HARMONY BIOSCIENCES ANNOUNCES EXCLUSIVE AGREEMENT TO DEVELOP AND COMMERCIALIZE TPM-1116, A HIGHLY POTENT AND SELECTIVE ORAL OREXIN-2 RECEPTOR AGONIST

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TPM-1116 preclinical data suggest a potential best-in-class profile that could transform the treatment of narcolepsy and other sleep/wake disorders

Expands Harmony's innovative neuroscience pipeline and strengthens its leadership position in sleep medicine

PLYMOUTH MEETING, Pa., April 11, 2024 /PRNewswire/ -- Harmony Biosciences Holdings, Inc. (Nasdaq: HRMY) today announced an exclusive licensing agreement with Bioprojet to develop, manufacture and commercialize TPM-1116, a highly potent and selective oral orexin-2 receptor (OX2R) agonist that will be evaluated for the treatment of narcolepsy and other sleep/wake disorders. TPM-1116 represents a new chemical series of OX2R agonists with the potential for a best-in-class clinical profile.

Narcolepsy and other hypersomnolence disorders continue to be a large market opportunity with significant unmet medical need. The agreement will accelerate the development of this orexin-2 receptor agonist and is expected to further Harmony's leadership in the sleep/wake space, reinforcing its commitment to advancing innovative treatments for patients living with unmet medical needs, according to Jeffrey M. Dayno, M.D., Harmony Biosciences President and CEO.

"Orexin agonism is an exciting area of sleep disorder research and represents the next novel mechanism of action for the treatment of narcolepsy since the launch of WAKIX. We also see potential synergies between TPM-1116 and our lead product, WAKIX, and new formulations of pitolisant, because of the interplay between histamine and orexin in the hypothalamus," Dayno said. "We believe TPM-1116, a new chemical series of orexin 2 agonist, could emerge with a potential best-in-class clinical profile based on its potency and selectivity, along with its strong preclinical safety profile and potential for once daily dosing. We look forward to working with Bioprojet and advancing the development program for TPM-1116 as part of our growth strategy."

"We are pleased that this new project to develop a potentially best-in-class orexin-2 receptor agonist will extend the productive collaboration between Bioprojet and Harmony in the field of sleep medicine beyond the successful commercialization of WAKIX in narcolepsy and the discovery of novel formulations of pitolisant to extend the pitolisant franchise," said Professor Jean-Charles Schwartz, Co-Founder of Bioprojet and member of the French and European Academies of Science.

Under the agreement, Harmony will pay Bioprojet an upfront license fee of $25.5 million for the exclusive right to develop, manufacture and commercialize TPM-1116 in the U.S. and Latin American territories. In addition, Harmony is obligated to pay up to $127.5 million upon achievement of development and regulatory milestones and up to $240 million upon achievement of sales-based milestones. Finally, Harmony will pay a royalty rate in the mid-teens on sales of product in the licensed territories.

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.

About Bioprojet
Bioprojet is a pharmaceutical company headquartered in Paris, France. Its activity is focused on the design, synthesis and development of novel classes of drugs for unmet medical needs, such as Pitolisant (Wakix®). Bioprojet is commercially active in 7 western European countries through its own organization and commercially covering the rest of the world through distributors and licensees.

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**.

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 product WAKIX and our license for TPM-1116. 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 regarding pitolisant and TPM-1116; our ongoing and planned clinical trials; our commercialization, marketing and manufacturing capabilities and strategy; and failure to successfully execute our strategy, including any delays in our planned future growth. 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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