HARMONY BIOSCIENCES ACKNOWLEDGES U.S. FOOD & DRUG ADMINISTRATION (FDA) ACTION DENYING THE CITIZEN PETITION FOR WAKIX® (PITOLISANT)

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FDA confirms the favorable benefit-risk profile of WAKIX

Harmony Biosciences focused on continuing to advance its pipeline assets across three rare CNS franchises; anticipates at least one new product or indication launch annually over the next five years

PLYMOUTH MEETING, Pa., June 25, 2024 /PRNewswire/ -- Harmony Biosciences Holdings, Inc. (Nasdaq: HRMY), today announced that the U.S. Food and Drug Administration denied the Citizen Petition filed by a short seller claiming that WAKIX is not safe and effective for the treatment of excessive daytime sleepiness (EDS) and cataplexy in adults with narcolepsy. The Agency's decision to reject the Petition was anticipated and confirms the Company's long-held position that the allegations in the Petition were unfounded and without merit.

In its denial, the FDA rejected all three requests from the Petitioner including withdrawal for all indications, immediate alert distribution ('Dear HCP Letter') to prescribers, and transitioning to a Compassionate Use Program with a REMS protocol, and stated "the FDA determined that WAKIX has a favorable benefit-risk profile under its approved conditions of use, and your Petition did not provide information that changes that assessment."[1]

The FDA denied the Petition after approving the supplemental New Drug Application (sNDA) for WAKIX on June 21, 2024, which expanded the indication for WAKIX to include the treatment of EDS in pediatric patients 6 years of age and older with narcolepsy. The denial letter states, "the FDA has carefully considered the information submitted in the Petition, other data available to the Agency, and relevant published literature. Based on our review of these materials and for the reasons stated, the Petition is denied."[2]

Harmony Biosciences stated:

> "We are pleased with the FDA's decision to deny the short seller Petition filed in March 2023, which tried to cast doubt on a safe and effective treatment while deliberately attempting to impact our stock price for profit. We appreciate the Agency's careful review of the unfounded claims in the Petition and its definitive action to deny the claims and resolve any potential doubt about the favorable benefit-risk profile of WAKIX.
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> Looking ahead, we confirm our outlook that WAKIX represents a billion-dollar plus market opportunity in adult narcolepsy alone, and we are well on our way to achieving further growth in the pitolisant franchise. We are also on track toward filing an sNDA for WAKIX in idiopathic hypersomnia later this year (2H 2024). In anticipation of the confirmation of the favorable benefit-risk profile of WAKIX, we have already been working on the next-generation formulations of pitolisant to address unmet medical needs. These formulations are designed to provide meaningful improvement, such as an enhanced pharmacokinetic (PK) profile and higher dosage range to drive greater efficacy. These innovations are expected to generate new IP to extend the pitolisant franchise out beyond 2040.
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> Beyond WAKIX, we have expanded our pipeline and diversified our portfolio resulting in three promising orphan rare CNS franchises in advanced stages of development, each with the potential to generate $1 billion to $2 billion in peak sales. These franchises are protected by patents extending into the late 2030s to mid-2040s. As we continue to execute our growth strategy, we are now poised to lead as a patient-centered CNS biotechnology company, providing innovative treatments for patients with unmet medical needs while driving substantial and durable value creation. Our pipeline consists of eight assets being studied across 13 development programs within these three CNS franchises.

Three of our development programs are in Phase 3 trials and we have two Phase 3 ready assets that we are working on. With this late-stage pipeline, we anticipate launching at least one new product or indication annually over the next five years and have the potential to bring new treatment options to hundreds of thousands of people living with rare diseases."

The FDA's detailed response letter can be found at the following link: https://downloads.regulations.gov/FDA-2023-P-1273-0005/attachment_1.pdf.

[1] FDA Response Letter, Docket No: FDA-2023-P-1273, Page 12, Paragraph 3, Sentence 3.

[2] FDA Response Letter, Docket No: FDA-2023-P-1273, Page 1, Paragraph 3, Sentence 1-2.

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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