Harmony Biosciences Reports Strong 2024 Revenues, Provides 2025 Revenue Guidance and Highlights Key Pipeline Catalysts

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WAKIX® (pitolisant) Preliminary Net Revenue of ~$201 Million for Fourth Quarter and ~$714 Million for Full Year 2024; Representing Growth of ~23% in Year-Five of Launch

2025 WAKIX Net Revenue Guidance Between $820 - $860 Million; On Track to a Potential $1 Billion+ Opportunity

Value-Creating Catalysts Anticipated Every Quarter in 2025:

Q1 – FDA Decision on File Acceptance of Pitolisant sNDA for Idiopathic Hypersomnia; Potential Approval in 2025
Q2 – Orexin/BP1.15205 Data Presentation at SLEEP 2025 Conference
Q3 – Pivotal Phase 3 Topline Data for ZYN002 in Fragile X Syndrome
Q4 – Initiation of Pitolisant-HD Pivotal Phase 3 Trial in Narcolepsy

Robust, Catalyst-Rich Pipeline Includes Up to Six Phase 3 Clinical Programs by Year End 2025

PLYMOUTH MEETING, Pa.--(BUSINESS WIRE)--Jan. 13, 2025-- Harmony Biosciences Holdings, Inc. (Nasdaq: HRMY) today announced strong preliminary, unaudited net product revenues for Q4 and full year 2024 of $201 million and $714 million, respectively. Building on this performance, the company is well positioned for a catalyst-rich 2025, with value-creating milestones anticipated every quarter. Harmony will be highlighting its catalysts for 2025 and other key milestones during its presentation at the 43rd Annual J.P. Morgan Healthcare Conference on Wednesday, January 15, 2025, at 11:15 a.m. PT / 2:15 p.m. ET.

“2025 is a pivotal year for Harmony Biosciences, as we focus on unlocking the full potential of our catalyst-rich neuroscience pipeline,” said Jeffrey M. Dayno, M.D., President and Chief Executive Officer of Harmony Biosciences. “Building upon our foundation of strong and continued revenue growth for WAKIX, our multi-franchise pipeline has come into focus with value-creating catalysts expected each and every quarter this year. We are entering 2025 with strong momentum and a clear path toward long-term growth, building a company with the potential to deliver over $3 billion in net revenue going forward."

Fourth Quarter and Full Year 2024 Net Product Revenue for WAKIX (Preliminary and Unaudited)

- Preliminary, unaudited net product revenue for the quarter ended December 31, 2024, was approximately $201 million, compared to $168.4 million for the same period in 2023
- Preliminary, unaudited net product revenue for the full year ended December 31, 2024, was approximately $714 million, compared to $582 million for the same period in 2023, representing ~23% growth in its fifth year on the market
- The average number of patients on WAKIX increased by approximately 300 sequentially to approximately 7,100 for the quarter ended December 31, 2024

2025 Net Revenue Guidance

- Net revenue projected between $820 to $860 million

Key Catalysts for 2025

- **Q1** – FDA decision on file acceptance of pitolisant sNDA for Idiopathic Hypersomnia (IH)
  - IH sNDA for pitolisant submitted in Q4 2024
  - Potential FDA approval in 2025
- **Q2** – Preclinical data for BP1.15205 (OX2R agonist) to be presented at SLEEP 2025
  - Data to include preclinical safety and efficacy
  - BP1.15205 on track for first-in-human study in Q3 2025
- **Q3** – Topline data readout for ZYN002 from pivotal Phase 3 trial in Fragile X syndrome (FXS)
  - Potential for first and only approved treatment for patients with FXS
  - Estimated 80,000 people living with FXS in the US; worldwide rights
- **Q4** – Initiation of Pitolisant-HD Pivotal Phase 3 trial in Narcolepsy
  - Designed to address the largest unmet need in patients with narcolepsy by providing greater efficacy for both excessive daytime sleepiness and cataplexy
  - Program to include novel endpoint to assess narcolepsy-related fatigue
  - Preliminary IP filed out to 2044 to extend the pitolisant franchise

Robust, Multi-Franchise Pipeline

- Anticipates up to six phase 3 clinical development programs by year end 2025
    - Initiated pivotal phase 3 study in Lennox-Gastaut syndrome (LGS) for EPX-100 in Q4 2024
        - EPX-100 is the most advanced 5HT2 (serotonin) agonist in clinical development
    - Initiation of Pitolisant-GR pivotal bioequivalence study in Q1 2025 with readout anticipated Q3 2025
- Pipeline poised to deliver at least one new product or indication approval every year for the next four years (2028)
- Current pipeline has the potential to generate over $3B in net revenue
- Additional program updates to be provided during the Management presentation at the upcoming J.P. Morgan Healthcare Conference on January 15, 2025, at 11:15 a.m. PT / 2:15 p.m. ET. Presentation slides are available on the investor page of the Harmony Biosciences website: https://ir.harmonybiosciences.com/

The financial information included in this press release is preliminary, unaudited, and subject to change. It does not present all the information necessary for an understanding of the company's financial results for the fourth quarter or full year 2024.

