The New England Journal of Medicine Publishes Results from Phase 1/2 MARINA® Trial of Delpacibart Etedesiran (del-desiran) for Treatment of Myotonic Dystrophy Type 1

Del-desiran effectively delivered siRNA to muscle, resulting in approximately 40% mean reduction in DMPK mRNA and amelioration of missplicing

Treatment demonstrated improvements in multiple measures including myotonia, muscle function and strength, mobility and patient-reported outcomes

Del-desiran showed acceptable safety and tolerability with most adverse events mild or moderate

SAN DIEGO, Feb. 18, 2026 /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 final results from the completed Phase 1/2 MARINA® trial of delpacibart etedesiran (del-desiran) in people living with myotonic dystrophy type 1 (DM1) will be published in the February 19 issue of *The New England Journal of Medicine* (*NEJM*). The manuscript is titled "An Antibody Oligonucleotide Conjugate for Myotonic Dystrophy Type 1."

DM1 is an underrecognized, progressive and often fatal neuromuscular disease with no disease modifying therapies. Del-desiran is an investigational treatment designed to address the underlying genetic root cause of DM1 by reducing total levels of the toxic, *DMPK* (myotonic dystrophy protein kinase) mRNA. The accumulation of these toxic mRNA sequester key RNA-regulatory proteins that subsequently lead to missplicing of several downstream genes, resulting in the diverse clinical manifestations of disease.

The Phase 1/2 MARINA trial was a randomized, double-blind, placebo-controlled study designed to evaluate the safety and tolerability of single and multiple ascending doses of del-desiran administered intravenously in adults with DM1 for six months. Data were assessed from 38 participants who were randomized 3:1 to receive one dose of 1 mg/kg del-desiran, three doses of either 2 mg/kg del-desiran or 4 mg/kg del-desiran (reflected as siRNA dose), or placebo. The primary endpoint of the study was to evaluate the safety and tolerability of del-desiran. Exploratory endpoints were to evaluate the clinical activity of del-desiran across multiple efficacy measures.

"These final results from the MARINA study further reinforce del-desiran data reported thus far showing acceptable safety profile and improvements across a range of key functional assessments including myotonia, a hallmark symptom of DM1," said Nicholas E. Johnson, M.D., M.Sci., FAAN, professor and vice chair of research in the Department of Neurology at Virginia Commonwealth University, lead author and primary investigator of the MARINA trial. "DM1 is a progressive disorder that is often fatal, increases in severity from generation to generation, and impacts thousands of people and families in the U.S. alone. There is an urgent need for an approved therapy that can address the underlying genetic cause of this disease, and these del-desiran data, as well as available data from the ongoing OLE study, are very encouraging for the DM1 community."

Results from the Phase 1/2 MARINA study of del-desiran published in *NEJM* demonstrated:

- Effective delivery of del-desiran (siRNA) to muscle, with a mean ~ 40% reduction in DMPK mRNA across all treated participants.
- Splicing improvements in a key set of muscle-specific genes following treatment with del-desiran 2 mg/kg and 4 mg/kg.
- Improvements in exploratory functional measures including:
    - Hand function/myotonia (video hand opening time, or vHOT)
    - Muscle strength (Quantitative Muscle Testing, or QMT total score)
    - Mobility (10-Meter Walk/Run Test, or 10mWRT, and Timed Up and Go test, or TUG)
    - DM1-Activ, a patient-reported outcome that measures activities of daily living (e.g., taking a shower, visiting family or friends, and walking up stairs)
- Acceptable safety and tolerability with most treatment emergent adverse events (TEAEs) mild or moderate in participants with DM1 and did not result in discontinuation.
- Two severe, serious AEs occurred in two participants in the 2 mg/kg and 4 mg/kg dose cohorts, with one participant discontinuing the study in the 4 mg/kg cohort. One of these SAEs was deemed drug-related.

