Avidity Biosciences Announces Positive Topline Del-zota Data Demonstrating Consistent, Statistically Significant Improvements in Dystrophin, Exon Skipping and Creatine Kinase in People Living with Duchenne Muscular Dystrophy Amenable to Exon 44 Skipping in Phase 1/2 EXPLORE44® Trial

On track for year end 2025 BLA submission for accelerated approval of 5 mg/kg every six weeks of del-zota in DMD44

Consistent favorable safety and tolerability across del-zota dose cohorts

Plan to present functional data in fourth quarter of 2025

Investor and analyst webcast event today at 8:00 a.m. ET

SAN DIEGO, March 17, 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 positive del-zota topline data from the Phase 1/2 EXPLORE44® trial in people living with Duchenne muscular dystrophy amenable to exon 44 skipping (DMD44) demonstrating consistent, statistically significant improvements in dystrophin, exon skipping and creatine kinase as well as favorable safety and tolerability across the dose cohorts. The data will be highlighted in an oral and poster presentation at the 2025 Muscular Dystrophy Association (MDA) Clinical & Scientific Conference, being held March 16-19, 2025, in Dallas, Texas.

"Del-zota has shown remarkable improvements across multiple measures, including a substantial increase in dystrophin production and a significant reduction in serum creatine kinase levels to near normal after just three doses. The consistency of these results in such a short time frame, coupled with favorable safety and tolerability, underscores the potential of del-zota to become a groundbreaking treatment for individuals living with DMD with genetic variants amenable to exon 44 skipping," said Aravindhan Veerapandiyan, M.D., Associate Professor of Pediatrics, University of Arkansas for Medical Sciences and Arkansas Children's Hospital. "These results bring new hope for patients and families affected by DMD who are in urgent need of targeted therapies that can preserve muscle integrity and possibly prevent or delay the progression of muscle weakness and loss of function associated with this disease."

Del-zota is designed to deliver phosphorodiamidate morpholino oligomers (PMOs) to skeletal and cardiac muscle tissue to specifically skip exon 44 of the dystrophin gene and enable production of near-full length dystrophin. Del-zota has been granted Orphan designation by the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA). The FDA has also granted del-zota Rare Pediatric Disease and Fast Track designations. Del-zota is the first of multiple AOCs currently in development at Avidity for the treatment of DMD.

"These data are a true testament to the power of our AOC platform and the potential of del-zota to change the course of this relentless and devastating rare disease," said Sarah Boyce, president and chief executive officer at Avidity. "We are particularly encouraged that these data demonstrate the consistent effects of del-zota across a variety of participants, including broad age range, genotypes and ambulatory and non-ambulatory participants. The early and durable effects observed with del-zota further strengthen our commitment to rapidly bring this potentially transformative therapy to people living with DMD44. Based on our interactions with FDA on accelerated approval, we believe dystrophin data from EXPLORE44 combined with the safety data from our fully enrolled EXPLORE44-OLE trial will support our planned BLA submission at the end of this year. We are immensely grateful for the continued dedication of our team, the investigators and, most importantly, the participants in our clinical trials and their families."

The topline data from the randomized, double-blind, placebo-controlled Phase 1/2 EXPLORE44 trial demonstrated consistent, statistically significant improvements across key biomarkers as well as safety and tolerability of del-zota across two dose levels, 5 mg/kg and 10 mg/kg.

Participants received three doses of either 5 mg/kg del-zota or placebo every six weeks, or 10 mg/kg del-zota or placebo every eight weeks. Data on muscle delivery, exon skipping, dystrophin production and creatine kinase levels were assessed from seven (7) participants in the 5 mg/kg cohort, 10 participants in the 10 mg/kg cohort, and six (6) placebo participants, 28 days after the third dose. Safety and tolerability data were assessed from 26 participants in the completed Phase 1/2 EXPLORE44 trial and 38 participants in the ongoing EXPLORE44 Open-Label Extension (OLE) trial, as of January 22, 2025.

The data presented at MDA highlight the consistent data across all parameters in both the 5 mg/kg and 10 mg/kg cohorts of del-zota, including:

- Targeted delivery of PMOs resulting in tissue concentrations of approximately 200nM in skeletal muscle;
- Statistically significant increases of approximately 40% in exon 44 skipping;
- Statistically significant increase of approximately 25% of normal in dystrophin production and restored total dystrophin up to 58% of normal;
- Reduction in creatine kinase levels to near normal with greater than 80% reductions compared to baseline:
    - Similarly, placebo participants demonstrated a reduction in creatine kinase levels to near normal upon treatment with del-zota;
    - Significant reductions in creatine kinase levels were sustained in the EXPLORE44-OLE trial with continued treatment up to one year; and,
- Del-zota demonstrated favorable safety and tolerability at both doses, with most treatment emergent adverse events (TEAEs) mild or moderate.

Based on the consistent data between the 5 mg/kg every six weeks and the 10mg/kg every eight weeks groups across all parameters, Avidity has selected the dose of 5 mg/kg every six weeks of del-zota for the Biologics License Application (BLA) submission and future clinical studies. Participants currently receiving the 10 mg/kg dose in the EXPLORE44-OLE trial are in the process of being transitioned to 5 mg/kg every six weeks.

Following alignment with FDA on the accelerated approval path late last year, including dose selection, Avidity's commercial preparations for a potential U.S. launch of del-zota in DMD44 are well underway. Del-zota's anticipated launch sets the foundation for sequential launches of Avidity's three neuromuscular programs, including del-desiran for myotonic dystrophy type 1 (DM1) and del-brax for facioscapulohumeral muscular dystrophy (FSHD).

