



## HARMONY BIOSCIENCES INITIATES PHASE 3 TRIAL OF PITOLISANT IN ADULT PATIENTS WITH IDIOPATHIC HYPERSOMNIA

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PLYMOUTH MEETING, Pa., April 27, 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 the initiation of its Phase 3 trial evaluating the efficacy and safety of pitolisant in adult patients with idiopathic hypersomnia (IH), known as the INTUNE study.



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"There has been much interest by both the patient community and healthcare professionals in pitolisant for the treatment of IH and we are excited about the initiation of our Phase 3 INTUNE study in adult patients with this rare neurological disorder," said Harmony's Chief Medical Officer, Jeffrey Dayno, M.D. "Given the novel mechanism of action of pitolisant, which works through histamine, an important wake-promoting neurotransmitter in the brain, we are looking to translate innovative science into therapeutic possibilities that have the potential to improve the health of people living with IH."

IH is a rare and chronic neurological disease that is characterized by excessive daytime sleepiness (EDS) despite sufficient or even long sleep time. People living with IH experience significant EDS along with the symptoms of sleep inertia (prolonged difficulty waking up from sleep) and 'brain fog' (impaired cognition, attention, and alertness). Based on insurance claims data, the number of patients diagnosed with IH in the U.S. ranges from 30,000 – 40,000.

"We are excited to initiate this Phase 3 trial and we are hopeful these efforts, if successful, will lead to Harmony seeking U.S. regulatory approval for the next indication for WAKIX<sup>®</sup>," said John C. Jacobs, President and Chief Executive Officer of Harmony Biosciences. "Patient needs drive our team's drug development efforts and with this in mind, it is our goal to bring WAKIX forward to help the IH patient community as we have done for patients who are living with narcolepsy."

The INTUNE study is a double-blind, placebo-controlled, randomized withdrawal study in approximately 200 IH patients which will be conducted at 60 to 80 clinical trial sites across the U.S. The primary objective is to evaluate the efficacy and safety of pitolisant compared with placebo in treating EDS in adult patients with IH. Secondary objectives of the study include the impact of pitolisant on other important symptoms of IH, such as sleep inertia and cognitive impairment. Other outcomes, including patient impression of overall change in symptoms, investigator assessment of overall disease severity, and functional status will also be evaluated in the study.

"Our mission and values are centered around both supporting people with hypersomnias like IH and scientific discovery. We are excited Harmony is moving forward with a Phase 3 clinical trial in people with idiopathic hypersomnia, which may bring us one step closer to finding an important therapeutic advancement for a community with limited treatment options," said David Burley, Board Chair at the Hypersomnia Foundation.

Pitolisant is marketed as WAKIX® in the U.S. for the treatment of EDS or cataplexy in adult patients with narcolepsy.

### **About Idiopathic Hypersomnia**

Idiopathic Hypersomnia (IH) is a rare and chronic neurological disease that is characterized by excessive daytime sleepiness (EDS) despite sufficient or even long sleep time. EDS in IH cannot be alleviated by naps, longer sleep or more efficient sleep. People living with IH experience significant EDS along with the symptoms of sleep inertia (prolonged difficulty waking up from sleep) and 'brain fog' (impaired cognition, attention, and alertness). The cause of IH is unknown, but it is likely due to alterations in areas of the brain that stabilize states of sleep and wakefulness. IH is one of the central disorders of hypersomnolence and, like narcolepsy, is a debilitating sleep disorder that can result in significant disruption in daily functioning.

### **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 ( $\geq 5\%$  and twice placebo) for WAKIX were insomnia (6%), nausea (6%), and anxiety (5%). Other adverse reactions that occurred at  $\geq 2\%$  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](http://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](http://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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 View original content to download multimedia: <https://www.prnewswire.com/news-releases/harmony-biosciences-initiates-phase-3-trial-of-pitolisant-in-adult-patients-with-idiopathic-hypersomnia-301533625.html>

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