Avidity Biosciences Completes Enrollment in Biomarker Cohort in Phase 1/2 FORTITUDE™ Trial for Delpacibart Braxlosiran (del-brax) in People Living with Facioscapulohumeral Muscular Dystrophy

Del-brax FORTITUDE biomarker cohort designed for potential accelerated approval; plan to share regulatory update in Q2 2025

Regulatory alignment on global Phase 3 del-brax trial design and study initiation anticipated in Q2 2025

Plan to present topline data from FORTITUDE dose escalation cohorts in Q2 2025

On track to be first globally approved drug for FSHD

SAN DIEGO, March 31, 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 the completion of enrollment in the biomarker cohort in the Phase 1/2 FORTITUDE™ clinical trial of delpacibart braxlosiran (del-brax) in people living with facioscapulohumeral muscular dystrophy (FSHD). A total of 51 participants were enrolled in the FORTITUDE biomarker cohort.

"Completing enrollment in the FORTITUDE biomarker cohort is an important milestone as we pursue a potential accelerated approval path in the U.S. for del-brax and work to bring the first approved drug to people living with this rare, devastating neuromuscular disease who have no treatment options as quickly as possible," said Steve Hughes, M.D., chief medical officer at Avidity. "We are very encouraged by the del-brax 2 mg/kg data thus far, demonstrating unprecedented and consistent reductions in DUX4-regulated genes, significant decreases in novel circulating biomarker and creatine kinase, trends of functional improvement, and favorable safety and tolerability, and look forward to sharing additional data as well as other key milestones in the second quarter of this year."

Avidity is on track to deliver multiple updates from the del-brax program in Q2 including:

- Regulatory alignment on a potential accelerated approval path in the U.S. for the ongoing FORTITUDE biomarker cohort;
- Regulatory alignment on the design of the global Phase 3 trial as well as initiation of the trial; and
- Topline data from the dose escalation cohorts in the FORTITUDE trial.

Del-brax is the first investigational therapy designed to treat the underlying cause of FSHD by directly targeting the mRNA transcript of 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. FSHD affects approximately 45,000 to 87,000 people in the United States and European Union.

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* in 90 participants with facioscapulohumeral muscular dystrophy (FSHD). FORTITUDE is evaluating the safety, tolerability, pharmacokinetics, and pharmacodynamics of del-brax administered intravenously. Activity of del-brax is being 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 explores the clinical activity of del-brax including measures of mobility and muscle strength as well as patient reported outcomes and quality of life measures.

The trial has a total of three dose cohorts. The first two dose escalation cohorts evaluated 2 mg/kg or 4 mg/kg of del-brax versus placebo and were designed to assess safety as well as inform the dose and dose regimen of del-brax for additional studies. Avidity has completed enrollment in the dose escalation cohorts and identified 2 mg/kg every six weeks of del-brax as the dose for future clinical trials.

The third, ongoing biomarker cohort in the FORTITUDE trial is designed for a potential accelerated approval path in the U.S. It is assessing the impact of del-brax 2 mg/kg every six weeks versus placebo for 12 months in people living with FSHD, ages 16-70. The primary endpoints of the study cohort are changes in DUX4-regulated gene expression and DUX4-regulated circulating biomarker. Enrollment in the biomarker cohort is complete.

Participants who complete FORTITUDE have the option to enroll in the ongoing FORTITUDE open-label extension (FORTITUDE-OLE™) study evaluating the long-term safety and tolerability of del-brax in participants living with FSHD. 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* in participants with facioscapulohumeral muscular dystrophy (FSHD) who were previously enrolled in the Phase 1/2 FORTITUDE™ trial. This trial will continue to evaluate the safety, tolerability, PK, PD, and efficacy of del-brax in participants who 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

Del-brax 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 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: Avidity's plans to present topline data from the dose escalation cohorts of the FORTITUDE study and the timing thereof; Avidity's plans to pursue an accelerated approval path for del-brax and the anticipation of regulatory alignment with such plans; the status of the FORTITUDE trial and cohorts therein, including but not limited to initiation, enrollment, design and goals; the ability for del-brax to achieve accelerated approval; the characterization of data associated with del-brax and the FORTITUDE trial, the conclusions drawn therefrom, the impact of such data on the advancement of del-brax and its abilities to treat FSHD; and the possibility of del-brax becoming the first globally approved drug for FSHD.

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 FORTITUDE trial

and FORTITUDE-OLE as of the most recent respective cutoff dates may not be indicative of final results, may not support BLA submissions or accelerated approvals, 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; even if approved, Avidity may not be able to execute a successful product launch for del-brax; unexpected adverse side effects to, or inadequate efficacy of, del-brax 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; 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 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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