Harmony Biosciences Presents Preclinical Data Demonstrating Significant Wake-Promoting and Cataplexy-Suppressing Effects of BP1.15205 in Narcolepsy at SLEEP 2025

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BP1.15205 is a potentially best-in-class OX2R agonist being investigated in narcolepsy and other central disorders of hypersomnolence

A first-in-human study is planned to start in 2H 2025; topline clinical data is anticipated in 2026

PLYMOUTH MEETING, Pa.--(BUSINESS WIRE)--Jun. 11, 2025-- Harmony Biosciences Holdings, Inc. (Nasdaq: HRMY) today announced the presentation of preclinical pharmacological effect data for BP1.15205, an investigational, highly potent, and potentially best-in-class orexin 2 receptor (OX2R) agonist, which demonstrated significant wake-promoting and cataplexy-suppressing effects in a standard transgenic mouse model of narcolepsy type 1. The data will be presented at the 39th Annual Meeting of the Associated Professional Sleep Societies (APSS) "SLEEP" on Wednesday, June 11, 2025, at 10:00 AM PDT in Seattle.

"We are encouraged by the robust preclinical data being presented at SLEEP, highlighting BP1.15205 as a potentially best-in-class OX2R agonist," said Kumar Budur, MD, MS, Chief Medical and Scientific Officer at Harmony Biosciences. "BP1.15205 is a new and unique chemical scaffold optimized for high potency that demonstrated statistically significant wake-promoting effects at very low doses administered orally in the standard transgenic mouse model. These findings are supportive of dosing flexibility to potentially treat all three central disorders of hypersomnolence at low doses, which could offer an optimized benefit / risk profile. The 3-month GLP toxicity study in two species revealed no concerning adverse events and supports a favorable safety and tolerability profile."

Orexin receptor functional studies showed that BP1.15205 is a highly potent, selective OX2R receptor agonist with no off-target effects expected and a >600-fold selectivity over human OX1R. BP1.15205 is orally bioavailable and has the potential for once-daily dosing.

Absorption, distribution, metabolism, and excretion (ADME) properties and preliminary toxicology studies showed that BP1.15205 is a differentiated OX2R agonist drug candidate. In the GLP toxicity study, no adverse events or biochemical changes were observed following a 3-month treatment period at doses up to 300 mg/kg/day, pending histopathology data.

An Investigational Medicinal Product Dossier (IMPD) application with the European Medicines Agency (EMA) is being completed for BP1.15205. A first-in-human study is planned to begin in 2H 2025 with topline data anticipated in 2026. Additionally, an Investigational New Drug (IND) application for BP1.15205 will be filed with the U.S. Food and Drug Administration (FDA).

"We are very excited to advance our potentially best-in-class OX2R program and support the strategic expansion of our sleep-wake franchise. We are dedicated to investigating this potential new solution further with the hope of bringing a novel treatment to market that can help even more people with narcolepsy and other central disorders of hypersomnolence," Budur added.

The poster entitled, "BP1.15205, a Novel Orexin-2 Receptor Agonist, Demonstrates Pharmacological Effects in a Mouse Model of Narcolepsy," will be presented at P-38; Poster Board Number 1; on June 11, 2025, at 10:00 AM PDT.

KEY FINDINGS FROM THE STUDIES INCLUDE:

In Vitro Orexin Receptor Functional Studies:

- BP1.15205 is a highly potent agonist at OX2R receptors: EC_{50} = 0.015 nM.
- BP1.15205 is highly selective for human OX2R receptors: >600-fold selectivity over human OX1R receptors.
- Minimal interspecies difference in agonist functional properties was observed between human and mouse orexin-2 receptors.

In Vivo Pharmacology Studies:

- Single oral dose administration of BP1.15205 in transgenic mice at the beginning of the 12-hour dark period of a 24-hour light/dark cycle produced significant and dose-dependent increases in total wakefulness time and sleep latency at every dose tested beginning at 0.03 and 0.1 mg/kg, respectfully, as compared to vehicle-treated animals.

- Significant and dose-dependent decreases in the total number and duration of cataplexy-like episodes were measured following single dose, oral administration of BP1.15205 beginning at 1mg/kg, as compared to vehicle.

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 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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