HARMONY BIOSCIENCES PRESENTS NEW SECONDARY OUTCOME DATA FROM PHASE 2 SIGNAL DETECTION STUDY IN PATIENTS WITH PRADER-WILLI SYNDROME

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Data presented at 2023 Foundation for Prader-Willi Research Symposium and Family Conference

PLYMOUTH MEETING, Pa., Oct. 5, 2023 /PRNewswire/ -- Harmony Biosciences Holdings, Inc. ("Harmony" or the "Company") (Nasdaq: HRMY), a pharmaceutical company dedicated to developing and commercializing innovative therapies for patients with rare neurological diseases, today announced the presentation of new secondary endpoint data, including improvements in behavioral disturbances, from its Phase 2 signal-detection study evaluating pitolisant for the treatment of excessive daytime sleepiness (EDS) in Prader-Willi syndrome (PWS), at the 2023 Foundation for Prader-Willi Research (FPWR) Symposium and Family Conference. The company also announced that it anticipates initiating its Phase 3 registrational TEMPO study in Q4 2023.

The poster presentation of secondary outcomes data included improvements in behavioral symptoms (as measured by the Aberrant Behavioral Checklist-2), especially in the higher-dose pitolisant group. Reductions in the caregiver rating of EDS severity were also observed as were some improvements in hyperphagia, even though baseline hyperphagia scores were in the normal to mild range. The overall rate of adverse events was similar for pitolisant and placebo, and the safety/tolerability profile was consistent with the known profile for pitolisant.

"We recognize the urgency for innovative treatments that help alleviate the profound unmet medical needs of individuals with PWS and their dedicated caregivers," said Kumar Budur, MD, Chief Medical Officer at Harmony Biosciences. "This is particularly crucial given the absence of an FDA-approved treatment for EDS in PWS, coupled with the prevalent and severe behavioral symptoms associated with this condition. We are encouraged by these findings from our Phase 2 signal-detection study, which build upon the favorable primary study outcome and provide additional hope to this community as we pursue a potential new indication for pitolisant."

The results from the Phase 2 signal-detection study informed the protocol design for the upcoming Phase 3 registrational TEMPO study, a randomized, double-blind, placebo-controlled, multicenter, global clinical study that will further assess the safety and efficacy of pitolisant in patients with PWS, ages ≥ 6 years. This study is expected to be initiated in Q4 2023. There are currently 15,000 – 20,000 people in the US living with PWS. More than half of them experience EDS and the majority of them have behavioral disturbances.

Poster: Secondary Outcomes from a Phase 2, Double-Blind, Placebo-Controlled Signal-Detection, Proof-of-Concept Study of Pitolisant in Prader-Willi Syndrome

The Phase 2 clinical trial was a randomized, double-blind, placebo-controlled signal-detection, proof-of-concept study designed to assess the safety and efficacy of pitolisant in people living with PWS. In the trial, eligible patients who were genetically confirmed to have PWS and who had EDS were enrolled in an 11-week double-blind treatment phase that included a 3-week titration phase and eight weeks of stable dosing. Participants (n=65) were randomized (1:1:1) to receive lower- or higher-dose pitolisant, or a matching placebo based on age. Secondary/exploratory endpoints included change from baseline in Caregiver Global Impression of Severity (CaGI-S) for EDS; behavioral disturbance, as measured using the Aberrant Behavior Checklist-2 (ABC-2); and Hyperphagia, assessed using the Hyperphagia Questionnaire for Clinical Trials (HQ-CT) in conjunction with the Food Safe Zone Questionnaire.

This proof-of-concept study was not powered to demonstrate statistical significance and was designed for signal detection.

Key results include:

- Reductions in behavioral disturbances among the youngest age group (6 to <12 years) were observed across all ABC-2 domains especially in the higher-dose pitolisant group.

