HETLIOZ® (Tasimelteon) Driving Study Demonstrates No Impairment in Next Morning Performance

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WASHINGTON, Sept. 12, 2018 /PRNewswire/ -- Vanda Pharmaceuticals Inc. (Vanda) (Nasdaq: VNDA) today announced the results of a HETLIOZ® (tasimelteon) driving study to measure next day performance. Tasimelteon did not impair measures of driving performance, whereas the active control, zopiclone, showed significant impairment.

In this triple crossover study, 48 healthy volunteers drove 100 km in a validated driving simulator the morning after taking a bedtime dose of either tasimelteon 20 mg, zopiclone 7.5 mg or placebo. The volunteers were instructed to operate the driving simulator for approximately 1 hour with a speed of 55 mph while maintaining lane position.

Treatment with tasimelteon 20 mg at bedtime demonstrated no next day driving impairment compared to placebo. Treatment with zopiclone 7.5 mg dosed at bedtime was associated with a meaningful and significant increase in Standard Deviation of Lateral Position (SDLP), a measure of lane weaving, compared to the placebo treatment. Results for SDLP, the primary endpoint, are shown below.

Driving Study Results Summary

Treatment Comparison	SDLP Difference* (cm)	95% CI	p-value
Tasimelteon vs Placebo	1.22	(-0.29, 2.74)	p=0.1119
Zopiclone vs Placebo	4.14	(2.60, 5.68)	p<0.0001
Tasimelteon vs Zopiclone	-2.92	(-4.43, -1.41)	p=0.0002

*Least squares means

A secondary analysis of the paired differences between treatments (a symmetry analysis) confirmed that tasimelteon did not impair next day driving while there was an impairment with zopiclone. A difference of 4.4 cm is considered equivalent to the driving impairment associated with a blood alcohol (BAC) level of 0.05%, a level associated with increased crash risk.[1]

"Compared to other sleep agents where we've investigated next-day residual effects on driving, tasimelteon demonstrated no impairment when evaluated 9 hours after dosing," said Gary G. Kay, Ph.D., President of Cognitive Research Corporation, the contract research organization who ran the study. Dr. Kay serves as a consultant for the National Highway Transportation Safety Administration (NHTSA) and is a recognized expert in drug impaired driving.[2]

HETLIOZ® is currently approved for the treatment of Non-24 Hour Sleep Wake Disorder. Vanda plans to file a supplemental New Drug Application for HETLIOZ® for the treatment of Jet Lag Disorder with the FDA in 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 Zopiclone

Zopiclone is a non-benzodiazepine sleep agent marketed at a dose of 7.5 mg in countries outside the U.S. In the U.S., eszopiclone the s-enantiomer of zopiclone, is available under the brand name Lunesta®.

About Driving Safety and Sleep Promoting Agents

Next day driving impairment has been reported for a number of sleep promoting agents including Ambien (zolpidem), the most commonly used prescription drug in the class,[3] as well as for the most commonly used over the counter sleep aids containing diphenhydramine (e.g., Excedrin PM®).[4]

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

SDLP	Standard Deviation of Lateral Position
CI	Confidence Interval

References

1. Compton, R. P. & Berning, A. (2015, February). Drug and alcohol crash risk. (Traffic Safety Facts Research Note. DOT HS 812 117). Washington, DC: National Highway Traffic Safety Administration.
2. Kay, G. G., & Logan, B. K., (2011). Drugged Driving Expert Panel report: A consensus protocol for assessing the potential of drugs to impair driving. (DOT HS 811 438).
3. Farkas, R.H., Unger, E.F., Temple, R. (2013). Zolpidem and Driving Impairment — Identifying Persons at Risk. N ENGL J MED 369;8.
4. Kay, G.G., Schwartz, H.I., Wingertzahn, M.A., Jayawardena, S., Rosenberg, R.P. (2016). Next-day residual effects of gabapentin, diphenhydramine, and triazolam on simulated driving performance in healthy volunteers: a phase 3, randomized, double-blind, placebo-controlled, crossover trial. Hum. Psychopharmacol Clin Exp.

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