HARMONY BIOSCIENCES PRESENTS POST-HOC ANALYSIS OF WAKIX® (PITOLISANT) PIVOTAL DATA IN ADULTS WITH HIGH BURDEN OF NARCOLEPSY SYMPTOMS

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PLYMOUTH MEETING, Pa., June 6, 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 results of a post-hoc analysis from the pivotal data evaluating the clinical impact of WAKIX® (pitolisant) on the reduction of excessive daytime sleepiness (EDS) and cataplexy in adults with a high burden of narcolepsy symptoms. The analysis was presented as a poster at the 36th Annual Meeting of the Associated Professional Sleep Societies (APSS), known as "SLEEP 2022," held in Charlotte, NC June 4-8.

"The results from this post-hoc analysis of data from randomized, controlled trials in the clinical development program for WAKIX presented at SLEEP 2022 reinforce the clinical effectiveness of WAKIX in patients with a high burden of narcolepsy symptoms," said Harmony's Chief Medical Officer, Jeffrey Dayno, M.D. "Clinical impact, quantified through effect size metrics, lends another perspective on the efficacy profile of WAKIX, especially when assessed in patients with high symptom burden."

Clinical Impact of Pitolisant on Excessive Daytime Sleepiness and Cataplexy in Adults with High Burden of Narcolepsy Symptoms

The poster presents a post-hoc analysis of pooled data from patients in the pivotal clinical trials with WAKIX who had a high burden of EDS and cataplexy. The data were pooled from HARMONY 1 and HARMONY CTP, two randomized, placebo-controlled seven- and eight-week studies in adult patients with narcolepsy from the clinical development program for WAKIX. Patients enrolled in the trial were individually titrated over a three-week period, with a potential maximum dose of 35.6mg/day, after which the dose remained stable. Three independent patient subgroups were analyzed based on the following criteria for high burden of narcolepsy symptoms:

- High burden of EDS as defined by an Epworth Sleepiness Scale (ESS) baseline score ≥16 (n = 118; pitolisant, n = 60; placebo, n = 58);
- High burden of EDS as defined by a sleep latency at baseline ≤8 minutes on the Maintenance of Wakefulness Test (MWT) (n = 105; pitolisant, n = 59; placebo, n = 46); and,
- High burden of cataplexy as defined by a baseline frequency of ≥15 cataplexy attacks per week (n = 31; pitolisant, n = 20; placebo, n = 11).

The clinical impact of a treatment can be quantified using effect size metrics, including Cohen's *d* (the standardized drug-placebo difference for an effect) and number needed to treat (NNT; number of patients that need to be treated with study medication instead of placebo to achieve a specific outcome for one additional person). Change from baseline to the end of treatment was evaluated for pitolisant compared with placebo in each patient subgroup using these effect size metrics and generated the following results:

- Cohen's *d* effect size values for pitolisant versus placebo were 0.80 for ESS, 0.31 for MWT, and 1.31 for weekly rate of cataplexy (WRC);

- NNT for pitolisant for improvement in EDS, as defined as a ≥3-point decrease from baseline on the ESS or final score ≤10, was 3;
- NNT for pitolisant for improvement in cataplexy, as defined by a reduction in WRC ≥50% decrease from baseline, was 2; and,
- For clinician ratings of "much" or "very much" improved on the clinical global impression of change (CGI-C) assessment, NNT was 5 in the ESS subgroup, 4 in the MWT subgroup, and 3 in the WRC subgroup.

About Narcolepsy
Narcolepsy is a rare, chronic, debilitating neurological disease of sleep-wake state instability that impacts approximately 165,000 Americans and is primarily characterized by excessive daytime sleepiness (EDS) and cataplexy – its two cardinal symptoms – along with other manifestations of REM sleep dysregulation (hallucinations and sleep paralysis), which intrude into wakefulness. EDS is the inability to stay awake and alert during the day and is the symptom that is present in all people living with narcolepsy. In most patients, narcolepsy is caused by the loss of hypocretin/orexin, a neuropeptide in the brain that supports sleep-wake state stability. This disease affects men and women equally, with typical symptom onset in adolescence or young adulthood; however, it can take up to a decade to be properly diagnosed.

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 (H3) receptor antagonist/inverse agonist. The mechanism of action of WAKIX is unclear; however, its efficacy could be mediated through its activity at H3 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 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. 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 plans to explore the therapeutic potential of pitolisant in additional indications; our ongoing and planned clinical trials; our ability to expand the scope of our license agreement with Bioprojet; 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 other product candidates; 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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