Avidity Biosciences Pursues Potential Accelerated Approval Path with Initiation of Biomarker Cohort in FORTITUDE™ Trial for Delpacibart Braxlosiran (del-brax/AOC 1020) in People Living with Facioscapulohumeral Muscular Dystrophy

Biomarker cohort for delpacibart braxlosiran (del-brax), the first potential therapy to target DUX4, is measuring changes in DUX4 regulated biomarkers; del-brax 2 mg/kg will be administered every six weeks

Enrollment in the del-brax biomarker cohort expected to be completed in 1H 2025; on track to initiate del-brax functional cohort in 1H 2025

In previously reported initial data, del-brax 2 mg/kg every six weeks showed unprecedented and consistent reductions of DUX4 regulated genes, significant decreases in novel circulating biomarker and creatine kinase, and trends of functional improvement at the four-month timepoint

SAN DIEGO, Oct. 30, 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 the initiation of a biomarker cohort in the Phase 1/2 FORTITUDE™ trial of delpacibart braxlosiran (del-brax/AOC 1020) in people living with facioscapulohumeral muscular dystrophy (FSHD). Avidity is pursuing a potential accelerated approval path for del-brax and expects enrollment in the biomarker cohort to be completed in the first half of 2025. Avidity also remains on track to initiate a functional cohort in the first half of 2025. In addition, enrollment of the FORTITUDE Open-label Extension study (OLE) is ongoing.

Del-brax is the first investigational therapy designed to treat the underlying cause of FSHD by directly targeting the disease-causing gene, double homeobox 4 (DUX4). Currently, there are no approved therapies for the treatment of FSHD, a rare, hereditary disorder marked by life-long, relentless loss of muscle function, significant pain, fatigue, and progressive disability.

"The initiation of the biomarker cohort marks a key step in our strategy to pursue a potential accelerated approval path for del-brax, the first potential treatment to directly target the root cause of FSHD," said Steve Hughes, M.D., chief medical officer at Avidity. "We are very pleased with the del-brax 2 mg/kg data which showed unprecedented and consistent reductions of DUX4-regulated genes, significant decreases in novel circulating biomarker and creatine kinase, and trends of functional improvement with favorable safety and tolerability at the four-month timepoint. We are advancing our clinical studies for del-brax as quickly as possible as we understand the urgency to bring a potential new treatment to people living with FSHD who have no treatment options."

The biomarker cohort in the FORTITUDE trial will assess the impact of del-brax 2 mg/kg every six weeks in people living with FSHD, ages 16-70. The primary endpoints of the study are changes in DUX4 regulated gene expression and DUX4 regulated circulating biomarker.

For people living with FSHD it is important to maintain suppression of DUX4 at all times as aberrant gene expression is toxic to the muscles. Favorable safety and tolerability, as well as decreases in circulating biomarker and creatine kinase levels were similar for patients treated with 2mg/kg or 4mg/kg of del-brax. Due to this similarity, Avidity selected 2 mg/kg of del-brax to be administered every six weeks, designed to ensure continuous suppression of DUX4 for the biomarker and functional cohorts.

In June of this year, Avidity reported positive initial del-brax 2 mg/kg data at four months from the Phase 1/2 FORTITUDE trial demonstrating unprecedented and consistent reductions of greater than 50% in DUX4 regulated genes, mean reductions of 25% or greater in novel circulating biomarker and creatine kinase, trends of functional improvement, and favorable safety and tolerability in people living with FSHD at the 31st Annual FSHD Society International Research Congress.

About the Phase 1/2 FORTITUDE™ trial
The FORTITUDE™ trial is a randomized, placebo-controlled, double-blind, Phase 1/2 clinical trial designed to evaluate single and multiple doses of delpacibart braxlosiran or *del-brax* (AOC 1020) in approximately 100 participants with facioscapulohumeral muscular dystrophy (FSHD). FORTITUDE will evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of *del-brax* administered intravenously. Activity of *del-brax* will be assessed using key biomarkers, including DUX4-regulated muscle and circulating biomarkers and 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 *del-brax* 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 FORTITUDE-OLE, an open-label extension study once participation in the FORTITUDE study is complete. For more information about the FORTITUDE trial, visit the FORTITUDE study website or visit http://www.clinicaltrials.gov and search for NCT05747924.

