Avidity Announces Unprecedented AOC 1020 Data from Phase 1/2 FORTITUDE™ Trial Demonstrating Greater Than 50 Percent Reduction in DUX4 Regulated Genes and Trends of Functional Improvement in People Living with Facioscapulohumeral Muscular Dystrophy

Avidity plans to accelerate the initiation of registrational cohorts in FORTITUDE™ trial

Delpacibart braxlosiran (AOC 1020), the first investigational therapy to target the underlying cause of FSHD, provided greater than 50% mean reduction across multiple DUX4 regulated gene panels (2 mg/kg at four months)

Trends of functional improvement including muscle strength, reachable workspace, and positive trends in patient and clinician reported outcomes demonstrated in people treated with delpacibart braxlosiran 2 mg/kg at four months

Delpacibart braxlosiran data demonstrate favorable safety and tolerability with all adverse events mild or moderate

Volume 9 of virtual investor and analyst series today, Wednesday, June 12 at 8:00 a.m. ET

SAN DIEGO, June 12, 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 positive initial AOC 1020 data 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 facioscapulohumeral muscular dystrophy (FSHD). Avidity plans to accelerate initiation of registrational cohorts in the FORTITUDE™ study. Avidity also announced *delpacibart braxlosiran* as the approved international nonproprietary name of AOC 1020, abbreviated as *del-brax*.

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

"As the first therapy to directly target DUX4, it is very encouraging to see that the *del-brax* data demonstrate consistent reductions in DUX4 regulated genes and provided trends of functional improvement in patients with FSHD at the four-month timepoint. These early data would support the notion that *del-brax* has the potential to change the course of disease for people living with FSHD," said Jeffrey M. Statland, M.D., Professor of Neurology, University of Kansas Medical Center, and FORTITUDE™ trial investigator. "Early data showing trends in *del-brax* to improve muscle strength and function are very encouraging for patients with FSHD who are in need of treatments to prevent the muscle weakness and disability that is associated with this relentlessly, progressive disease."

The AOC 1020 initial data will be highlighted in an oral presentation at the 31st Annual FSHD Society International Research Congress, being held June 13-14, 2024, in Denver, Colorado.

"With the unprecedented *del-brax* data from the FORTITUDE trial, we are now focused on accelerating our registrational plans as we understand the urgency to develop a treatment for people living with FSHD who have no treatment options," said Sarah Boyce, president and chief executive officer at Avidity. "By directly targeting the root cause of FSHD, we believe that *del-brax* has the potential to be a first-in-class, best-in-class therapy for people living with FSHD. This is our third rare muscle disease program to show delivery to muscle and target engagement and second therapy to provide signs of functional improvement in patients with rare neuromuscular diseases, further reinforcing the promise of our AOC platform to profoundly improve people's lives by revolutionizing the delivery of RNA therapeutics."

The initial assessment from the randomized, double-blind, placebo-controlled Phase 1/2 FORTITUDE trial of *del-brax* provides a four-month look at the safety and tolerability for all 39 participants across two dose levels (2 mg/kg and 4 mg/kg). For the four-month assessment in the 2 mg/kg cohort, participants received a single-dose of 1 mg/kg *del-brax* followed by two doses of 2 mg/kg *del-brax* (siRNA dose), or placebo. Data on DUX4 regulated genes, circulating biomarkers and muscle strength and function were assessed from 12 participants in the 2 mg/kg cohort.

In the Phase 1/2 FORTITUDE study, *del-brax* demonstrated:

- Greater than 50% mean reductions in DUX4 regulated genes across multiple panels for DUX4 regulated gene expression in muscle
- All participants treated with *del-brax* showed reductions greater than 20% in DUX4 regulated genes

- Mean reductions of 25% or greater in novel circulating biomarker and creatine kinase
- Trends of functional improvements including increased strength in upper and lower limb muscles, and muscle function as measured by reachable workspace (RWS) compared to placebo and the ReSolve natural history study
- Trends of improvement in patient and clinician reported outcomes
- Favorable safety and tolerability with all adverse events (AEs) mild or moderate, no serious adverse events and no discontinuations

"Data from the FORTITUDE trial are very promising for people living with FSHD as the progression of the disease can make it increasingly difficult to perform critical day-to-day activities, pursue work and can affect many aspects of life, including family and social life," said Mark Stone, president and chief executive officer of FSHD Society. "FSHD is one of the most prevalent forms of muscular dystrophy and currently, there are no treatment options. The initial *del-brax* data offers real hope for those living with the disease, their families, and their caregivers, who are desperately waiting for a treatment."

Video Webcast Information
The company is hosting Volume 9 of its investor and analyst event series on June 12, 2024, beginning at 8:00 a.m. ET to discuss the initial data from the FORTITUDE™ trial of *del-brax* in people living with FSHD. 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.

The management team will be joined by Jeffrey M. Statland, M.D., Professor of Neurology, University of Kansas Medical Center, and FORTITUDE™ trial investigator. Dr. Statland is one of the principal investigators in the ReSolve study, an ongoing natural history study being led by the FSHD Clinical Trial Research Network (CTRN).

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 39 adult participants with facioscapulohumeral muscular dystrophy (FSHD). FORTITUDE will evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of *del-brax* administered intravenously, with the primary objective being the safety and tolerability of *del-brax* in FSHD patients. Activity of *del-brax* 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 *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 an open-label extension study at the end of the treatment period in the FORTITUDE study. For more information about the FORTITUDE trial, visit the FORTITUDE study website or visit http://www.clinicaltrials.gov and search for NCT05747924.

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. In preclinical studies, a single intravenous dose with the murine version of *del-brax* prevented development of muscle weakness demonstrated by three functional assays - treadmill running, in vivo force and compound muscle action potential. *Del-brax* is currently in Phase 1/2 development as part of the FORTITUDE™ trial in adults 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 significant pain, fatigue, and 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 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 cohorts for the FORTITUDE trial and such cohorts potentially serving as the basis for registration; the status and potential of *del-brax* as a first-in-class, best-in-class treatment for FSHD; 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. 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 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 additional clinical holds which may not be timely lifted, recalls or product liability claims; Avidity's planned additional 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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