# HARMONY BIOSCIENCES PRESENTS EFFICACY AND SAFETY ANALYSES FOR WAKIX® (PITOLISANT) AT VIRTUAL SLEEP 2020

August 28, 2020

**Post-hoc analyses evaluate time-to-response, efficacy in high burden of narcolepsy symptoms, and overall cardiovascular safety profile in patients with narcolepsy**

**PLYMOUTH MEETING, PA, and CHICAGO, IL, August 28, 2020 —**Harmony Biosciences Holdings, Inc. ("Harmony") (Nasdaq: HRMY), a pharmaceutical company dedicated to developing and commercializing innovative therapies for patients living with rare neurological disorders who have unmet medical needs, announced today results from post-hoc analyses of the efficacy and safety data for WAKIX® (pitolisant) presented at the 34th Annual Meeting of the Associated Professional Sleep Societies (APSS), known as "SLEEP 2020." The meeting is being held virtually from August 27—30. Harmony is presenting a total of four posters in the Virtual SLEEP 2020 Exhibit Hall, three of which are post-hoc analyses of the efficacy and safety data from the clinical development program for WAKIX.

"We are pleased to participate in this year's SLEEP 2020 virtual meeting and share clinically relevant data supporting WAKIX with healthcare professionals and the sleep medicine community," said Harmony's Chief Medical Officer, Jeffrey Dayno, M.D. "The results presented from post-hoc analyses of the clinical data help further characterize the efficacy and safety profile of WAKIX to assist healthcare professionals in making treatment decisions for their patients living with narcolepsy."

**Time-to-Response in Excessive Daytime Sleepiness and Cataplexy During Treatment with Pitolisant in Patients with Narcolepsy**

This poster presents results from a post-hoc analysis that examined the time-to-response to pitolisant on improvement in both excessive daytime sleepiness (EDS) and reduction in cataplexy based on pooled data from the HARMONY 1 and HARMONY CTP randomized, controlled clinical trials. Pitolisant was titrated to a maximum dose of 35.6 mg/day and the change from baseline in mean Epworth Sleepiness Scale (ESS) scores (in both studies) and mean weekly rate of cataplexy (WRC; in HARMONY CTP) was compared for pitolisant versus placebo.

In the HARMONY 1 (pitolisant, n=31; placebo, n=30) and HARMONY CTP (pitolisant, n=54; placebo, n=51) trials, the ESS score improvement was significantly greater with pitolisant versus placebo beginning at Week 2 (LS mean difference, -2.8; p=0.015) and Week 3 (LS mean difference, -2.0; p=0.005), respectively. In HARMONY CTP, the LS mean WRC with pitolisant was 11.7 at baseline, 4.6 at end-of treatment, and 5.1 after a one-week, placebo-washout period. Improvement in the WRC was significantly greater with pitolisant versus placebo beginning at Week 2 (LS mean difference, -5.3; p=0.004) and continued through end-of-treatment (LS mean difference, -6.2; p<0.001 ); there was no evidence of rebound cataplexy after placebo-washout (LS mean difference, -4.9; p=0.027).

**Efficacy of Pitolisant in Patients with High Burden of Narcolepsy Symptoms**

This post-hoc analysis, based on pooled data from the HARMONY 1 and HARMONY CTP clinical trials, examined the efficacy of pitolisant in patients with narcolepsy who had a high symptom burden of EDS and cataplexy at baseline. The analyses included three independent patient subgroups: baseline score of >16 on the ESS (pitolisant, n=54; placebo, n=54), sleep latency of ≤8 minutes on the Maintenance of Wakefulness Test (MWT) (pitolisant, n=59; placebo, n=46), and ≥15 cataplexy attacks per week (pitolisant, n=20; placebo, n=11).

Mean change in ESS from baseline was significantly greater for pitolisant (-6.1) compared with placebo (-2.6; p=0.0002). A significantly greater percentage of pitolisant-treated patients were classified as treatment responders: for ESS score reduction ≥3, 68.5 percent in the pitolisant group versus 35.2 percent in the placebo group (p=0.0006); for final ESS score ≤10, 35.2 percent versus 9.3 percent, respectively (p=0.0026). Mean increase in sleep latency on the MWT was significantly greater for pitolisant (7.0 minutes) compared with placebo (3.4 minutes; p=0.0089). Decrease in mean WRC was significantly greater for pitolisant (baseline, 21.8; final, 3.9) compared with placebo (baseline, 20.9; final, 18.2); the rate ratio was 0.35 (95% CI, 0.26–0.47; p<0.001). Adverse events in the analysis populations were consistent with the known safety profile of pitolisant; headache was the most common adverse event in pitolisant-treated patients (10.0–20.4 percent).

**Cardiac Safety Profile of Pitolisant in Patients with Narcolepsy**

The third post-hoc analysis examined the cardiac safety events associated with pitolisant based on a pooled analysis of the HARMONY 1 (8-week) and HARMONY CTP (7-week) clinical trials, and from the 12-month, open-label HARMONY 3 trial. Cardiovascular adverse effects are of concern with narcolepsy medications, as cardiovascular diseases are comorbid conditions in some patients with narcolepsy, and these patients usually require lifelong pharmacotherapy for both narcolepsy and cardiovascular disorders.

The pooled analysis included 166 patients (pitolisant, n=85; placebo, n=81). Mean change in heart rate from baseline to end-of-treatment was -0.5 beats/min with pitolisant and -0.2 beats/min with placebo (LS mean difference, -0.4; p=0.744). Mean change was also similar for pitolisant versus placebo in systolic (LS mean difference, 0.0; p=0.983) and diastolic (LS mean difference, -0.6; p=0.552) blood pressure, as was mean change in QTc interval (LS mean difference, 0.4; p=0.911). Cardiac adverse events with pitolisant included heart rate increase (n=4), right bundle branch block (n=1), sinus tachycardia (n=1), and palpitations (n=1), and with placebo included blood pressure increase (n=1). In the long-term study, mean change from baseline in QTc interval was 3.1 msec at Month 6 (n=70) and 6.1 msec at Month 12 (n=67); three patients had a post-baseline increase >60 msec but none had an increase in QTc >500 msec.

**About WAKIX® (pitolisant) Tablets**
WAKIX is a first-in-class medication approved by the U.S. Food and Drug Administration in August 2019 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.

**Important Safety Information**
WAKIX is contraindicated in patients with severe hepatic impairment. WAKIX is extensively metabolized by the liver and there is a significant increase in WAKIX exposure in patients with moderate impairment.

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 not recommended in patients with end-stage renal disease (ESRD).

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.

Please see the **Full Prescribing Information** for WAKIX for more information.

**About Narcolepsy**
Narcolepsy is a rare, chronic, debilitating neurologic disorder of sleep-wake state instability that impacts up to 165,000 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.

**About Harmony Biosciences**
Harmony Biosciences is a pharmaceutical company headquartered in Plymouth Meeting, PA and Chicago, IL. The company was established in October 2017 by Paragon Biosciences, LLC, with a vision to provide novel treatment options for people living with rare, neurological disorders who have unmet medical needs. For more information on Harmony Biosciences, visit www.harmonybiosciences.com.

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