News Release

Edgewise Therapeutics Announces Positive 4-Month Interim Results from the ARCH Open Label Study of EDG-5506 in Adults with Becker Muscular Dystrophy (BMD)

– Remarkable North Star Ambulatory Assessment scale (NSAA) improvements relative to BMD natural history trajectories –

– Significant decrease in levels of serum creatine kinase (CK) and fast skeletal muscle troponin I (TNNI2), enzyme biomarkers strongly associated with muscle damage caused by BMD –

– EDG-5506 continues to be well-tolerated with no serious adverse events observed –

– Management hosting webcast to discuss findings on September 12 at 8:30 a.m. Eastern Time –

Boulder, Colo., *(September 11, 2022)* – Edgewise Therapeutics, Inc., (NASDAQ: EWTX), a clinical-stage biopharmaceutical company focused on developing orally bioavailable, small molecule therapies for the treatment of rare muscle disorders, announced today positive 4-month interim results from the ongoing ARCH study, an open label, single-center study assessing the safety, tolerability, impact on muscle damage biomarkers, and pharmacokinetics (PK) of EDG-5506 in adults with BMD. EDG-5506 is an investigational orally administered small molecule myosin modulator designed to protect injury-susceptible fast skeletal muscle fibers in dystrophinopathies such as Duchenne muscular dystrophy (DMD) and BMD.

The twelve adults with BMD enrolled in the ARCH study were dose escalated to daily 15 mg oral doses of EDG-5506 at night after having initially received a 10 mg dose during the first 2 months of the study. Plasma PK at 4 months reached the target exposures observed in the Phase 1b study where BMD participants were dosed with 20 mg EDG-5506 once-daily for two weeks. EDG-5506 was well-tolerated in all participants with no discontinuations or dose reductions. The most common adverse events observed to date were dizziness, drowsiness, and headache. All eligible patients have subsequently been dose escalated to 20 mg daily as per protocol.

Treatment with EDG-5506 led to a significant decrease in key biomarkers of muscle damage when assessed by laboratory assays. Importantly, CK and fast skeletal muscle troponin I were reduced by an average of 29% and 74%, respectively, after 4 months. While CK reductions were sustained and in line with observations made at 2 months, mean fast skeletal muscle troponin I levels decreased with continued exposure to EDG-5506. Similar to observations made after 2 months, both CK and fast skeletal muscle troponin I were significantly decreased in the context of typical everyday activity levels as measured with a pedometer.

After 4 months of EDG-5506 dosing, NSAA increased by an average of 1.17 points compared to pre-therapy baseline. Remarkably, nine of the twelve participants showed either a functional improvement or exhibited no decline on NSAA relative to their baselines. The NSAA improvements observed after only 4 months of EDG-5506 dosing differ from trajectories observed in the natural history study reported by Bello *et al.* (2016)[1], one of the most comprehensively characterized BMD cohorts, in which the yearly decline was 1.22 NSAA points. These observations were further corroborated by an independent study from van de Velde *et al.* (2021)[2], which showed a decline of 2.5 NSAA points over 2 years.

The Company believes the 4-month ARCH study data with EDG-5506 provide further support that reducing contraction-induced damage in dystrophic muscle has the potential to preserve and improve muscle function while preventing disease progression in dystrophinopathies.

“Those with BMD have no approved options to treat their condition,” said Joanne Donovan, M.D., Ph.D., Chief Medical Officer of Edgewise. “We continue to be encouraged by EDG-5506’s safety profile and these interim 4-month data allow us to make some critical decisions on how to potentially accelerate our clinical programs in BMD and DMD.”

“We appreciate the individuals with BMD who are participating in the ARCH open label study,” added Kevin Koch, Ph.D., President and Chief Executive Officer of Edgewise. “These early NSAA results, along with the steep decline in biomarkers of muscle damage, are very encouraging and highlight EDG-5506’s potential to alter the course of the disease.”

Data Review Conference Call

Members of the Edgewise management team will hold a conference call and webcast on **Monday, September 12, at 8:30 am ET** to discuss the ARCH interim data. To participate, please dial **844-200-6205** (domestic) or **646-904-5544** (international) and refer to access code **413021**. Visit the Edgewise events page to access the webcast, including replay and conference call slides.

About the ARCH Open Label Study

The ARCH open label study is evaluating EDG-5506 in 12 adult males with BMD. All those who participated in the Phase 1b first-in-human study of EDG-5506 enrolled in the ARCH study after at least a 3-month washout following their participation in the Phase 1b trial. The study is evaluating escalating doses of EDG-5506 administered daily over 12 months. Safety, pharmacokinetics (PK), changes in biomarkers of muscle damage such as CK and fast skeletal muscle troponin I, measures of function with NSAA and North Star Assessment for Limb Girdle Type Muscular Dystrophies (NSAD), time function tests and patient-reported outcomes, are being evaluated. Go to clinicaltrials.gov to learn more about this study (NCT05160415).

About Becker Muscular Dystrophy

BMD is a serious, progressively debilitating, and potentially fatal inherited X-linked neuromuscular disorder. BMD results from mutation of the dystrophin gene yielding unstable and/or dysfunctional dystrophin expression in muscles. Individuals with BMD, typically males, have ongoing muscle fiber (myofiber) degeneration that eventually leads to fibrosis, progressive loss of skeletal muscle function, and that can lead to severe disability and early death. BMD typically presents with juvenile onset of

muscle wasting and progressive symmetrical, proximal muscle weakness, calf hypertrophy, activity-induced muscle cramping and elevated creatine kinase activity. While the course of BMD is variable, it is unidirectional in terms of the inevitable progressive limb weakness resulting in severe disability. BMD is also associated with early mortality from cardiac disease. The incidence of BMD is approximately 1 in every 18,450 live male births. It is estimated that there are between 4,000 to 5,000 individuals with BMD in the U.S., with similar numbers of individuals living with BMD in the EU and UK. Despite the seriousness of the disease, for many with BMD, the disease remains one of considerable unmet medical need as there are no approved therapies in the U.S.

