Harmony Biosciences Acquires Asset With Novel Mechanism Of Action For The Potential Treatment Of Narcolepsy And Other Rare Neurological Diseases

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Acquisition represents the first step in Harmony's plan to build a robust portfolio of products to treat patients living with rare neurological diseases who have significant unmet medical needs

PLYMOUTH MEETING, Pa., Aug. 9, 2021 /PRNewswire/ -- Harmony Biosciences Holdings, Inc. ("Harmony") (Nasdaq: HRMY), a pharmaceutical company dedicated to developing and commercializing innovative therapies for patients living with rare neurological diseases, today announced the acquisition of HBS-102 (formerly CSTI-100), a potential first-in-class molecule with a novel mechanism of action, from ConSynance Therapeutics, Inc., a clinical stage biotechnology company focused on rare central nervous system diseases. Under the terms of the agreement, Harmony will acquire full development and commercialization rights globally, with the exception of Greater China, with financial terms including an upfront payment of $3.5 million and potential development and regulatory milestone payments and royalties.

"The acquisition of HBS-102 represents our first addition to the pipeline beyond WAKIX® (pitolisant), and our intention is to continue to pursue additional assets in line with our vision of becoming a leading rare neurological disease company with a robust portfolio of products," said John C. Jacobs, President and Chief Executive Officer of Harmony.

HBS-102 is a Melanin Concentrating Hormone Receptor 1 (MCHR1) antagonist that has the potential to offer a novel approach to the treatment of narcolepsy including the symptoms of Rapid Eye Movement (REM) sleep dysregulation, such as cataplexy, hallucinations and sleep paralysis. HBS-102 blocks the activity of melanin concentrating hormone (MCH) neurons, which scientific evidence indicates is the generator of REM sleep and its associated behaviors. Therefore, HBS-102 could potentially reduce REM intrusions into wakefulness and reduce the frequency of cataplexy, hallucinations, and sleep paralysis. In a preclinical proof-of-concept study, Dr. Thomas Scammell, Professor, Department of Neurology, Beth Israel Deaconess Medical Center and Division of Sleep Medicine, Harvard Medical School, and his team demonstrated that an MCHR1 antagonist molecule resulted in a significant reduction in cataplexy events in an orexin knockout mouse model of narcolepsy.[1] Harmony will complete additional work to prepare and submit an Investigational New Drug (IND) application with the plan to initiate a Phase 2 clinical trial once the IND is open.

"Similar to WAKIX, this asset offers Harmony another opportunity to lead with the science and potentially bring another first-in-class treatment option to patients living with narcolepsy and other rare neurological diseases," said Jeffrey Dayno, M.D., Chief Medical Officer of Harmony. "The majority of people living with narcolepsy experience symptoms of REM dysregulation that have a significant impact on their lives. The acquisition and successful development of HBS-102 could represent a next-generation therapy for narcolepsy patients by offering a novel approach, directly targeting the control center for REM sleep and its associated behaviors."

About Narcolepsy

Narcolepsy is a rare, chronic, debilitating neurological disease of sleep-wake state instability that impacts approximately 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 (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 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 or cataplexy in adult patients with narcolepsy. WAKIX has been commercially available in the U.S. since Q4 2019. 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.

Important Safety Information
WAKIX is contraindicated in patients with known hypersensitivity to pitolisant or any component of the formulation and 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 of WAKIX 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 HBS-102
HBS-102 is an investigational compound being developed as a potential treatment for narcolepsy and other rare neurological diseases. HBS-102 is a potential first-in-class molecule with a novel mechanism of action which targets melanin concentrating hormone (MCH) neurons in the hypothalamus, which make up the control center for REM sleep and related behaviors. In the setting of orexin deficiency (as occurs in patients with type 1 narcolepsy), there is an imbalance between orexin and MCH which could result in the control center for REM sleep going unchecked that could lead to REM sleep intruding into wakefulness. If that occurs, the clinical symptoms are experienced as cataplexy, hallucinations, and/or sleep paralysis. HBS-102, an MCHR1 antagonist, blocks the activity of the MCH neurons, which could potentially reduce REM intrusions into wakefulness and therefore reduce the debilitating symptoms of cataplexy, hallucinations and sleep paralysis.

About Harmony Biosciences
Harmony Biosciences is a pharmaceutical company headquartered in Plymouth Meeting, PA. The Company was established by Paragon Biosciences, LLC, with a vision to provide novel treatment options for people living with rare neurological diseases who have unmet medical needs. For more information on Harmony, please visit the company's website: www.harmonybiosciences.com.

About ConSynance
ConSynance Therapeutics is a clinical-stage, biopharmaceutical company targeting rare central nervous system diseases. The Company focuses on innovative therapeutics for rare hypothalamic disorders including narcolepsy, Prader-Willi Syndrome and hypothalamic injury-induced obesity. For more information on ConSynance, please visit the company's website: www.consynance.com.

Forward Looking Statement
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 product WAKIX. 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 WAKIX, 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 agreement with Bioprojet; the availability of favorable insurance coverage and reimbursement for WAKIX; the impact of the COVID-19 pandemic; 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 needs for additional financing; our ability to identify 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; and 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; 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 March 25, 2021, 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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[1] Naganuma, F., Bandaru, S. S., Absi, G., Mahoney, C. E., Scammell, T. E., & Vetrivelan, R. (2018). Melanin-concentrating hormone neurons contribute to dysregulation of rapid eye movement sleep in narcolepsy. *Neurobiology of Disease, 120*, 12-20. https://doi.org/10.1016/j.nbd.2018.08.012

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