Video Webcast Information
The company is hosting an investor and analyst event today at 8:00 am ET and will be joined by Kevin M. Flanigan, MD, Director, Center for Gene Therapy and Robert F. & Edgar T. Wolfe Foundation Endowed Chair in Neuromuscular Research at Nationwide Children's Hospital, and Professor of Pediatrics and Neurology at Ohio State University, to discuss del-zota topline data from the EXPLORE44 trial. The 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.

About the EXPLORE44® Phase 1/2 Trial
The EXPLORE44® trial was a randomized, placebo-controlled, double-blind, Phase 1/2 clinical trial that enrolled 26 participants with Duchenne muscular dystrophy mutations amenable to exon 44 skipping (DMD44). The study was designed to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamic effects of single and multiple ascending doses of *del-zota* (formerly AOC 1044) administered intravenously in healthy volunteers and participants living with DMD44. The EXPLORE44 trial assessed exon skipping and dystrophin protein levels in participants with DMD44. Participants with DMD44 had the option to enroll into EXPLORE44-OLE™, an open-label extension study, at the end of the post-treatment period. For more information about the EXPLORE44 trial, visit the EXPLORE44 study website or visit https://www.clinicaltrials.gov and search for NCT05670730.

About the Phase 2 EXPLORE44-OLE™ Study
EXPLORE44-OLE™ is an open-label, multi-center trial designed to evaluate the long-term safety, tolerability, pharmacokinetics, pharmacodynamic effects and efficacy of *del-zota* in participants with DMD44. Enrollment has been completed in the EXPLORE44-OLE study, with 23 participants who were previously enrolled in the Phase 1/2 EXPLORE44® trial and 16 participants who directly enrolled in the EXPLORE44-OLE study. Participants in the EXPLORE44-OLE study will receive 5 mg/kg of *del-zota* every six weeks. The total duration of active treatment with *del-zota* in the EXPLORE44-OLE study is approximately 24 months. Once participants have completed active treatment, there will be a three-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 NCT06244082.

About Duchenne muscular dystrophy (DMD)
Duchenne muscular dystrophy (DMD) causes a lack of functional dystrophin that leads to stress and tears of muscle cell membranes, resulting in muscle cell death and the progressive loss of muscle function. The dystrophin protein maintains the integrity of muscle fibers and acts as a shock absorber through its role as the foundation of a group of proteins that connects the inner and outer elements of muscle cells. People living with DMD suffer from progressive muscle weakness that typically starts at a very young age. Over time, people with Duchenne will develop problems walking and breathing, and eventually, the heart and respiratory muscles will stop working. Those living with the condition often require special aid and assistance throughout their lives and have significantly shortened life expectancy. While there are treatments approved to treat people with DMD, there remains a very high unmet need. DMD is a monogenic, X-linked, recessive disease that primarily affects males, with one in 3,500 to 5,000 boys born worldwide having Duchenne.

About *Del-zota*
Del-zota is designed to deliver phosphorodiamidate morpholino oligomers (PMOs) to skeletal muscle and heart tissue to

specifically skip exon 44 of the dystrophin gene to enable dystrophin production in people living with Duchenne muscular dystrophy with mutations amenable to exon 44 skipping (DMD44). DMD is characterized by progressive muscle degeneration and weakness due to alterations of a protein called dystrophin that protects muscle cells from injury during contraction. *Del-zota* consists of a proprietary monoclonal antibody that binds to the transferrin receptor 1 (TfR1) conjugated with a PMO targeting exon 44. The Phase 1/2 EXPLORE44® trial of *del-zota* has been completed, and the EXPLORE44 Open-Label Extension trial (OLE™) of *del-zota* is currently ongoing. Topline data from the completed*del-zota* Phase 1/2 EXPLORE44 trial demonstrated unsurpassed delivery of PMOs to skeletal muscle, robust increases in dystrophin production, significant increases in exon 44 skipping, and significant and sustained decreases of creatine kinase levels to near normal in people living with DMD44. *Del-zota* has received Rare Pediatric Disease, 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 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: the characterization of data associated with del-zota and the EXPLORE44® trial; the safety and tolerability of del-zota; the dose selection and frequency of administration of del-zota in the EXPLORE44-OLE study; the active treatment and safety follow-up periods in EXPLORE44-OLE; Avidity's plans for a BLA submission for del-zota and the timing thereof; the design and goals of the EXPLORE44 and EXPLORE44-OLE trials; the ability for del-zota to achieve accelerated approval; the status of Avidity's commercialization efforts; the ability for del-zota to treat DMD44 and Avidity's product candidates to treat their intended indications; and the potential of the AOC platform. 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: the data and results produced in the EXPLORE44 trial as of the most recent cutoff date may not be indicative of final results, may not support a BLA submission or accelerated approval, may not be satisfactory to the FDA and other regulators, and new analyses of existing data and results may produce different conclusions than established as of the date hereof; the FDA and other regulators may change their positions on the status of del-zota and its clinical development; 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, Avidity's product candidates that may delay or limit their development, regulatory approval and/or commercialization; Avidity's approach to the discovery and development of product candidates based on its AOC platform is unproven; potential delays in the commencement, enrollment, data readouts and completion of Avidity's ongoing clinical trials; 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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https://investors.aviditybiosciences.com/2025-03-17-Avidity-Biosciences-Announces-Positive-Topline-Del-zota-Data-Demonstrating-Consistent,-Statistically-Significant-Improvements-in-Dystrophin,-Exon-Skipping-and-Creatine-Kinase-in-People-Living-with-Duchenne-Muscular-Dystrophy-Amenable-to-Exon-44