  Irritability: higher-dose, -5.5; lower-dose, -3.0; placebo, -1.5
  Social withdrawal: higher-dose, -4.9; lower-dose, -1.6; placebo, -3.1
  Hyperactivity/noncompliance: higher-dose, -4.6; lower-dose, -0.9; placebo, -3.0
  Inappropriate speech: higher-dose, -2.0; lower-dose, -0.4; placebo, -0.6
  Stereotypic behavior: higher-dose, -1.0; lower-dose, -0.2; placebo, -0.6

- Reductions in CaGI-S scores were greater for pitolisant compared with placebo in the children (higher-dose, -1.1; lower-dose, -1.0; placebo, -0.5) and adult (higher-dose, -1.0; lower-dose, -2.0; placebo, -0.7) age groups.

  A reduction of -1.0 or more was seen in the mean change from baseline to week 11 in the children and adult subgroups, meeting the clinical significance threshold per The American Academy of Sleep Medicine (AASM).

- Some improvements in hyperphagia were noted in children (higher-dose, -2.0; lower-dose, -2.5; placebo, 0.1) and adults (higher-dose, -3.4; lower-dose, -3.0; placebo, -1.7) even though baseline hyperphagia scores were in the normal/mild range.

  Despite the trial not enriching for hyperphagia and HQ-CT scores being relatively low at baseline, encouraging trends toward improvements were seen compared with placebo, especially in the children age group.

- There was an unusually large placebo response in the adolescent age group, due to data from a single outlier, resulting in an outsized impact on the magnitude of the placebo response not only in the adolescent age group but also in the overall study population.

Pitolisant is marketed as WAKIX® in the U.S. and is FDA approved to treat EDS or cataplexy in adult patients with narcolepsy. Pitolisant is not approved for use in patients with PWS and is currently being evaluated as an investigational agent in this patient population.

About Prader-Willi Syndrome
PWS is an orphan/rare, genetic neurological disorder with many of the symptoms resulting from hypothalamic dysfunction. The hypothalamus is the part of the brain that controls both sleep-wake state stability and signals that mediate the balance between hunger and satiety, resulting in two of the main symptoms in patients with PWS, EDS and hyperphagia (an intense persistent sensation of hunger accompanied by food preoccupations, an extreme drive to consume food, food-related behavior problems, and a lack of normal satiety). Other features include low muscle tone, short stature, behavioral problems, and cognitive impairment. Approximately 15,000 to 20,000 people in the U.S. live with PWS, and over half of them experience EDS and the majority of them have behavioral disturbances.

About WAKIX® (pitolisant) Tablets
WAKIX, a first-in-class medication, is approved by the U.S. Food and Drug Administration for the treatment of excessive daytime sleepiness or cataplexy in adult patients with narcolepsy and has been commercially available in the U.S. since Q4 2019. It was granted orphan drug designation for the treatment of narcolepsy in 2010, and breakthrough therapy designation for the treatment of cataplexy in 2018. WAKIX is a selective histamine 3 (H_3) receptor antagonist/inverse agonist. The mechanism of action of WAKIX is unclear; however, its efficacy could be mediated through its activity at H_3 receptors, thereby increasing the synthesis and release of histamine, a wake promoting neurotransmitter. WAKIX was designed and developed by Bioprojet (France). Harmony has an exclusive license from Bioprojet to develop, manufacture and commercialize pitolisant in the United States.

INDICATIONS AND USAGE
WAKIX is indicated for the treatment of excessive daytime sleepiness or cataplexy in adult patients with narcolepsy.

IMPORTANT SAFETY INFORMATION

Contraindications
WAKIX is contraindicated in patients with known hypersensitivity to pitolisant or any component of the formulation. Anaphylaxis

has been reported. WAKIX is also contraindicated in patients with severe hepatic impairment.

Warnings and Precautions
WAKIX prolongs the QT interval; avoid use of WAKIX in patients with known QT prolongation or in combination with other drugs known to prolong the QT interval. Avoid use in patients with a history of cardiac arrhythmias, as well as other circumstances that may increase the risk of the occurrence of torsade de pointes or sudden death, including symptomatic bradycardia, hypokalemia or hypomagnesemia, and the presence of congenital prolongation of the QT interval.

The risk of QT prolongation may be greater in patients with hepatic or renal impairment due to higher concentrations of pitolisant; monitor these patients for increased QTc. Dosage modification is recommended in patients with moderate hepatic impairment and moderate or severe renal impairment (see full prescribing information). WAKIX is not recommended in patients with end-stage renal disease (ESRD).

