HETLIOZ® (tasimelteon) Effective in Treating Jet Lag during Transatlantic Travel

May 23, 2018

- HETLIOZ® demonstrates significant improvement in objective and subjective measures of Jet Lag during 5 hour and 8 hour time zone transatlantic travel from the US to the UK

WASHINGTON, May 23, 2018 /PRNewswire/ -- Vanda Pharmaceuticals Inc. (Vanda) (Nasdaq: VNDA) today announced results from the JET Study (VP-VEC-162-2102), a 3-night transatlantic travel study of the effects of tasimelteon on Jet Lag Disorder. Tasimelteon was shown to be effective in treating Jet Lag Disorder in travelers who flew from the US to the UK.

"The results of the JET study are supportive and add to the body of evidence of the effects of tasimelteon on Jet Lag in the context of 5 and 8 hour time zone transatlantic travel," said Mihael H. Polymeropoulos, MD, Vanda's President and CEO.

The JET study was a two-phase transatlantic travel study, with an observational travel phase (baseline) followed by a treatment phase. Study participants traveled either 5 or 8 time zones from Washington, DC to London and San Francisco or Los Angeles to London, respectively. They stayed in London for 3 nights and 4 days, and during randomization they received tasimelteon 20mg for 3 consecutive nights prior to their bedtime. Efficacy was monitored by polysomnography (PSG) as well as sleep and wake questionnaire scales. Due to the complexity of the study, the study was terminated before it reached the original enrollment goal of 90 patients, with only 25 patients completing both phases of the study (tasimelteon n=13, placebo n=12).

Despite the small sample size (n=25) of this study, tasimelteon succeeded in demonstrating significant and meaningful effects across a number of sleep and wake measures, as summarized in Table 1.

Tasimelteon significantly improved total sleep time of the first 2/3 of the night (TST 2/3) on night 3, in both objective and subjective measures of sleep. Tasimelteon-treated patients slept 76 minutes longer during their second trip as compared to their first. Cumulatively over the 3 travel nights of their second trip, tasimelteon-treated patients added 131 minutes of sleep (TST 2/3) as compared to the 3 travel nights of the first trip.

Similar results favoring tasimelteon were seen in outcomes of the Post Sleep Questionnaire (PSQ), including subjective TST, subjective Sleep Latency, subjective Wake after Sleep Onset and subjective Sleep Quality. Measures of global function, including Patient Global Impression of Severity (PGI-S) and the Karolinska Sleepiness scale (KSS), also favored tasimelteon.

Table 1: Summary of Results

		Change from baseline			
	Endpoint	**HETLIOZ®**	**Placebo**	**Difference**	**p-value**
Objective Sleep	$TST_{2/3}$ Night 3 *	76.2	41.4	34.8	p=0.0354
	$TST_{2/3}$ All 3 Nights	131.4	40.9	90.6	p=0.0785
Subjective Sleep	TST Night 3	111.9	33.5	78.5	p=0.0225
	TST All 3 Nights	240.0	65.1	174.9	p=0.0423
	Sleep Quality (1-5) Night 3	1.31	0.36	0.95	p=0.0198
	Sleep Latency Night 3	-20.6	6.0	-26.5	p=0.0347
	WASO Night 3	-81.1	-24.7	-56.4	p=0.0840
Global Functioning	PGI-S (1-4) Day 3	-0.71	-0.07	-0.63	p=0.0168
	KSS (1-9) Day 4	-1.69	-0.69	-1.00	p=0.0765

*The primary endpoint of the study was Total Sleep Time for the first 2/3 (TST 2/3)[2] of the night(s) most likely to be disrupted. Examination of the observational phase baseline data demonstrated that Night 3 was the night most disrupted with 197 minutes in TST 2/3, followed by Night 1 and Night 2 with 218 minutes and 250 minutes, respectively. TST, Sleep Latency, and WASO shown in minutes.

The results of the JET study support the previously reported pivotal JET5 and JET8 Phase III studies, which demonstrated significant effects in circadian advances of 5 and 8 hours, respectively.[1,2]

Jet Lag Disorder affects millions of individuals annually who cross multiple time zones during their travel. Jet Lag Disorder symptoms are more severe during eastward travel. It is reported that more than 30 million US residents make trips abroad each year to overseas destinations. Of these, 60% (approximately 20 million) travel to destinations in Europe, the Middle East and Asia. It is also reported that of these 20 million travelers, 8% (approximately 1.6 million) travel in either Business or First Class.[3]

Vanda intends to seek marketing approval for the use of HETLIOZ® in the treatment of Jet Lag Disorder. Vanda believes that if HETLIOZ® is approved by regulatory authorities for the treatment of Jet Lag Disorder, it will potentially offer a therapeutic solution to many travelers and may represent an important commercial opportunity for the company. Vanda plans to file a supplemental New Drug Application for the treatment of Jet Lag Disorder with the FDA during the second half of 2018. For a review of the current prescribing information of HETLIOZ® please visit www.hetlioz.com.

HETLIOZ® IS NOT CURRENTLY APPROVED BY ANY REGULATORY AUTHORITY FOR THE TREATMENT OF JET LAG 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.

Important Safety Information

The most common adverse reactions (incidence >5% and at least twice as high on HETLIOZ® (tasimelteon) than on placebo) were headache, increased alanine aminotransferase, nightmares or unusual dreams, and 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.

Indication

HETLIOZ® is indicated for the treatment of Non-24-Hour Sleep-Wake Disorder (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 potentially impair the performance of activities requiring complete mental alertness.

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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.

About Vanda

Vanda is a global biopharmaceutical company focused on the development and commercialization of innovative therapies to address high unmet medical needs and improve the lives of patients. For more on Vanda Pharmaceuticals Inc., please visit www.vandapharma.com.

Abbreviations

PSG	Polysomnography
TST	Total Sleep Time
$TST_{2/3}$	Total Sleep Time First Two Thirds
WASO	Wake After Sleep Onset
PGI-S	Patient Global Impression of Severity
KSS	Karolinska Sleepiness Scale

References

1. Rajaratnam SM, Polymeropoulos MH, Fisher DM, Roth T, Scott C, Birznieks G, Klerman E. Melatonin agonist tasimelteon (VEC-162) for transient insomnia after sleep-time shift: two randomized controlled multicenter trials. The Lancet. 2009: 373: 433-516.

2. HETLIOZ® (tasimelteon) Demonstrates Efficacy to Treat Jet Lag Disorder in an 8 Hour Phase Advance Clinical Study. https://www.prnewswire.com/news-releases/hetlioz-tasimelteon-demonstrates-efficacy-to-treat-jet-lag-disorder-in-an-8-hour-phase-advance-clinical-study-300607853.html

3. US Department of Commerce, International Trade Administration, National Travel and Tourism Office. Profile of U.S. Resident Travelers Visiting Overseas Destinations: 2015 Outbound. http://tinet.ita.doc.gov/outreachpages/download_data_table/2015_Outbound_Profile.pdf

FORWARD LOOKING STATEMENTS

Various statements in this release 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 statements include, among others: the ability of HETIOZ® to provide significant benefit in the treatment of the symptoms of Jet Lag Disorder; Vanda's ability to obtain marketing approval for the use of HETLIOZ® in the treatment of Jet Lag Disorder; and other factors that are described 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, 2017 and quarterly report on Form 10-Q for the fiscal quarter ended March 31, 2018, 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.

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