About the Phase 2 FORTITUDE-OLE™ trial
FORTITUDE-OLE™ is an open-label, multi-center trial designed to evaluate the long-term safety and tolerability of delpacibart braxlosiran or *del-brax* (AOC 1020) in participants with facioscapulohumeral muscular dystrophy (FSHD) who were previously enrolled in the FORTITUDE Phase 1/2 trial. This trial will continue to evaluate the safety, tolerability, PK, PD, and efficacy of del-brax in participants that enrolled in the randomized, placebo-controlled, Phase 1/2 FORTITUDE clinical trial. Participants who enroll in the FORTITUDE-OLE study will receive del-brax regardless of whether they received active treatment or placebo in the FORTITUDE study. The total duration of active treatment with del-brax in the FORTITUDE-OLE is approximately 24 months. Avidity may extend active treatment beyond 24 months at a future timepoint. For more information on the FORTITUDE-OLE study click here or visit http://www.clinicaltrials.gov and search for NCT06547216.

About *Del-brax* (AOC 1020)
Del-brax (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. Del-brax aims to reduce the expression of DUX4 mRNA and DUX4 protein in muscles in people with FSHD. Del-brax consists of a proprietary monoclonal antibody that binds to the transferrin receptor 1 (TfR1) conjugated with a siRNA targeting DUX4 mRNA. Avidity reported positive initial del-brax 2 mg/kg data at four months from the Phase 1/2 FORTITUDE trial demonstrating unprecedented and consistent reductions of greater than 50% in DUX4 regulated genes, trends of functional improvement, and favorable safety and tolerability in people living with FSHD. Del-brax is currently in Phase 1/2 development as part of the FORTITUDE™ trial in individuals with FSHD. The U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) have granted Orphan designation for del-brax and the FDA has granted del-brax Fast Track designation.

About Facioscapulohumeral Muscular Dystrophy (FSHD)
Facioscapulohumeral muscular dystrophy (FSHD) is a rare, progressive, and variable hereditary muscle-weakening condition marked by life-long, relentless loss of muscle function, significant pain, fatigue, and progressive disability. It is characterized by progressive and often asymmetric skeletal muscle loss that initially causes weakness in muscles in the face, shoulders, arms and trunk and progresses to weakness in muscles in the lower body. FSHD is an autosomal dominant disease caused by the aberrant expression of the DUX4 (double homeobox 4) gene in the skeletal muscle, which activates genes that are toxic to muscle cells and leads to a series of downstream events that result in skeletal muscle wasting and compromised muscle function. Skeletal muscle weakness results in physical limitations throughout the whole body, 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 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.

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 primary endpoints, design, goals and other details related to the FORTITUDE™ trial and each of its cohorts; the status and clinical development of *del-brax*, including any potential accelerated approval; Avidity's plans for the FORTITUDE-OLE™ study and the timing thereof; the characterization of safety, tolerability and functional data associated with *del-brax* from the Phase 1/2 FORTITUDE trial; the impact of such data on the advancement of *del-brax*; the plans and timing of adding a functional cohort for the FORTITUDE trial and the biomarker and functional cohorts potentially serving as the basis for registration; the potential of Avidity's product candidates to treat rare diseases and Avidity's efforts to bring them to people suffering from applicable diseases; and the potential of AOCs to target a range of different cells and tissues beyond the liver, and to treat cardiac and immunological 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 Avidity's business and those beyond its control, including, without limitation: preliminary results of a clinical trial are not necessarily indicative of final results and additional participant data related to *del-brax* 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 data cutoff; 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 clinical holds which may not be timely lifted, recalls or product liability claims; Avidity's current and planned cohorts in the FORTITUDE trial may not support the registration of *del-brax*; 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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