HARMONY BIOSCIENCES TO PRESENT CLINICAL DATA ON WAKIX (PITOLISANT) AT UPCOMING WORLD SLEEP 2019

September 16, 2019 12:00 PM EDT

One oral presentation and seven posters will highlight human abuse potential data, new analysis on the efficacy of pitolisant in patients with a high burden of narcolepsy symptoms, and efficacy and safety data from the pivotal trials

WAKIX is a first-in-class medication with a novel mechanism of action and is the first and only non-scheduled treatment approved for patients with narcolepsy in the U.S.

PLYMOUTH MEETING, PA, September 16, 2019 —Harmony Biosciences, LLC, (Harmony) announced today it will present clinical data on the efficacy and safety of WAKIX® (pitolisant) at the World Sleep 2019 meeting in Vancouver, Canada, from September 20-25, 2019. In an oral presentation, results will be presented from a randomized, double-blind, active- and placebo-controlled, four-sequence, four-way crossover study that evaluated the abuse potential of pitolisant compared with the stimulant phentermine HCl (C-IV) and placebo in non-dependent, recreational stimulant users. In addition, seven scientific posters will be presented, including a new post-hoc analysis of pooled data from two randomized, placebo-controlled, seven- and eight-week studies of pitolisant in adults with narcolepsy that evaluated the efficacy of WAKIX in patients with a high burden of narcolepsy symptoms.

WAKIX was recently approved by the U.S. Food and Drug Administration (FDA) for the treatment of excessive daytime sleepiness (EDS) in adult patients with narcolepsy. WAKIX is the first and only treatment approved for patients with narcolepsy that is not scheduled as a controlled substance by the U.S. Drug Enforcement Administration (DEA).

“Harmony looks forward to sharing clinical data for WAKIX at the World Sleep 2019 meeting, which will shed light on its product profile as the first and only approved treatment for patients with narcolepsy that is not scheduled as a controlled substance,” said Harmony’s Chief Medical Officer, Jeffrey Dayno, M.D. “These data reflect the breadth of scientific evidence in support of WAKIX, and further demonstrate its uniqueness as a first-in-class molecule with a novel mechanism of action. We look forward to presenting these data to a global audience.”

Data being presented by Harmony include:

- **Oral Presentation: Evaluation of Abuse Potential of the Narcolepsy Medication Pitolisant** (Session Oral 28, September 25, 4:30-6pm) *J Dayno, C Scart-Grès, P Robert, J-C Schwartz, B Setnik*.
    - Results from a randomized, double-blind, active- and placebo-controlled, four-sequence, four-way crossover study evaluating the abuse potential of single-dose pitolisant compared with the stimulant phentermine HCl (C-IV) and placebo in non-dependent, recreational stimulant users.
- **Poster Presentation: Efficacy of Pitolisant in Patients with High Burden of Narcolepsy Symptoms** (Session P3, September 24, 5:30-7pm) *C Davis, L Krahn, B Vaughn, M Thorpy*.
    - Results from a post-hoc analysis evaluating the efficacy of pitolisant in patients with a high burden of narcolepsy symptoms. Data were pooled from two randomized, placebo-controlled, seven- and eight-week studies of pitolisant in adults with narcolepsy.
- **Poster Presentation: The Safety and Tolerability of Pitolisant in the Treatment of Excessive Daytime Sleepiness and Cataplexy in Adult Patients with Narcolepsy: An Open-Label, Expanded Access Program in the United States** (Session P3, September 24, 5:30-7pm) *E Bauer, C Davis, A Patroneva, J Dayno, M Thorpy*.
    - Results from an interim data collection of the Pitolisant Expanded Access Clinical Evaluation (PEACE) Program, which provided adult patients in the U.S. living with narcolepsy access to treatment with pitolisant before its approval by FDA.
- **Poster Presentation: Long-Term Evaluation of Safety and Efficacy of Pitolisant in Narcolepsy: HARMONY 3 Study** (Session P2, September 23, 5:30-7pm) *Y Dauvilliers, I Arnulf, C Scart-Grès, I Lecomte, C Caussé, J Dayno, J-C Schwartz*.
    - HARMONY 3 was an open-label, long-term (up to five years) study of pitolisant in patients with

narcolepsy. This presentation will focus on findings from a one-year analysis that assessed the long-term safety and efficacy of pitolisant in the treatment of excessive daytime sleepiness (EDS) and cataplexy in patients with narcolepsy.

