HETLIOZ® (tasimelteon) Phase III SET and RESET Trial Results Published in The Lancet

August 5, 2015

-- HETLIOZ®, when taken daily at a fixed time, promotes master body clock entrainment (synchronization) resulting in significant improvement across a number of sleep and wake parameters.

-- Discontinuation of HETLIOZ® results in reversed clinical benefits reinforcing the importance of chronic therapy.

WASHINGTON, Aug. 5, 2015 /PRNewswire/ -- Vanda Pharmaceuticals Inc. (Vanda) (NASDAQ: VNDA) today announced publication of pivotal trial results related to patient entrainment in the August issue of The Lancet. The published trial results are from the SET (Safety and Efficacy of Tasimelteon) and RESET (Randomized-withdrawal study of the Efficacy and Safety of Tasimelteon to treat Non-24-Hour Sleep-Wake Disorder (Non-24)) Phase III studies of HETLIOZ® (tasimelteon), a circadian regulator for the treatment of individuals suffering from Non-24. Non-24 is a serious, rare and chronic circadian rhythm disorder that affects a majority of totally blind individuals who lack light perception, and consequently cannot entrain (synchronize) their master body clock to the 24-hour day. Tasimelteon, marketed under the tradename HETLIOZ®, is currently approved for use in the United States and in the European Union.

In the SET study, HETLIOZ® achieved the primary endpoints of entrainment of the melatonin rhythm as compared to placebo and clinical response as measured by entrainment plus a score of greater than or equal to 3 on the Non-24 Clinical Response Scale. HETLIOZ® also demonstrated significant improvement versus placebo across a number of sleep and wake parameters including measures of total sleep time, daytime sleep duration, and timing of sleep, as well as in the Clinical Global Impression of Change, an overall global functioning scale. In treated patients, daytime sleep decreased by 46 minutes per day in the worst 25% of days and nighttime sleep increased by 57 minutes per day during the worst 25% of nights.

The RESET study demonstrated that continued treatment with 20mg of HETLIOZ® is required to maintain entrainment of the master body clock as measured by melatonin and cortisol circadian rhythms in individuals with Non-24. Patients treated with HETLIOZ® maintained their clinical benefits while patients who received placebo showed significant deterioration in measures of nighttime sleep, daytime sleep and timing of sleep. Furthermore, discontinuation of HETLIOZ® resulted in a rapid loss of circadian entrainment and a return to non-entrained circadian rhythms, reinforcing the importance of chronic therapy.

"The studies published today represent years of collaborative work between Vanda, leading researchers in the field and patients with Non 24," said Mihael H. Polymeropoulos, M.D., President and CEO of Vanda. "These clinical studies of Hetlioz in Non 24 led to approval in the U.S. in 2014, and with the recent European marketing authorization for Hetlioz, we are very excited about the opportunity to make this much-needed treatment available to the thousands of patients in Europe who are suffering from this debilitating condition."

Twenty-four-hour biological rhythms are regulated by interaction between environmental time cues and the internal circadian timing system. The environmental light-dark cycle interacts with the circadian timing system, and is the major time keeper for the master body clock which regulates many biological rhythms. Non-24 patients frequently struggle with severe disruptions to the sleep-wake cycle when the master body clock is out-of-sync with the 24-hour world.

"These results show HETLIOZ's efficacy as a circadian regulator, which can serve as an alternative to light as a 24-hour time cue in order to synchronize the circadian clock in the blind," said lead investigator Steven W. Lockley, Ph.D., Division of Sleep and Circadian Disorders, Brigham and Women's Hospital, a teaching affiliate of Harvard Medical School. "These results also show the importance of treating at a fixed clock time every day in order to maintain entrainment of one's circadian body clock."

About Non-24-Hour Sleep-Wake Disorder

Non-24 is a chronic circadian rhythm disorder resulting from loss of entrainment of the master body clock to the 24-hour day, disrupting the sleep-wake cycle. The sleep disturbance causes significant distress and/or impairment in social, occupational and other important areas of functioning. Non-24 affects the majority of totally blind individuals and it has been estimated that approximately 80,000 people in the United States suffer from Non-24 and 130,000 people in the European Union have the disorder.

