HARMONY BIOSCIENCES PRESENTS POSITIVE DATA FOR PITOLISANT IN THE TREATMENT OF EXCESSIVE DAYTIME SLEEPINESS AND FATIGUE IN MYOTONIC DYSTROPHY TYPE 1

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Phase 2 signal detection study presented at the annual meeting of the Associated Professional Sleep Societies, "SLEEP 2024"

PLYMOUTH MEETING, Pa., June 5, 2024 /PRNewswire/ -- Harmony Biosciences (Nasdaq: HRMY) presented data from its Phase 2 signal detection study showing that pitolisant reduced excessive daytime sleepiness (EDS) and fatigue in adults with Myotonic dystrophy Type 1 (DM1).

"More than 80 percent of DM1 patients experience EDS and fatigue, which patient-reported outcomes research has shown to be nearly as debilitating as the primary symptoms of DM1, namely myotonia and muscle weakness,"[1] said Kumar Budur, M.D., M.S., Chief Medical and Scientific Officer of Harmony Biosciences. "The findings from our signal detection study evaluating pitolisant, which is believed to promote wakefulness through histamine, present an exciting opportunity to develop new treatments for EDS and fatigue in DM1, narcolepsy, and the other sleep/wake disorders we are investigating through our lifecycle management programs that will involve Next-Generation formulations of pitolisant."

Notably, there was greater mean improvement from baseline to Week 11 in both EDS (as measured by the Daytime Sleepiness Scale) and fatigue (as measured by the Fatigue Severity Scale) compared to placebo. The overall disease burden also signaled greater improvement for pitolisant compared to placebo, with the higher dose pitolisant group showing a stronger efficacy signal. This study was designed for signal detection and was not powered to demonstrate statistical significance.

Estimates suggest there are 40,000 people currently diagnosed with DM1 in the U.S. with up to 90% of them reporting EDS and fatigue.

"Given the potential opportunity of pitolisant for treating EDS and fatigue in patients with DM1, we plan to progress our DM1 development program through a pivotal Phase 3 study using the Next-Generation 2 (NG2) formulation of pitolisant, which is designed to deliver an optimized pharmacokinetic profile and higher dosage strength," Budur added. "The NG2 formulation could be promising given the positive findings we observed across the EDS and fatigue endpoints within the higher dose pitolisant treatment arm. These efforts are integral to our broader life cycle management programs, which, if successful, could benefit over 100,000 patients living with unmet medical needs."

Poster 378: Primary Efficacy and Safety Results of a Phase 2, Double-Blind, Placebo-Controlled, Proof of Concept, Signal Detection Study of Pitolisant in Myotonic Dystrophy

The Phase 2 signal detection study was a randomized, double-blind, placebo-controlled study designed to evaluate the efficacy and safety of pitolisant in the treatment of EDS and other non-muscular symptoms in adults with DM1. Eligible patients were confirmed to have DM1 and enrolled in an 11-week double-blind treatment phase that included a 3-week titration period and an 8-week stable dose period. Participants were randomized to receive higher or lower dose pitolisant, or a matching placebo.

The primary efficacy endpoint was the change from baseline to Week 11 in Daytime Sleepiness Scale score. Additional efficacy endpoints included the change from baseline to Week 11 in Epworth Sleepiness Scale score, Fatigue Severity Scale score, Clinical Global Impression of Severity (for EDS) score, and Myotonic Dystrophy Health Index score.

Results from the study include:

- Mean improvement on the Daytime Sleepiness Scale (primary endpoint) was greater for pitolisant. Compared with placebo, a dose-response relationship was observed from baseline to Week 11:
    - Higher Dose Pitolisant (n=8): -2.5
    - Lower Dose Pitolisant (n=8): -1.0
    - Placebo (n=9): -0.2

- Mean improvement on the other secondary efficacy endpoints (EDS, fatigue, disease burden) was also greater for pitolisant versus placebo, with higher dose pitolisant showing a stronger efficacy signal from baseline to Week 11.
    - Epworth Sleepiness Scale:
        - Higher Dose Pitolisant (n=8): -4.9
        - Lower Dose Pitolisant (n=9): 1.3
        - Placebo (n=10): -0.1
    - Fatigue Severity Scale:
        - Higher Dose Pitolisant (n=8): -0.9
        - Lower Dose Pitolisant (n=9): -0.4
        - Placebo (n=10): -0.1
    - Clinical Global Impression of Severity (for EDS):
        - Higher Dose Pitolisant (n=8): -0.9
        - Lower Dose Pitolisant (n=9): -0.2
        - Placebo (n=10): -0.1
    - Myotonic Dystrophy Health Index
        - Higher Dose Pitolisant (n=8): -9.1
        - Lower Dose Pitolisant (n=9): -2.9
        - Placebo (n=10): 0.4

- The rate of adverse events was similar for pitolisant and placebo. The safety and tolerability of pitolisant in patients with DM1 were consistent with its known safety profile.

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 DM1 and is currently being evaluated as an investigational agent in this patient population.

[1] Heatwole C, Bode R, Johnson N, et al. Patient-reported impact of symptoms in myotonic dystrophy type 1 (PRISM-1). Neurology. 2012; 79(4):348-57. Erratum in: Neurology. 2012; 79(13):1411.

About Myotonic Dystrophy Type 1
Myotonic dystrophy Type 1 (DM1) is the most common form of adult-onset muscular dystrophy. It is a genetic disorder inherited in an autosomal-dominant pattern. Latest estimates suggest a prevalence of about one per 2,100 people with the genetic defect for DM1. This equates to about 150,000 people in the U.S. with the genetic defect for DM1.

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 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 full year 2024 net product revenue, expectations for the growth and value of WAKIX, plans to submit an sNDA for pitolisant in idiopathic hypersomnia; our future results of operations and financial position, business strategy, products, prospective products, product approvals, the plans and objectives of management for future operations and future results of anticipated products. 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 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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