Avidity Biosciences Receives Orphan Drug Designation in Japan for Delpacibart Etedesiran (del-desiran) for Treatment of Myotonic Dystrophy Type 1

Del-desiran first-ever investigational treatment for DM1 to receive Orphan Drug designation in Japan

SAN DIEGO, April 8, 2025 /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 that the Japan Ministry of Health, Labour and Welfare (MHLW) has granted Orphan Drug designation (ODD) to delpacibart etedesiran (del-desiran) for the treatment of myotonic dystrophy type 1 (DM1), an investigational treatment designed to address the root cause of DM1, an underrecognized, progressive and often fatal neuromuscular disease with no approved therapies. Del-desiran is the first investigational treatment for DM1 to receive Orphan Drug designation in Japan. Del-desiran has also received Breakthrough Therapy, Orphan Drug and Fast Track designations by the U.S. Food and Drug Administration (FDA) and Orphan designation by the European Medicines Agency (EMA).

"This decision by MHLW further reinforces the significant potential of del-desiran to address the root cause of DM1 and the urgent need to bring an approved therapy to the many people impacted by this devastating rare disease in Japan and around the world," said Steve Hughes, M.D., chief medical officer at Avidity. "We are very encouraged by del-desiran data reported from the MARINA and MARINA-OLE studies thus far, demonstrating favorable long-term safety and tolerability, reversal of disease progression, and consistent and durable improvements in multiple clinical endpoints. Looking ahead, there are multiple key milestones this year as we complete enrollment in the phase 3 HARBOR trial and continue to advance our global commercialization preparations to potentially deliver the first globally approved drug for people living with DM1."

Avidity has aligned with global regulators on the registrational path for del-desiran for the treatment of DM1, which informed the design of the ongoing Phase 3 HARBOR™ study. Avidity expects to complete participant enrollment in the Phase 3 HARBOR study in mid-2025 and submit marketing applications starting 2026 in the U.S., European Union and Japan.

Japan's MHLW grants Orphan Drug designation to drugs in development for the treatment of diseases that affect fewer than 50,000 patients in Japan and for which there is a high unmet medical need. An investigational therapy is eligible to qualify for Orphan Drug designation if there is no approved alternative treatment option or if there is high efficacy or safety expected compared to existing treatment options. Orphan Drug designation provides certain benefits, including prioritized consultation regarding clinical development, reduced consultation fees, tax incentives, priority review of applications, reduced application fees, and extended registration validity period.

About the Phase 3 HARBOR™ Trial
The global Phase 3 HARBOR™ trial is a randomized, placebo-controlled, double blind pivotal study designed to evaluate*del-desiran* in approximately 150 people (age 16 and older) living with DM1. The trial will be conducted at approximately 40 sites globally. Patients will be administered either *del-desiran* or placebo (1:1) every eight weeks. HARBOR is designed to assess multiple key functional aspects of DM1. The primary endpoint is video hand opening time (vHOT), a measurement of myotonia, which is a hallmark symptom of DM1. Key secondary endpoints include muscle strength as measured by hand grip strength and quantitative muscle testing (QMT) total score, and activities of daily living as measured by DM1-Activ. All study participants, regardless of whether they receive active treatment or placebo, will have the option to enroll into an open-label extension trial. For more information about the HARBOR trial, visit the HARBOR study website or visit http://www.clinicaltrials.gov and search for NCT06411288.

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 del-desiran in participants with 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 del-desiran in participants enrolled in the randomized, placebo-controlled, Phase 1/2 MARINA clinical trial. Participants enrolled in the MARINA-OLE study receive quarterly doses of del-desiran regardless of whether they received active treatment or placebo in the MARINA study. The total duration of active treatment with del-desiran in the MARINA-OLE study is approximately 24 months. Once patients have completed active treatment, there will be a nine-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 Del-desiran
Del-desiran, 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. Del-desiran consists of a proprietary monoclonal antibody that binds to the transferrin receptor 1 (TfR1) conjugated with a siRNA targeting DMPK mRNA. Del-desiran is currently being assessed in the global Phase 3 HARBOR™ trial and in the ongoing MARINA-OLE™ trial in people with DM1. Long-term data from the MARINA-OLE trial showed reversal of disease progression in people living with DM1 across multiple endpoints including video

hand opening time (vHOT) as a measure of hand function and myotonia, muscle strength and activities of daily living when compared to END-DM1 natural history data. Del-desiran has received Breakthrough Therapy, Orphan Drug and Fast Track designations by the U.S. Food and Drug Administration (FDA) and Orphan designation by the European Medicines Agency (EMA).

About Myotonic Dystrophy Type 1
Myotonic dystrophy type 1 (DM1) is an underrecognized, autosomal dominantly inherited, 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 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 neuromuscular diseases: myotonic dystrophy type 1 (DM1), Duchenne muscular dystrophy (DMD) and facioscapulohumeral muscular dystrophy (FSHD). Avidity is also advancing two wholly-owned precision cardiology development candidates addressing rare genetic cardiomyopathies. In addition, Avidity is broadening the reach of AOCs with its advancing and expanding pipeline including programs in cardiology and immunology through 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: planned marketing applications for del-desiran in the U.S., European Union and Japan, and the timing thereof; Avidity's plans to become a global commercial organization and the status of its commercialization efforts; the characterization of data associated with del-desiran in the MARINA and MARINA-OLE studies, the conclusions drawn therefrom, and the impact of such data on the advancement of del-desiran and its ability to treat DM1; the designs, goals, statuses and enrollment levels of, and plans for, the MARINA-OLE and HARBOR studies; Avidity's platform, planned operations and programs; and Avidity's cash position and runway.

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 beyond its control, including, without limitation: Avidity may not realize any benefit from Orphan Drug designation of del-desiran by global health authorities; the data and results produced in Avidity's ongoing studies of del-desiran as of the most recent respective cutoff dates may not be indicative of final results, may not support a BLA submission, may not be satisfactory to the MHLW and other regulators, and new analyses of existing data and results may produce different conclusions than established as of the date hereof; even if approved, Avidity may not be able to execute any successful product launches; Avidity's efforts to build a global commercial organization may be unsuccessful; unexpected adverse side effects to, or inadequate efficacy of, del-desiran that may delay or limit its development, regulatory approval and/or commercialization; later developments with the MHLW and other global regulators that could be inconsistent with the feedback received to date; Avidity's approach to the discovery and development of product candidates based on its AOC™ platform is unproven and may not produce any products of commercial value; potential delays in the commencement, enrollment, data readouts and completion of the MARINA-OLE and HARBOR studies; Avidity's dependence on third parties in connection with preclinical and clinical testing and product manufacturing; legislative, judicial and regulatory developments in the United States and foreign countries; Avidity could exhaust its available capital resources sooner than it currently expects; and other risks described in Avidity's Annual Report on Form 10-K for the fiscal year ended December 31, 2024. 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:
Kat Lange
(619) 837-5014
investors@aviditybio.com

Media Contact:
(619) 837-5016

media@aviditybio.com

SOURCE Avidity Biosciences, Inc.
