Harmony Biosciences Provides Update From Its Phase 3 RECONNECT Study of ZYN002 in Fragile X Syndrome

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PLYMOUTH MEETING, Pa.--(BUSINESS WIRE)--Sep. 24, 2025-- Harmony Biosciences Holdings, Inc. (Nasdaq: HRMY), today announced topline results from its Phase 3 registrational clinical trial (the RECONNECT Study) of ZYN002 in Fragile X syndrome (FXS). The RECONNECT Study did not meet the primary endpoint of improvement in social avoidance primarily due to a higher than expected placebo response rate.

Kumar Budur, M.D., M.S., Chief Medical and Scientific Officer at Harmony Biosciences said, “Although the study did not achieve its primary endpoint, the findings from this study provide valuable insights into Fragile X syndrome, a rare neurobehavioral condition with significant unmet medical need and no FDA-approved therapies. We will conduct a comprehensive analysis of the full dataset to better understand the results as part of our continued commitment to the Fragile X community.” Dr. Budur added, “We are grateful to the patients, families, caregivers, clinicians, and researchers who made this trial possible.”

The RECONNECT Study was a Phase 3 randomized, double-blind, placebo-controlled, multiple-center study, to assess the efficacy and safety of ZYN002, a pharmaceutically manufactured cannabidiol administered as a transdermal gel to patients with FXS ages 3 to under 30 years old.

“While these results are not what we anticipated, we remain confident in our ability to bring innovative therapies to patients while creating long-term value for shareholders,” said Jeffrey M. Dayno, M.D., President and CEO of Harmony Biosciences. “We have a late-stage, catalyst-rich pipeline with multiple Phase 3 programs in the clinic and continue to be on track to initiate our Phase 3 trials for pitolisant HD in narcolepsy and idiopathic hypersomnia in the fourth quarter of this year. Harmony’s unique profile as a profitable self-funding biotech company with strong cash-generation positions us well to drive future growth.”

About the RECONNECT Study

The RECONNECT Study was a randomized, double-blind, placebo-controlled, multiple-center study, to assess the efficacy and safety of ZYN002. A total of 215 male and female patients, ages 3 to < 30 years, were randomized 1:1 to receive study drug or placebo during an 18-week treatment period. Doses of treatments were weight-based. The primary endpoint for the RECONNECT Study was change from baseline to week 18 in the ABC-C_{FXS} Social Avoidance subscale score in patients with complete methylation (≥90%) in the *FMR1* gene. Key secondary endpoints included change from baseline to week 18 in the ABC-C_{FXS} Irritability subscale score in patients with complete methylation (≥90%) in the *FMR1* gene.

About ZYN002

ZYN002 is the first-and-only pharmaceutically manufactured synthetic cannabidiol devoid of THC and formulated as a patent-protected permeation-enhanced gel for transdermal delivery through the skin and into the circulatory system. The product is manufactured through a synthetic process in a cGMP facility and is not extracted from the cannabis plant. ZYN002 does not contain THC, the compound that causes the euphoric effect of cannabis, and has the potential to be a nonscheduled product if approved. Cannabidiol, the active ingredient in ZYN002, has been granted orphan drug designation by the United States Food and Drug Administration (FDA) and the European Medicines Agency (EMA) for the treatment of FXS and for the treatment of 22q. Additionally, ZYN002 has received FDA Fast Track designation for the treatment of behavioral symptoms in patients with FXS.

About Fragile X Syndrome

Fragile X syndrome (FXS) is a rare genetic disorder that is the leading known cause of both inherited intellectual disability and autism spectrum disorder. The disorder negatively affects synaptic function, plasticity and neuronal connections, and results in a spectrum of intellectual disabilities and behavioral symptoms, such as social avoidance and irritability. While the exact prevalence is unknown, upwards of 80,000 patients in the US and 121,000 patients in the European Union and the UK are believed to have FXS, based on FXS prevalence estimates of approximately 1 in 4,000 to 7,000 in males and approximately 1 in 8,000 to 11,000 in females. There is a significant unmet medical need in patients living with FXS as there are currently no FDA-approved treatments for this disorder.

FXS is caused by a mutation in *FMR1*, a gene which modulates a number of systems, including the endocannabinoid system, and most critically, codes for a protein called FMRP. The *FMR1* mutation manifests as multiple repeats of a DNA segment, known as the CGG triplet repeat, resulting in deficiency or lack of FMRP. FMRP helps regulate the production of other proteins and plays a role in the development of synapses, which are critical for relaying nerve impulses, and in regulating synaptic plasticity. In people

with full mutation of the *FMR1* gene, the CGG segment is repeated more than 200 times, and in most cases causes the gene to not function. Methylation of the *FMR1* gene also plays a role in determining functionality of the gene. In approximately 70% - 75% of patients with FXS, who have complete methylation of the *FMR1* gene, no FMRP is produced, resulting in dysregulation of the endocannabinoid system and severe neurobehavioral symptoms.

About Harmony Biosciences

Harmony Biosciences is a pharmaceutical company dedicated to developing and commercializing innovative therapies for patients with rare neurological diseases who have unmet medical needs. Driven by novel science, visionary thinking, and a commitment to those who feel overlooked, Harmony Biosciences is nurturing a future full of therapeutic possibilities that may enable patients with rare neurological diseases to truly thrive. Established by Paragon Biosciences, LLC, in 2017 and headquartered in Plymouth Meeting, Pa., we believe that when empathy and innovation meet, a better future can begin; a vision evident in the therapeutic innovations we advance, the culture we cultivate, and the community programs we foster. For more information, please visit www.harmonybiosciences.com.

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