About HETLIOZ®

HETLIOZ® is a melatonin receptor agonist. HETLIOZ® has been granted market authorization by the U.S. Food and Drug Administration and the European Medicines Agency. For full U.S. prescribing information, please visit www.hetlioz.com.

U.S. Indication and Important Safety Information About HETLIOZ®

Indication

HETLIOZ® is indicated for the treatment of Non-24.

Important Safety Information

HETLIOZ® may cause somnolence: After taking HETLIOZ®, patients should limit their activity to preparing for going to bed, because HETLIOZ® can impair the performance of activities requiring complete mental alertness.

The most common adverse reactions (incidence >5% and at least twice as high on HETLIOZ® than on placebo) were headache, increased alanine aminotransferase, nightmares or unusual dreams, upper respiratory or urinary tract infection. The risk of adverse reactions may be greater in elderly (>65 years) patients than younger patients because exposure to HETLIOZ® is increased by approximately 2-fold compared with younger patients.

Use of HETLIOZ® should be avoided in combination with fluvoxamine or other strong CYP1A2 inhibitors, because of a potentially large increase in exposure of HETLIOZ®, and a greater risk of adverse reactions. HETLIOZ® should be avoided in combination with rifampin or other CYP3A4

inducers, because of a potentially large decrease in exposure of HETLIOZ®, with reduced efficacy.

There are no adequate and well-controlled studies of HETLIOZ® in pregnant women. Based on animal data, HETLIOZ® may cause fetal harm. HETLIOZ® should be used during pregnancy only if the potential benefit justifies the potential risks. Caution should be exercised when HETLIOZ® is administered to a nursing woman.

HETLIOZ® has not been studied in patients with severe hepatic impairment and is not recommended in these patients.

Safety and effectiveness of HETLIOZ® in pediatric patients have not been established.

Full U.S. HETLIOZ® Prescribing Information can be found at: www.HETLIOZ.com.

About Vanda Pharmaceuticals Inc.
Vanda Pharmaceuticals Inc. is a biopharmaceutical company focused on the development and commercialization of products for the treatment of central nervous system disorders. For more on Vanda, please visit www.vandapharma.com.

CAUTIONARY NOTE REGARDING FORWARD LOOKING STATEMENTS

Various statements in this release, including, without limitation, Vanda's assumptions regarding the efficacy of HETLIOZ® as a circadian regulator, are "forward-looking statements" under the securities laws. Forward-looking statements are based upon current expectations that involve risks, changes in circumstances, assumptions and uncertainties. Important factors that could cause actual results to differ materially from those reflected in Vanda's forward-looking are set forth in the "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" sections of Vanda's annual report on Form 10-K for the fiscal year ended December 31, 2014 and quarterly report on Form 10-Q for the quarter ended June 30, 2015, which are on file with the SEC and available on the SEC's website at www.sec.gov. In addition to the risks described above and in Vanda's annual report on Form 10-K and quarterly reports on Form 10-Q, other unknown or unpredictable factors also could affect Vanda's results. There can be no assurance that the actual results or developments anticipated by Vanda will be realized or, even if substantially realized, that they will have the expected consequences to, or effects on, Vanda. Therefore, no assurance can be given that the outcomes stated in such forward-looking statements and estimates will be achieved.

All written and verbal forward-looking statements attributable to Vanda or any person acting on its behalf are expressly qualified in their entirety by the cautionary statements contained or referred to herein. Vanda cautions investors not to rely too heavily on the forward-looking statements Vanda makes or that are made on its behalf. The information in this release is provided only as of the date of this release, and Vanda undertakes no obligation, and specifically declines any obligation, to update or revise publicly any forward-looking statements, whether as a result of new information, future events or otherwise.

HETLIOZ® is a registered trademark of Vanda Pharmaceuticals Inc.

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To view the original version on PR Newswire, visit:http://www.prnewswire.com/news-releases/hetlioz-tasimelteon-phase-iii-set-and-reset-trial-results-published-in-the-lancet-300123799.html

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