ trial demonstrating the first-ever successful targeted delivery of RNA into muscle, a revolutionary advancement for the field of RNA therapeutics. The effective targeted delivery of siRNA into muscle further reinforces the broad and disruptive potential of Avidity's proprietary AOC platform and expands the ability to address targets and diseases previously unreachable with existing RNA therapies. AOC 1001, Avidity's lead clinical program utilizing its AOC platform, is designed to address the root cause of myotonic dystrophy type 1 (DM1), an underrecognized, progressive and often fatal neuromuscular disease with no approved therapies.

"Utilizing our AOC platform technology, we have demonstrated for the first time ever the successful targeted delivery of siRNA to muscle in humans, a major breakthrough for the field of RNA therapeutics," said Art Levin, Ph.D., chief scientific officer at Avidity. "These unprecedented data open up the RNA field and underscore the potential of our AOC platform to expand the possibilities of how we can treat diseases and target a range of different cells and tissues beyond the liver, which up until now have been inaccessible with existing RNA-based therapeutics. At Avidity, we look forward to advancing our three AOC clinical programs for the treatment of muscle diseases and to continuing to expand our pipeline and programs in cardiac, immunology and other diseases."

The preliminary assessment from the randomized, double-blind, placebo-controlled Phase 1/2 MARINA trial of AOC 1001 provides first in-human data and a mid-study look at the safety and tolerability of all 38 participants and key biomarkers in 19 participants. The preliminary assessment includes biomarker data six weeks after dosing. Participants received a single dose of 1 mg/kg AOC 1001, two doses of 2 mg/kg AOC 1001 (reflected as siRNA dose), or placebo. AOC 1001 Phase 1/2 data from the preliminary assessment demonstrated:

- Targeted delivery of siRNA to muscle, a tissue previously untreatable with existing RNA therapeutics;
- Meaningful DMPK reduction in 100% of participants treated with AOC 1001;
- Mean reduction of 45% in DMPK after only a single dose of 1 mg/kg or two doses of 2 mg/kg of AOC 1001;
- Splicing improvement of 31% in a key set of muscle-specific genes and splicing improvement of 16% across a broad 22-gene panel in the 2 mg/kg cohort. Splicing improvements demonstrate AOC 1001 activity in the nucleus;
- Early signs of clinical activity with improvement in myotonia in some participants. Myotonia was measured by video hand opening time (vHOT) and is a hallmark of DM1 where relaxation of key muscle groups is impaired; and
- Safety and tolerability data with majority of adverse events (AEs) mild or moderate.

"We are very pleased with this early data set of AOC 1001 from the MARINA trial. We have demonstrated the cascade of delivery to muscle, DMPK reduction and splicing improvements with AOC 1001 and are seeing early signs of clinical activity with improvement in myotonia, just weeks after only one or two doses of AOC 1001," said Sarah Boyce, president and chief executive officer at Avidity. "AOC 1001 has the potential to deliver on the promise of the AOC platform and significantly impact the underlying disease mechanism of DM1, a devastating disease where there are currently no approved therapies. We look forward to sharing top-line data from the MARINA trial in 2023 and advancing our other clinical programs for the treatment of DMD and FSHD."

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. AOC 1001 consists of a proprietary monoclonal antibody (mAb) that binds to the transferrin receptor 1 (TfR1) conjugated with a siRNA targeting DMPK mRNA to address the underlying cause in DM1.

In September 2022, the U.S. Food and Drug Administration (FDA) placed a partial clinical hold on new participant enrollment in

the Phase 1/2 MARINA trial of AOC 1001 in adults with DM1 due to a serious adverse event reported in a single participant in the 4 mg/kg dose cohort. Avidity continues to work to resolve the partial hold on new participant enrollment as swiftly as possible. All current participants, whether they are on AOC 1001 or placebo, may continue in their current dosing cohort and roll over into the MARINA-OLE™ trial where they will receive AOC 1001. To date, 100% of participants who have completed the MARINA trial have opted to roll over into the MARINA open label extension (MARINA-OLE™).

Avidity has three distinct rare disease programs in the clinic: AOC 1001 for DM1 is currently being evaluated in the Phase 1/2 clinical trial and the MARINA-OLE; AOC 1020 is advancing into the Phase 1/2 FORTITUDE™ trial for the treatment of facioscapulohumeral muscular dystrophy (FSHD); and, AOC 1044 is advancing into the Phase 1/2 EXPLORE44™ trial for the treatment of Duchenne muscular dystrophy (DMD) mutations amenable to Exon 44 skipping (DMD44).

Video Webcast Information
The company is hosting Volume 6 of their virtual investor and analyst series on December 14, 2022, beginning at 8:00 a.m. ET to discuss the preliminary results from the MARINA trial of AOC 1001. The event is 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.

The management team will be joined by Dr. Nicholas E. Johnson, MD, MSCI, FAAN. Dr. Johnson is one of the principal investigators in END-DM1, an ongoing natural history study being run by the Myotonic Dystrophy Clinical Research Network (DMCRN) and is the lead investigator in the AOC 1001 Phase 1/2 MARINA trial. Dr. Johnson is an associate professor, division chief of neuromuscular, and vice chair of research in the department of neurology at Virginia Commonwealth University.

About the Phase 1/2 MARINA™ Trial

The MARINA™ trial is a randomized, double-blind, placebo-controlled, Phase 1/2 clinical trial 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 Avidity's ability to resolve the partial clinical hold and resume enrollment in and complete the MARINA™ trial, the continuation of participants in the MARINA trial and enrollment of participants into the MARINA-OLE™; and the timing thereof; the progression of clinical programs for AOC 1001, AOC 1044 and AOC 1020 and the timing thereof; the initiation of the FORTITUDE™ and EXPLORE44™ trials; the potential of Avidity's product candidates to treat rare diseases; the potential of AOCs to target a range of different cells and tissues beyond the liver; the potential of AOCs to treat cardiac and immunological diseases; and Avidity's plans to expand its AOC platform into additional muscle diseases. 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 the business, including, without limitation: Avidity may not be able to resolve the partial clinical hold and the analysis related to the underlying cause of the serious adverse event may result in delays in the MARINA study or an inability to compete the study; the Phase 1/2 MARINA trial results are based on a preliminary analysis of interim data available as of the data cutoffs, and the interim results do not predict final results of the trial, and one or more of the safety or biomarker results may materially change following more comprehensive reviews of the data, as follow-up on the outcome of any particular patient continues, as and if additional patients enroll in the trial and as more patient data become available, any of which may materially alter the findings and conclusions from Avidity's preliminary analysis; unexpected adverse side effects or inadequate efficacy of its product candidates that may delay or limit their development, regulatory approval and/or commercialization, or may result in 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; disruption to its operations from the COVID-19 pandemic or the war in Ukraine; Avidity could use its available capital resources sooner than it currently expects; and other risks described in prior press releases and in filings with the Securities and Exchange Commission (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 exist 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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