About EDG-5506

EDG-5506 is an orally administered small molecule designed to address muscle damage induced by mechanical stress in dystrophinopathies including DMD and BMD. EDG-5506 presents a novel mechanism of action designed to selectively limit the exaggerated muscle damage caused by the absence or loss of functional dystrophin. By impacting the progressive muscle damage that leads to functional impairment, EDG-5506 has the potential to benefit a broad range of patients suffering from debilitating rare neuromuscular disorders. It is anticipated to be used as a single agent therapy, but it may also provide a synergistic or additive effect in combination with available therapies and therapies currently in development. In August 2021, the U.S. Food and Drug Administration (FDA) granted Fast Track designation to EDG-5506 for the treatment of individuals with BMD.

The Company has completed a Phase 1 clinical trial of EDG-5506 designed to evaluate safety, tolerability, PK and pharmacodynamics of EDG-5506 in adult healthy volunteers (Phase 1a) and in adults with BMD (Phase 1b) (NCT04585464). In ARCH, a follow-on open-label, single-center trial (NCT05160415) assessing long-term safety and PK, decreases in biomarkers of muscle damage and improvements in NSAA have been demonstrated. CANYON, a Phase 2 trial (NCT05291091) is assessing safety, PK, biomarkers and functional measures in participants with BMD. Recently, the FDA authorized LYNX, a Phase 2 trial of EDG-5506 for the treatment of DMD that will assess safety, PK and biomarkers of muscle damage.

About Edgewise Therapeutics

Edgewise Therapeutics is a clinical-stage biopharmaceutical company focused on the discovery, development, and commercialization of innovative treatments for severe, rare neuromuscular and cardiac disorders for which there is significant unmet medical need. Guided by its holistic drug discovery approach to targeting the muscle as an organ, Edgewise has combined its foundational expertise in muscle biology and small molecule engineering to build its proprietary, muscle-focused drug discovery platform. Edgewise's platform utilizes custom-built high throughput and translatable systems that measure integrated muscle function in whole organ extracts to identify small molecule precision medicines regulating key proteins in muscle tissue. To learn more, go to: www.edgewisetx.com or follow us on LinkedIn, Twitter and Facebook.

References

[1] Bello L, *et al.*, Functional Changes in Becker Muscular Dystrophy: Implications for Clinical Trials in Dystrophinopathies, *Scientific Reports*, 2016.

[2] van de Velde NM, *et al.*, Selection Approach to Identify the Optimal Biomarker Using Quantitative Muscle MRI and Functional Assessments in Becker Muscular Dystrophy, *Neurology*, 2021.

Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements as that term is defined in Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. Statements in this press release that are not purely historical are forward-looking statements. Such forward-looking statements include, among other things, statements regarding the potential of, and expectations regarding, Edgewise's drug discovery platform, product candidates and programs, including EDG-5506; statements regarding Edgewise's expectations relating to its clinical trials of EDG-5506; and statements by Edgewise's president and chief executive officer and chief medical officer. Words such as "believes," "anticipates," "plans," "expects," "intends," "will," "goal," "potential" and similar expressions are intended to identify forward-looking statements. The forward-looking statements contained herein are based upon Edgewise's current expectations and involve assumptions that may never materialize or may prove to be incorrect. Actual results could differ materially from those projected in any forward-looking statements due to numerous risks and uncertainties, including but not limited to: risks associated with the process of discovering, developing and commercializing drugs that are safe and effective for use as human therapeutics and operating as an early clinical stage company including the potential for Edgewise's product candidates to cause serious adverse events; Edgewise's ability to develop, initiate or complete preclinical studies and clinical trials for, obtain approvals for and commercialize any of its product candidates for muscular dystrophy patients or other patient populations; the timing, progress and results of clinical trials for EDG-5506 ; Edgewise's ability to raise any additional funding it will need to continue to pursue its business and product development plans; negative impacts of the COVID-19 pandemic on Edgewise's operations, including preclinical and clinical trials; the timing, scope and likelihood of regulatory filings and approvals; the potential for any clinical trial results to differ from preclinical, interim, preliminary, topline or expected results; Edgewise's ability to develop a proprietary drug discovery platform to build a pipeline of product candidates; Edgewise's ability to enroll and maintain patients in its ongoing and future clinical trials; Edgewise's manufacturing, commercialization and marketing capabilities and strategy; the size of the market opportunity for Edgewise's product candidates; the loss of key scientific or management personnel; competition in the industry in which Edgewise operates; Edgewise's reliance on third parties; Edgewise's ability to obtain and maintain intellectual property protection for its product candidates; general economic and market conditions; and other risks. Information regarding the foregoing and additional risks may be found in the section entitled "Risk Factors" in documents that Edgewise files from time to time with the Securities and Exchange Commission (the "SEC"). These forward-looking statements are made as of the date of this press release, and Edgewise assumes no obligation to update the forward-looking statements, or to update the reasons why actual results could differ from those projected in the forward-looking statements, except as required by law.

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