"We are pleased that *The New England Journal of Medicine* recognizes the significance of the Phase 1/2 MARINA data. The favorable safety profile, coupled with robust analyses of exploratory endpoints in our del-desiran program reinforce our belief that this investigational therapy may offer a transformational treatment option for people living with DM1 and their families," said Sarah Boyce, President and Chief Executive Officer at Avidity. "We remain focused on advancing the ongoing Phase 3 HARBOR study of del-desiran, which is on track to be the first globally approved drug for DM1."

Del-desiran (4 mg/kg) is currently being assessed in the global Phase 3 HARBOR™ study in people living with DM1 who are age 16 and older and in the ongoing HARBOR open-label extension (HARBOR-OLE™) trial with all the participants who completed the Phase 1/2 MARINA trial. The global Phase 3 HARBOR study completed enrollment in July 2025 and a 54-week topline data readout is expected in the second half of 2026.

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 is being conducted at approximately 40 sites globally. Patients are 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, have the option to enroll into the ongoing open-label extension trial. For more information about the HARBOR trial, visit http://www.clinicaltrials.gov and search for NCT06411288. For more information about the HARBOR-OLE trial, visit http://www.clinicaltrials.gov and search for (NCT07008469).

About the Phase 1/2 MARINA® Trial
The MARINA® trial was a randomized, double-blind, placebo-controlled, Phase 1/2 clinical trial that enrolled 38 adults with DM1. The primary objective of this study was to evaluate the safety and tolerability of single and multiple ascending doses of del-desiran (AOC 1001) administered intravenously. The MARINA trial assessed the activity of del-desiran (AOC 1001) across key biomarkers, including reduction of DMPK mRNA in skeletal muscle and amelioration of aberrant alternative splicing. Though the Phase 1/2 trial was not powered to assess functional benefit, it explored the clinical activity of del-desiran (AOC 1001) in multiple measures of muscle function including myotonia, muscle strength, measures of mobility as well as patient reported outcomes and quality of life measures. Patients had 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 Myotonic Dystrophy Type 1
Myotonic dystrophy type 1 (DM1) is a rare, hereditary (autosomal dominant), progressive neuromuscular disease that shortens life expectancy and requires life-long care 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. DM1 is characterized by multisystemic manifestations including myotonia and progressive muscle weakening and may be underrecognized because it presents heterogeneously across skeletal, cardiac, and smooth muscles, leading to impairment of the cardiovascular, gastrointestinal, respiratory, ocular, and/or endocrine systems. Currently, there are no approved drugs for people living with DM1.

About del-desiran
Del-desiran, utilizing Avidity's AOC platform technology, is designed to address the underlying genetic cause of DM1 by reducing levels of toxic DMPK mRNA. Del-desiran consists of a proprietary monoclonal antibody that binds to transferrin receptor 1 (TfR1) and is conjugated to a siRNA that targets DMPK mRNA. Del-desiran is currently being assessed in the global Phase 3 HARBOR™ trial and in the ongoing HARBOR-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). Del-desiran was also the first investigational treatment for DM1 to receive Orphan Drug designation in Japan.

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 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: the meaningfulness of the del-desiran data from the

MARINA® study; the potential for del-desiran to offer a transformational treatment option for DM1 and become the first globally approved drug to treat DM1; the status of the clinical study of del-desiran; Avidity's plans to present additional data from the HARBOR™ study and the timing thereof; the characterization of data associated with del-desiran from the MARINA study and the impact of such data on the advancement of del-desiran; the design, goals and status of the MARINA, MARINA-OLE™ and HARBOR studies; Avidity's plans and expectations to advance its clinical programs, and the timing thereof; and Avidity's platform, planned operations and programs. 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: analysis of new data may lead to conclusions different from those established in the MARINA trial of del-desiran, and such data may not meet Avidity's or regulators' expectations; 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 FDA and other global regulators that could be inconsistent with the feedback received to date regarding del-desiran and which could delay its currently anticipated timelines; Avidity's approach to the discovery and development of product candidates based on its AOC™ platform is unproven; potential delays in the HARBOR study; Avidity's dependence on third parties in connection with 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 and 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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