HARMONY BIOSCIENCES ANNOUNCES TOPLINE RESULTS FROM PHASE 2 PROOF-OF-CONCEPT STUDY EVALUATING PITOLISANT FOR EXCESSIVE DAYTIME SLEEPINESS IN PATIENTS WITH PRADER-WILLI SYNDROME

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Topline data show positive signal in treating excessive daytime sleepiness

PLYMOUTH MEETING, Pa., Nov. 1, 2022 /PRNewswire/ -- Harmony Biosciences Holdings, Inc. ("Harmony") (Nasdaq: HRMY), a pharmaceutical company dedicated to developing and commercializing innovative therapies for patients with rare neurological diseases, today announced initial topline results from its Phase 2 proof-of-concept study in patients with Prader-Willi syndrome (PWS), which showed a positive signal on improvement in the primary outcome related to excessive daytime sleepiness (EDS).

The Phase 2 clinical trial was a randomized, double-blind, placebo-controlled study designed to assess the safety and efficacy of pitolisant in patients with PWS. This proof-of-concept study was not powered to demonstrate statistical significance and was designed for signal detection. The study included patients ages 6 to 65 years and patients were randomized 1:1:1 to low dose pitolisant, high dose pitolisant, or placebo treatment groups. Pitolisant dosing was based on three age cohorts (children 6 to < 12; adolescents 12 to < 18; and adults 18 to 65) and another objective of the study was to evaluate for a dose-response to pitolisant in patients with PWS. The primary endpoint of this study was the evaluation of EDS as measured by change from baseline to end of treatment (EOT) on the Epworth Sleepiness Scale for Children and Adolescents (ESS-CHAD) Parent/Caregiver Version.

Topline study results include:

- 65 patients were enrolled in the trial; 91% completed treatment and all but one patient opted to continue into the open-label extension
- Mean baseline ESS-CHAD (Parent/Caregiver Version) ranged from 14.7 to 15.7
- Mean change from baseline to EOT on the ESS-CHAD Parent/Caregiver Version scores ranged from -3.7 to -5.5 across all age groups and treatment groups, representing a clinically meaningful change (which is defined as a ≥ 2-point improvement on this scale)
- In two of the three age groups (children and adults), there was a clinically meaningful difference (minimum of 2 points) between pitolisant and placebo, driven by the high dose pitolisant treatment group

  In the adolescent age group, there was a high placebo response of a magnitude three times that seen in the other two age groups, which resulted in no clinically meaningful difference between pitolisant and placebo in this age group

- A responder analysis (defined as an improvement on the ESS-CHAD Parent/Caregiver Version of ≥ 3-points or a

score at EOT of ≤10 for this analysis) showed response rates of 70% in the high dose pitolisant group, 55.6% in the low dose pitolisant group, and 52.6% in the placebo group
- Overall safety/tolerability profile was consistent with the known safety/tolerability profile of pitolisant

  Adverse events were reported in 57% of patients on pitolisant and 65% of patients on placebo
  Treatment-related adverse events were reported in 26% of patients on pitolisant and 30% of patients on placebo
  There was one serious adverse event in a patient in the placebo treatment group

These results represent the initial topline data with the full data set expected before the end of the year. The full data set will include the results on the secondary outcomes, including caregiver and clinician global impression scores, as well as measurements of behavioral symptoms, cognitive function, and hyperphagia. The full results will be presented at a future medical meeting and submitted for publication in a scientific journal.

"The positive signals observed on the primary outcome of EDS from this proof-of-concept study are encouraging," said Jeffrey M. Dayno, M.D., Chief Medical Officer at Harmony. "We look forward to receiving the full data set from this initial signal detection study which will further inform our understanding of the data as we plan to advance our clinical development program for pitolisant in PWS. In the meantime, I want to thank our clinical investigators and their teams, who partnered with us in the conduct of this trial, as well as the patients with PWS and their families who participated in the trial, for whom we are grateful."

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.

"Our organizations support and encourage research that can potentially help reduce the symptom burden for people living with PWS. We are pleased the results of this trial were clinically important and that Harmony intends to continue to study pitolisant in people with PWS, which may bring us one step closer to finding an important therapeutic advancement for a community with such limited treatment options," said Susan Hedstrom, Executive Director, Foundation for Prader-Willi Research and Paige Rivard, Chief Executive Officer, Prader-Willi Syndrome Association USA in a joint statement.

Pitolisant is marketed as WAKIX® in the U.S. and is FDA approved to treat excessive daytime sleepiness or cataplexy in adults 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 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.

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 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 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 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 and our 2022 LCA with Bioprojet. 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 impact of the COVID-19 pandemic, including any current and future variants; 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 under our 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; 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 28, 2022, 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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