Harmony Biosciences Presents Promising Open-Label Extension Data of ZYN002 in Fragile X Syndrome

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Data to be Presented at the Hot Topics in Child Neurology Podium Presentation Session at the American Academy of Neurology Annual Meeting

PLYMOUTH MEETING, Pa.--(BUSINESS WIRE)--Apr. 8, 2025-- Harmony Biosciences Holdings, Inc. (Nasdaq: HRMY) today announced the presentation of updated data from its Open-Label Extension (OLE) study (ZYN2-CL-017) evaluating the safety and effectiveness of ZYN002 in children, adolescents, and adults with Fragile X syndrome (FXS). The data showed clinically meaningful improvements in irritability-related symptoms prevalent in individuals with FXS. There are currently no U.S. Food & Drug Administration (FDA) approved treatments for FXS.

The data will be shared during a podium presentation at the American Academy of Neurology (AAN) 2025 Annual Meeting's "Hot Topics in Child Neurology" session on Tuesday, April 8, 2025, at 3:30 PM PT in San Diego, CA.

"The acceptance of our Fragile X syndrome OLE data as a podium presentation at AAN underlines the significant unmet need in FXS, and the potential for ZYN002 to become the first-and-only approved treatment for this condition," said Kumar Budur, MD, MS, Chief Medical and Scientific Officer at Harmony Biosciences. "These data are encouraging as we prepare for the topline data readout from our ongoing Phase 3 registrational trial, the RECONNECT study, in Q3 2025. Approximately 80,000 individuals are living with this rare neurological disease in the U.S. alone and Harmony is deeply committed to addressing the profound unmet medical needs of this community both in the U.S. and globally."

Participants entered the OLE trial from the Phase 2/3 CONNECT-FX trial, and the Phase 1/2 FAB-C signal detection open-label trial. Participants in the OLE trial demonstrated clinically meaningful improvements in behavioral symptoms as measured by the Aberrant Behavior Checklist – Community (ABC-C_{FXS} Irritability). This included participants who received active treatment in the double-blind, placebo-controlled CONNECT-FX trial, and those who transitioned from placebo to treatment in the OLE. More than 60% of participants in both groups achieved clinically meaningful improvement of at least 9 points on the ABC-C_{FXS} Irritability scores at two consecutive visits.

Additionally, 40.6% of participants who received active treatment in the CONNECT-FX trial were rated by their caregivers as demonstrating a clinically meaningful improvement in behavior based on the Caregiver Global Impression of Change (CaGI-C) scores, compared to 29.8% who received placebo in the CONNECT-FX trial. After three years, 73.3% of patients who continued on ZYN002, as well as 72% who transitioned from placebo to ZYN002, experienced clinically meaningful improvements.

Serious treatment-emergent adverse events were reported in 4.6% of patients in the OLE, with discontinuation occurring in 3.3% of patients. Treatment-related adverse events were observed in 12.9% of patients, none of which were serious, and the most common of these adverse events was pain at the treatment application site in 6.7% of patients.

The data presented at AAN covers the period from September 2018 to January 31, 2024, and included 240 patients administered ZYN002 at doses of 250, 500, or 750 mg per day based on their weight. The mean age of the patients was 9.7 years and ranged from 3 to 17 years.

ZYN002 is currently being evaluated as an investigational treatment for FXS in the RECONNECT study, a Phase 3 randomized, double-blind, placebo-controlled registrational trial evaluating the safety and efficacy of ZYN002 in patients with FXS ages 3 to under 30 years. ZYN002 is not approved by the FDA for the treatment of FXS.

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 22q11.2 deletion syndrome (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 inherited cause of both 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 U.S. 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 60% of patients with FXS, who have complete methylation of the FMR1 gene, no FMRP is produced, resulting in dysregulation of the systems modulated by FMRP.

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.

Forward-Looking Statements
This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this press release that do not relate to matters of historical fact should be considered forward-looking statements, including statements regarding our future results of operations and financial position, business strategy, products, prospective products, product approvals, the plans and objectives of management for future operations and future results of anticipated products. These statements are neither promises nor guarantees, but involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including, but not limited to, the following: the timing of, and our ability to obtain, regulatory approvals for our product candidates; our estimates regarding expenses, future revenue, capital requirements and additional financing needs; our ability to identify, acquire and integrate additional products or product candidates with significant commercial potential that are consistent with our commercial objectives; our commercialization, marketing and manufacturing capabilities and strategy; significant competition in our industry; our intellectual property position; loss or retirement of key members of management; failure to successfully execute our growth strategy, including any delays in our planned future growth; our failure to maintain effective internal controls; the impact of government laws and regulations; volatility and fluctuations in the price of our common stock; the significant costs and required management time as a result of operating as a public company; the fact that the price of Harmony's common stock may be volatile and fluctuate substantially; statements related to our intended share repurchases and repurchase timeframe and the significant costs and required management time as a result of operating as a public company. These and other important factors discussed under the caption "Risk Factors" in our Annual Report on Form 10-K filed with the Securities and Exchange Commission (the "SEC") on February 25, 2025, and our other filings with the SEC could cause actual results to differ materially from those indicated by the forward-looking statements made in this press release. Any such forward-looking statements represent management's estimates as of the date of this press release. While we may elect to update such forward-looking statements at some point in the future, we disclaim any obligation to do so, even if subsequent events cause our views to change.

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