Adverse Reactions
In the placebo-controlled clinical trials conducted in patients with narcolepsy with or without cataplexy, the most common adverse reactions (≥5% and at least twice placebo) for WAKIX were insomnia (6%), nausea (6%), and anxiety (5%). Other adverse reactions that occurred at ≥2% and more frequently than in patients treated with placebo included headache, upper respiratory tract infection, musculoskeletal pain, heart rate increased, hallucinations, irritability, abdominal pain, sleep disturbance, decreased appetite, cataplexy, dry mouth, and rash.

Drug Interactions
Concomitant administration of WAKIX with strong CYP2D6 inhibitors increases pitolisant exposure by 2.2-fold. Reduce the dose of WAKIX by half.

Concomitant use of WAKIX with strong CYP3A4 inducers decreases exposure of pitolisant by 50%. Dosage adjustments may be required (see full prescribing information).

H1 receptor antagonists that cross the blood-brain barrier may reduce the effectiveness of WAKIX. Patients should avoid centrally acting H1 receptor antagonists.

WAKIX is a borderline/weak inducer of CYP3A4. Therefore, reduced effectiveness of sensitive CYP3A4 substrates may occur when used concomitantly with WAKIX. The effectiveness of hormonal contraceptives may be reduced when used with WAKIX and effectiveness may be reduced for 21 days after discontinuation of therapy.

Use in Specific Populations
WAKIX may reduce the effectiveness of hormonal contraceptives. Patients using hormonal contraception should be advised to use an alternative non-hormonal contraceptive method during treatment with WAKIX and for at least 21 days after discontinuing treatment.

There is a pregnancy exposure registry that monitors pregnancy outcomes in women who are exposed to WAKIX during pregnancy. Patients should be encouraged to enroll in the WAKIX pregnancy registry if they become pregnant. To enroll or obtain information from the registry, patients can call 1-800-833-7460. The safety and effectiveness of WAKIX have not been established in patients less than 18 years of age.

WAKIX is extensively metabolized by the liver. WAKIX is contraindicated in patients with severe hepatic impairment. Dosage adjustment is required in patients with moderate hepatic impairment.

WAKIX is not recommended in patients with end-stage renal disease. Dosage adjustment of WAKIX is recommended in patients with moderate or severe renal impairment.

Dosage reduction is recommended in patients known to be poor CYP2D6 metabolizers; these patients have higher concentrations of WAKIX than normal CYP2D6 metabolizers.

Please see the **Full Prescribing Information** for WAKIX for more information.

To report suspected adverse reactions, contact Harmony Biosciences at 1-800-833-7460 or the FDA at 1-800-FDA-1088 or **www.fda.gov/medwatch**.

About Harmony Biosciences
At Harmony Biosciences, we specialize in developing and delivering treatments for rare neurological diseases that others often overlook. We believe that where empathy and innovation meet, a better life can begin for people living with neurological diseases. Established by Paragon Biosciences, LLC, in 2017 and headquartered in Plymouth Meeting, PA, our team of experts from a wide variety of disciplines and experiences is driven by our shared conviction that innovative science translates into therapeutic possibilities for our patients, who are at the heart of everything we do. For more information, please visit www.harmonybiosciences.com.

Forward Looking Statement

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 product WAKIX. 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: our commercialization efforts and strategy for WAKIX; the rate and degree of market acceptance and clinical utility of WAKIX, pitolisant in additional indications, if approved, and any other product candidates we may develop or acquire, if approved; our research and development plans, including our development activities with Bioprojet, and plans to explore the therapeutic potential of pitolisant in additional indications; our ongoing and planned clinical trials; the availability of favorable insurance coverage and reimbursement for WAKIX; the timing of and our ability to obtain regulatory approvals for pitolisant for other indications as well as any of our product candidates, including those we are developing with Bioprojet; our failure to achieve the potential benefits of the 2022 LCA with Bioprojet; our estimates regarding expenses, future revenue, capital requirements and needs for additional financing; our ability to identify 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 21, 2023, 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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