HARMONY BIOSCIENCES RECEIVES U.S. FOOD AND DRUG ADMINISTRATION APPROVAL FOR WAKIX® (PITOLISANT) IN PEDIATRIC PATIENTS WITH NARCOLEPSY

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WAKIX is the first-and-only FDA-approved non-scheduled treatment option for excessive daytime sleepiness in pediatric patients 6 years of age and older with narcolepsy

FDA granted priority review of the sNDA in February 2024

PLYMOUTH MEETING, Pa., June 24, 2024 /PRNewswire/ -- Harmony Biosciences (Nasdaq: HRMY) today announced that the U.S. Food and Drug Administration (FDA) has approved its supplemental New Drug Application (sNDA) for WAKIX® (pitolisant) tablets for the treatment of excessive daytime sleepiness (EDS) in pediatric patients 6 years of age and older with narcolepsy. The FDA separated the submission into two sNDAs for administrative purposes to issue an approval for the treatment of EDS and a complete response for the treatment of cataplexy in pediatric patients (6 to <18 years of age) with narcolepsy.

The FDA granted priority review of the sNDA based on a Phase 3 study conducted by Bioprojet, which evaluated the safety and efficacy of pitolisant in patients ages 6 to under 18 years with narcolepsy, with or without cataplexy. Based on the results of this study, Bioprojet received approval from the European Medicines Agency last year extending the indication for WAKIX to include the treatment of narcolepsy in children ages 6 years of age and older, with or without cataplexy.

"Following the FDA's decision to grant priority review, we are very pleased with the Agency's timely review and approval of WAKIX for pediatric narcolepsy patients with excessive daytime sleepiness," said Jeffrey M. Dayno, M.D., President and Chief Executive Officer of Harmony Biosciences. "EDS is the primary symptom experienced by all patients with narcolepsy and this approval for WAKIX, as the first-and-only FDA-approved non-scheduled treatment option for narcolepsy, makes this important treatment option available to pediatric patients 6 years and older living with narcolepsy."

WAKIX was first approved by the FDA in August 2019 for the treatment of EDS in adult patients with narcolepsy, followed by FDA approval for the treatment of cataplexy in adult patients with narcolepsy in October 2020. A first-in-class treatment with a novel mechanism of action, WAKIX functions as a selective histamine 3 (H_3) receptor antagonist/inverse agonist that is believed to target the histamine system to promote wakefulness.

Dayno added, "The unique mechanism of action of WAKIX and its non-scheduled status are especially important for a pediatric population that has had limited treatment options, all of which are controlled substances. The unique features of pitolisant present an exciting opportunity, and we are currently working on the next-generation formulations that could potentially offer additional benefits to patients, such as greater efficacy and new indications, extend the WAKIX franchise, and strengthen our leadership position in the treatment of rare sleep disorders."

"We plan to discuss with the Agency a path forward for a cataplexy indication in pediatric narcolepsy patients based on the strength of the existing data from Bioprojet's Phase 3 trial," said Kumar Budur, M.D., M.S., Chief Medical and Scientific Officer of Harmony Biosciences. "We appreciate the FDA's recognition of the unmet medical need in this patient population and their approval of the EDS indication, making WAKIX available to every appropriate pediatric patient 6 years and older living with narcolepsy."

"As a parent of a son who was diagnosed with narcolepsy in childhood, who continues to work in advocacy for all people living with narcolepsy of all ages, I applaud the FDA for approving WAKIX in pediatric patients 6 years of age and older," said Monica Gow, Co-Founder and Executive Director of Wake Up Narcolepsy. "This new approval offers a promising non-scheduled treatment option for children with narcolepsy, marking an important step

forward in addressing the unmet medical needs of these children."

About Narcolepsy
Narcolepsy is a rare, chronic, debilitating neurological disease of sleep-wake state instability that impacts approximately 170,000 Americans and is primarily characterized by its cardinal symptom excessive daytime sleepiness (EDS), with or without cataplexy – 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 (EDS) or cataplexy in adult patients with narcolepsy and for the treatment of EDS in pediatric patients 6 years of age and older with narcolepsy. 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 (EDS) or cataplexy in adult patients with narcolepsy and for the treatment of excessive daytime sleepiness (EDS) in pediatric patients 6 years of age and older 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. WAKIX is contraindicated in patients with severe hepatic impairment and not recommended in patients with end-stage renal disease (ESRD).

Adverse Reactions
In the placebo-controlled clinical trials conducted in adult 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.

In the placebo-controlled phase of the clinical trial conducted in pediatric patients 6 years and older with narcolepsy with or without cataplexy, the most common adverse reactions (≥5% and greater than placebo) for WAKIX were headache (19%) and insomnia (7%). The overall adverse reaction profile of WAKIX in the pediatric clinical trial was similar to that seen in the adult clinical trial program.

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.

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. WAKIX may reduce the effectiveness of sensitive CYP3A4 substrates, including 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.

Use in Specific Populations
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 for treatment of excessive daytime sleepiness in pediatric patients less than 6 years of age with narcolepsy.

The safety and effectiveness of WAKIX have not been established for treatment of cataplexy in pediatric patients with narcolepsy.

WAKIX is extensively metabolized by the liver. WAKIX is contraindicated in patients with severe hepatic impairment. Dosage adjustment is recommended 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 eGFR <60

mL/minute/1.73 m^2.

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 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 agreements with Bioprojet Société Civile de Recherche ("Bioprojet"); 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 other 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 22, 2024, 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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