



Harmony Biosciences Announces Positive Results From the Pivotal Bioequivalence Study for Pitolisant Gastro-Resistant Formulation

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New Drug Application to be submitted in early 2026; target PDUFA in Q1 2027

Utility patent applications filed with potential exclusivity to 2044

PLYMOUTH MEETING, Pa.--(BUSINESS WIRE)--Nov. 24, 2025-- Harmony Biosciences Holdings, Inc. (Nasdaq: HRMY) today announced positive results from its pivotal bioequivalence (BE) study evaluating pitolisant gastro-resistant (GR) formulation. With positive findings from both the pivotal BE and dosing optimization studies, Harmony is on track to submit a New Drug Application (NDA) for pitolisant GR in early 2026, targeting a PDUFA date in Q1 2027. With utility patent applications filed for pitolisant GR with potential exclusivity to 2044, Harmony is well positioned to extend the pitolisant franchise into the mid-2040s.

"We are very pleased to have demonstrated bioequivalence for pitolisant GR which, along with the positive findings from our dosing optimization study, confirms its potential as a differentiated next-generation treatment option for narcolepsy patients," said Kumar Budur, MD, MS, Chief Medical and Scientific Officer at Harmony Biosciences. "The combination of GR coating and ability to initiate treatment at the therapeutic dose without the need for titration, can potentially result in an enhanced overall treatment experience with pitolisant GR."

The pivotal BE study confirmed that 17.8mg of pitolisant GR is bioequivalent to existing 17.8mg WAKIX® tablets. The pitolisant GR vs. WAKIX AUC and Cmax ratios (%) were 108.46 h*ng/mL (90% CI 103.74 – 113.41) and 99.65 ng/mL (90% CI 91.95 – 108.00), respectively. No new safety or tolerability issues were reported. Importantly, the topline data from the dosing optimization study of pitolisant GR showed 100% of patients successfully initiated treatment at the therapeutic dose of 17.8mg, eliminating the need for dose titration.

This progress on pitolisant GR underscores the accelerating momentum of the pitolisant franchise, which is rapidly approaching blockbuster status in narcolepsy alone. Harmony Biosciences' commitment to innovation is further demonstrated by the development of pitolisant HD, a high-dose, enhanced formulation of pitolisant with an optimized pharmacokinetic profile, designed to deliver greater efficacy for excessive daytime sleepiness and other residual symptoms in narcolepsy and idiopathic hypersomnia. With utility patent applications for both pitolisant GR and pitolisant HD filed to potentially extend exclusivity to 2044, Harmony is well positioned for sustained market leadership and long-term value creation in the sleep/wake therapeutic space.

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 (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 (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 patients with narcolepsy with or without cataplexy, the most common adverse reactions ($\geq 5\%$ and at least 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 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 ($\geq 5\%$ 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 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 eGFR < 60 mL/minute/1.73 m².

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 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 excessive daytime sleepiness (EDS) and cataplexy – its two cardinal symptoms – 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 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 Harmony Biosciences

Harmony Biosciences is a pharmaceutical company dedicated to developing and commercializing innovative therapies for patients with rare neurological diseases who have unmet medical needs. Driven by novel science, visionary thinking, and a commitment to those who feel overlooked, Harmony Biosciences is nurturing a future full of therapeutic possibilities that may enable patients with rare neurological diseases to truly thrive. Established by Paragon Biosciences, LLC, in 2017 and headquartered in Plymouth Meeting, Pa., we believe that when empathy and innovation meet, a better future can begin; a vision evident in the therapeutic innovations we advance, the culture we cultivate, and the community programs we foster. 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 2025 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, including ZYN002 and EPX-100; 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 macroeconomic effects and changes in market conditions, including the impact of tariffs, inflation and the risk of recession. 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 25, 2025, 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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Harmony Biosciences Investor Contact:

Matthew Beck
917-415-1750
matthew.beck@astrpartners.com

Harmony Biosciences Media Contact:

Cate McCanless
202-641-6086
cmccanless@harmonybiosciences.com

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