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 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 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 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 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 ZYN002

ZYN002 is the first-and-only pharmaceutically manufactured synthetic cannabidiol devoid of THC and formulated as a patent-protected permeation-enhanced gel for transdermal delivery through the skin and into the circulatory system. The product is manufactured through a synthetic process in a cGMP facility and is not extracted from the cannabis plant. ZYN002 does not contain THC, the compound that causes the euphoric effect of cannabis, and has the potential to be a nonscheduled product if approved. Cannabidiol, the active ingredient in ZYN002, has been granted orphan drug designation by the United States Food and Drug Administration (FDA) and the European Medicines Agency (EMA) for the treatment of FXS and for the treatment of 22q. Additionally, ZYN002 has received FDA Fast Track designation for the treatment of behavioral symptoms in patients with FXS.

About Fragile X Syndrome

Fragile X syndrome (FXS) is a rare genetic disorder that is the leading known cause of both inherited intellectual disability and autism spectrum disorder. The disorder negatively affects synaptic function, plasticity and neuronal connections, and results in a spectrum of intellectual disabilities and behavioral symptoms, such as social avoidance and irritability. While the exact prevalence is unknown, upwards of 80,000 patients in the U.S. and 121,000 patients in the European Union and the UK are believed to have

FXS, based on FXS prevalence estimates of approximately 1 in 4,000 to 7,000 in males and approximately 1 in 8,000 to 11,000 in females. There is a significant unmet medical need in patients living with FXS as there are currently no FDA-approved treatments for this disorder.

FXS is caused by a mutation in FMR1, a gene which modulates a number of systems, including the endocannabinoid system, and most critically, codes for a protein called FMRP. The FMR1 mutation manifests as multiple repeats of a DNA segment, known as the CGG triplet repeat, resulting in deficiency or lack of FMRP. FMRP helps regulate the production of other proteins and plays a role in the development of synapses, which are critical for relaying nerve impulses, and in regulating synaptic plasticity. In people with full mutation of the FMR1 gene, the CGG segment is repeated more than 200 times, and in most cases causes the gene to not function. Methylation of the FMR1 gene also plays a role in determining functionality of the gene. In approximately 60% of patients with FXS, who have complete methylation of the FMR1 gene, no FMRP is produced, resulting in dysregulation of the systems modulated by FMRP.

About Clemizole Hydrochloride (EPX-100)

EPX-100, clemizole hydrochloride, is under development for the treatment of Dravet syndrome (DS) and Lennox-Gastaut syndrome (LGS). EPX-100 acts by targeting central 5-hydroxytryptamine receptors to modulate serotonin signaling. The drug candidate is administered orally twice a day in a liquid formulation and has been developed based on a proprietary phenotype-based zebrafish drug screening platform. DS is caused by a loss of function mutation in the SCN1A gene, and scn1 mutant zebrafish replicate the genetic etiology and phenotype observed in the majority of DS patients. The scn1Lab mutant zebrafish model that expresses voltage gated sodium channels has been used for high-throughput screening of compounds that modulate Nav1.1 in the central nervous system.

About Dravet Syndrome

Dravet syndrome (DS) is a severe and progressive epileptic encephalopathy that begins in infancy and causes significant impact on patient functioning. DS begins in the first year of life and is characterized by high seizure frequency and severity, intellectual disability, and a risk of sudden unexpected death in epilepsy. Approximately 85% of Dravet syndrome cases are caused by de novo loss-of-function (LOF) mutations in a voltage-gated sodium channel gene, SCN1A1. DS has an estimated incidence rate of 1:15,700.

About Lennox-Gastaut Syndrome

Lennox-Gastaut syndrome (LGS) is a rare and drug-resistant epileptic encephalopathy characterized by onset in children between 3-5 years of age. The underlying cause of LGS is unknown and can be related to a wide range of factors including genetic differences and structural differences in the brain. As a result, patients experience multiple seizure types, including atonic seizures, and developmental, cognitive, and behavioral issues. LGS affects approximately 48,000 patients in the U.S.

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 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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