Avidity Biosciences Announces the Phase 1/2 FORTITUDE™ Trial of AOC 1020 in Adults with Facioscapulohumeral Muscular Dystrophy

AOC 1020 is Avidity's second siRNA antibody oligonucleotide conjugate (AOC™) entering Phase 1/2 studies

Company now has three distinct rare disease programs in clinical development - myotonic dystrophy type 1 (DM1), facioscapulohumeral muscular dystrophy (FSHD), and Duchenne muscular dystrophy (DMD)

Volume 4 of virtual investor and analyst series on Monday, October 3, 2022 at 10:00 a.m. ET

SAN DIEGO, Sept. 29, 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 the Phase 1/2 FORTITUDE™ clinical trial of AOC 1020 in adults with facioscapulohumeral muscular dystrophy (FSHD). FSHD is a rare, hereditary muscle-weakening condition marked by life-long, progressive loss of muscle function and causes significant pain, fatigue, and disability. AOC 1020 is the second muscle-targeting small interfering RNA (siRNA) AOC from Avidity's pipeline to advance into clinical development.

Earlier this week, Avidity announced that the U.S. Food and Drug Administration (FDA) cleared the company's investigational new drug (IND) applications of AOC 1020 for FSHD and AOC 1044 for the treatment of Duchenne muscular dystrophy (DMD) mutations amenable to exon 44 skipping (DMD44). The company has now advanced three programs - DM1, FSHD and DMD44 – into clinical development in a 14-month period.

"Advancing AOC 1020 into the Phase 1/2 FORTITUDE study is a significant milestone for the FSHD community and our proprietary AOC platform. People living with FSHD have no approved treatments and experience life-long, progressive loss of muscle function leading to fatigue and disability," said Sarah Boyce, president and chief executive officer of Avidity. "AOC 1020, our second siRNA AOC, is designed to directly target the disease-causing gene, DUX4, with the goal of treating the underlying biological cause of FSHD. We now have three clinical programs in development for three distinct rare diseases that have no approved therapies."

FSHD affects approximately 16,000-38,000 people in the United States alone. It is an autosomal dominant disease caused by the abnormal expression of the gene DUX4 (double homeobox 4) that leads to skeletal muscle wasting and progressive loss of muscle function, with symptoms often beginning in adolescence and early adulthood.

"We are grateful for companies like Avidity that are working to address a significant unmet need in the FSHD community," said Mark A. Stone, chief executive officer at FSHD Society. "Patients as well as their caregivers and families live with the burden of this devastating disease every day and are in desperate need of treatment options that can improve quality of life. As FSHD is a progressive disease, the impact is debilitating and often results in an inability to do everyday activities like brushing teeth or getting dressed. There is a long road ahead, but today marks an important step and gives hope to everyone in our community impacted by FSHD."

In addition to AOC 1020 and AOC 1044, Avidity is developing AOC 1001 for the potential treatment of myotonic dystrophy type 1 (DM1). AOC 1001 is being evaluated in the Phase 1/2 MARINA™ trial and the MARINA open label-extension study (MARINA-OLE™). Earlier this week, Avidity announced that the FDA placed a partial clinical hold on new participant enrollment in the Phase 1/2 MARINA trial. 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 where they will receive AOC 1001 as planned.

Avidity remains on track to conduct a preliminary assessment of safety, tolerability and key biomarkers in approximately half of the study participants in the Phase 1/2 MARINA trial in the fourth quarter of 2022.

The FORTITUDE™ Phase 1/2 Trial of AOC 1020 in Adults with FSHD
The FORTITUDE trial is a randomized, placebo-controlled, double-blind, Phase 1/2 clinical trial designed to evaluate AOC 1020 in 68 adult participants with FSHD. FORTITUDE will evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of AOC 1020 administered intravenously, with the primary objective being the safety and tolerability of AOC 1020 in FSHD patients. Activity of AOC 1020 will be assessed using key biomarkers, including magnetic resonance imaging (MRI) measures of muscle volume and composition. Though the Phase 1/2 trial is not statistically powered to assess functional benefit, it will explore the clinical activity of AOC 1020 including measures of mobility and muscle strength as well as patient reported outcomes and quality of life measures. Participants will have the option to enroll in an open-label extension study at the end of the

treatment period in the FORTITUDE study.

Video Webcast Information – Monday, October 3, 2022
The company is hosting Volume 4 of their virtual investor and analyst series on Monday, October 3, 2022 beginning at 10 a.m. ET / 7 a.m. PT to further discuss the AOC 1020 clinical development program. 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.

About Facioscapulohumeral Muscular Dystrophy (FSHD)
Facioscapulohumeral muscular dystrophy (FSHD) is characterized by progressive and often asymmetric skeletal muscle loss that typically causes weakness initially in muscles in the face, shoulders, arms and trunk and progresses to weakness in muscles in the lower body. FSHD is an autosomal dominant genetic disease, meaning a single copy of the disease-associated gene, DUX4 (double homeobox 4), is enough to cause the disease. The abnormal expression of DUX4 leads to a series of downstream events that result in skeletal muscle wasting and progressive loss of muscle function, including an inability to lift arms for more than a few seconds, loss of ability to show facial expressions, and serious speech impediments. These symptoms cause many people affected by FSHD to become dependent on the use of a wheelchair for mobility. Currently, there are no approved treatments for people living with FSHD.

About AOC 1020
AOC 1020 is designed to treat the underlying cause of FSHD, which is caused by the abnormal expression of a gene called double homeobox 4 or DUX4. The abnormal expression of DUX4 protein leads to changes in gene expression in muscle cells that are associated with the life-long, progressive loss of muscle function in patients with FSHD. AOC 1020 aims to reduce the expression of DUX4 mRNA and DUX4 protein in muscles in patients with FSHD. AOC 1020 consists of a proprietary monoclonal antibody that binds to the transferrin receptor 1 (TfR1) conjugated with a siRNA targeting DUX4 mRNA. In preclinical studies, a single intravenous dose with the murine version of AOC 1020 prevented development of muscle weakness demonstrated by three functional assays - treadmill running, in vivo force and compound muscle action potential. AOC 1020 is currently in Phase 1/2 development as part of the FORTITUDE™ trial in adults with FSHD.

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 now has three programs in clinical development. The company's lead product candidate, AOC 1001, is designed to treat people with myotonic dystrophy type 1 (DM1). AOC 1001 is currently in Phase 1/2 development with the ongoing MARINA™ trial and MARINA-OLE™ in adults with DM1. The next programs in the company's advancing and expanding pipeline are AOC 1020, designed to treat people living with FSHD currently in Phase 1/2 development with the ongoing FORTITUDE™ trial, and AOC 1044, the lead of three programs for the treatment of 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: the initiation of clinical trials of AOC 1020 and AOC 1044 in patients with FSHD and DMD, respectively, and the timing thereof; AOC 1020's potential to address unmet needs in FSHD and to treat the underlying biological cause of FSHD; expectations for Avidity's interactions with the FDA, the ongoing investigation into the underlying cause of the SAE for the affected patient, and the anticipated impact of, and Avidity's ability to resolve, the partial clinical hold and resume enrollment in and complete the MARINA study, and to conduct and present data from the preliminary assessment of the MARINA study and the timing thereof; and the potential to broaden the reach of AOCs beyond skeletal muscle tissues. 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 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 clinical trials; Avidity may not be able to resolve the partial clinical hold and the analysis related to the underlying cause of the SAE may result in delays in the MARINA study or an inability to compete the study; 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; 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 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; 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.

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