- **Poster Presentation: Safety and Tolerability of Pitolisant in the Treatment of Adults with Narcolepsy: Integrated Data from Clinical Studies** (Session P2, September 23, 5:30-7pm) *C Scart-Grès, C Momah, M Roy, K Maski, S Piris, R Bogan*.
    - Analysis of integrated safety data from four randomized, placebo-controlled, clinical studies of pitolisant in adult patients with narcolepsy.
- **Poster Presentation: Efficacy and Safety of Pitolisant in Patients with Narcolepsy: A Review of Clinical Trials** (Session P3, September 24, 5:30-7pm) *Y Dauvilliers, J-C Schwartz, C Davis, J Dayno*.
    - Results from HARMONY 1 and HARMONY CTP: two randomized, double-blind, placebo-controlled pivotal studies that assessed the efficacy and safety of pitolisant for the treatment of EDS (HARMONY 1) and cataplexy (HARMONY CTP) in adult patients with narcolepsy.
- **Poster Presentation: Pitolisant in Combination with Other Medications for the Management of Narcolepsy** (Session P2, September 23, 5:30-7pm) *K Doghramji, C Davis, A Patroneva, J-C Schwartz, C Scart-Grès, P Robert, T Duvauchelle, S Wanaski, A Krystal*.
    - Results from a drug-drug interaction study that evaluated the pharmacokinetics of pitolisant when administered with sodium oxybate or modafinil. It also includes results from an open-label, long-term safety study of pitolisant (HARMONY 3) with analyses of effectiveness and adverse events in patients with narcolepsy treated with pitolisant as monotherapy, as well as in patients treated with pitolisant and concomitant psychostimulants and/or anticataplectics.
- **Poster Presentation: Burden of Narcolepsy: A Survey of Patients and Physicians** (Session P2, September 23, 5:30- 7pm) *M Thorpy, J Hopper, A Patroneva*.
    - Results from a survey on perceptions of healthcare professionals and patients living with narcolepsy regarding the burden, symptoms and treatment of narcolepsy. Discrepancies between patient and healthcare professional responses will also be described.

About WAKIX (pitolisant)
WAKIX is a first-in-class medication approved for use in the U.S. for the treatment of excessive daytime sleepiness in adult patients with narcolepsy. It was granted orphan drug designation for the treatment of narcolepsy in 2010. 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 Societe Civile de Recherche (Bioprojet), who has marketed the product in Europe since its approval by the European Medicines Agency in 2016. 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) in adult patients with narcolepsy.

IMPORTANT SAFETY INFORMATION

Contraindications
WAKIX is 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 (≥5% and 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 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).

H_1 receptor antagonists that cross the blood-brain barrier may reduce the effectiveness of WAKIX. Patients should avoid centrally acting H_1 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 at www.wakix.com.

To report suspected adverse reactions, contact Harmony Biosciences, LLC at 1-800-833-7460 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

About Narcolepsy
Narcolepsy is a rare, chronic, debilitating neurologic disorder of sleep-wake state instability that impacts up to 200,000 Americans and is primarily characterized by excessive daytime sleepiness (EDS) and cataplexy – its two cardinal symptoms – along with other manifestations of REM sleep dysregulation, 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, a neuropeptide in the brain that supports sleep-wake state stability. This disorder 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.

Harmony Biosciences, LLC
Harmony Biosciences, LLC, is a private biopharmaceutical company headquartered in Plymouth Meeting, PA. The company was established in October 2017 with a vision to provide novel treatment options for people living with rare and orphan diseases, with an emphasis on central nervous system disorders, starting with patients living with narcolepsy. Harmony Biosciences is committed to advancing the understanding of narcolepsy and providing information and resources to both the individuals who live with this disorder, and to the healthcare professionals who treat them. For more information on Harmony Biosciences, visit www.harmonybiosciences.com.

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