



## Press Releases

### **Phase III Data Show Vanda Pharmaceuticals' Tasimelteon (VEC-162) Significantly Improves Sleep in Patients with Chronic Insomnia**

Study Meets Primary Endpoint, with Positive Effect Sustained Through Duration of 4-Week Study  
ROCKVILLE, Md., June 26 /PRNewswire-FirstCall/ -- Vanda Pharmaceuticals Inc. (Nasdaq: VNDA) (Vanda) today announced positive top-line results from a Phase III trial showing that its investigational drug candidate, tasimelteon (VEC-162), a novel melatonin agonist, met the primary endpoint of the trial and significantly improved sleep in adult patients with chronic insomnia.

We are excited that the results of this Phase III chronic insomnia study demonstrate the clinical utility of tasimelteon and the ability of the compound to treat sleep disorders over a period of four weeks. The mechanism of action of tasimelteon as a circadian regulator gives Vanda the opportunity to explore its use for the treatment of circadian rhythm sleep disorders as well as chronic primary insomnia, stated Paolo Baroldi, MD, PhD, Vanda's Chief Medical Officer.

This Phase III, multi-center, placebo-controlled, 4-week trial evaluated 322 patients with chronic primary insomnia. Patients were randomized to receive either 20 mg or 50 mg of tasimelteon or placebo over the course of four weeks. The primary endpoint consisted of the evaluation of the immediate and short-term (average of Nights 1 and 8) ability of tasimelteon to improve sleep onset as measured by Latency to Persistent Sleep (LPS) through polysomnography (PSG). Secondary endpoints evaluated tasimelteon's ability to maintain improvements on sleep onset after long-term (average of Nights 22 and 29) use of the compound as well as measures of sleep duration (Total Sleep Time, TST) and sleep maintenance (Wake After Sleep Onset, WASO). Patients were eligible for the study if symptoms of insomnia were chronic and LPS was greater than 30 minutes.

#### Significant Improvement in Sleep Onset Sustained through Study Duration

These results demonstrate that tasimelteon was able to improve LPS significantly, and that this effect persisted for the 4 week duration of the study. The results on LPS at night 1 (N1)/night 8 (N8), and night 22 (N22)/night 29 (N29) are as follows.

-- Mean LPS at baseline (before drug treatment) was 78.8 minutes in the 20mg group, 76.4 minutes in the 50mg group, and 78.2 minutes in the placebo group. On Nights 1 and 8 of treatment, mean LPS improved by 45.0 minutes in the 20mg group ( $p < .001$ ), by 46.4 minutes in the 50mg group ( $p < .001$ ), and by 28.3 minutes in the placebo group. On Nights 22 and 29 of treatment, mean LPS improved by 49.4 minutes in the 20mg group ( $p < .001$ ), by 45.1 minutes in the 50mg group ( $p = .016$ ), and by 33.9 minutes in the placebo group. All statistical comparisons are between tasimelteon dose versus placebo.

Importantly, this effect was also seen acutely on the first night of treatment. Patients in the 20mg and 50mg groups fell asleep 22.9 minutes ( $p < .001$ ) and 25.9 minutes ( $p < .001$ ) faster, respectively, than those in the

placebo group, as measured objectively through PSG. Data from subjective patient self-reports on these nights were consistent with this finding.

#### Additional Phase III Results on Sleep Maintenance Parameters

The trial also evaluated parameters of sleep maintenance, including TST and WASO.

-- Mean TST at baseline (before drug treatment) was 325.7 minutes in the 20mg group, 327.0 minutes in the 50mg group, and 328.9 minutes in the placebo group. On Nights 1 and 8 of treatment, mean TST improved by 51.4 minutes in the 20mg group ( $p = .089$ ), by 52.0 minutes in the 50mg group ( $p = .074$ ), and by 40.0 minutes in the placebo group. On Nights 22 and 29 of treatment, mean TST improved by 60.3 minutes in the 20mg group ( $p = .057$ ), by 48.6 minutes in the 50mg group (not statistically significant, nss), and by 47.4 minutes in the placebo group. All statistical comparisons are between tasimelteon dose versus placebo.

-- Mean WASO at baseline (before drug treatment) was 92.6 minutes in the 20mg group, 93.8 minutes in the 50mg group, and 93.8 minutes in the placebo group. On Nights 1 and 8 of treatment, mean WASO improved by 12.2 minutes in the 20mg group (nss), by 14.1 minutes in the 50mg group (nss), and by 11.7 minutes in the placebo group. On Nights 22 and 29 of treatment, mean WASO improved by 17.7 minutes in the 20mg group (nss), by 10.2 minutes in the 50mg group (nss), and by 20.3 minutes in the placebo group. There were no significant differences in this secondary endpoint comparing tasimelteon versus placebo groups.

Analysis of the baseline PSG data revealed that the sleep disruption in this patient population occurred primarily during the first third of the 8-hour night. This is not unexpected given that the entry criteria in the study focused upon recruiting subjects with difficulty falling asleep and that there was no WASO entry criterion. At baseline, sleep efficiency (i.e. the percent of time spent asleep during the time available for sleep) during the first, second and last thirds of the night were 50.7%, 79.4% and 74.5%, respectively. Therefore, Vanda evaluated the effect of tasimelteon on sleep maintenance parameters in the first third of the night, when the sleep disruption was greatest in this population of chronic primary insomnia patients.

-- Mean TST during the first third of the night at baseline (before drug treatment) was 79.0 minutes in the 20mg group, 82.3 minutes in the 50mg group, and 82.2 minutes in the placebo group. On Nights 1 and 8 of treatment, mean TST during the first third of the night improved by 40.9 minutes in the 20mg group ( $p < .001$ ), by 39.4 minutes in the 50mg group ( $p < .001$ ), and by 26.6 minutes in the placebo group. On Nights 22 and 29 of treatment, mean TST during the first third of the night improved by 45.2 minutes in the 20mg group ( $p < .001$ ), by 40.1 minutes in the 50mg group ( $p < .01$ ), and by 30.6 minutes in the

placebo group. All statistical comparisons are between tasimelteon dose versus placebo.

-- Mean WASO during the first third of the night at baseline (before drug treatment) was 20.8 minutes in the 20mg group, 21.3 minutes in the 50mg group, and 21.3 minutes in the placebo group. On Nights 1 and 8 of treatment, mean WASO during the first third of the night improved by 2.3 minutes in the 20mg group ( $p < .01$ ), and by 1.8 minutes in the 50mg group ( $p < .05$ ), but worsened by 3.1 minutes in the placebo group. On Nights 22 and 29 of treatment, mean WASO during the first third of the night improved by 3.1 minutes in the 20mg group (nss), by 1.8 minutes in the 50mg group (nss) and by 0.6 minutes in the placebo group. All statistical comparisons are between tasimelteon dose versus placebo.

These results reveal that tasimelteon was able to achieve a number of statistically significant improvements on sleep maintenance parameters during the portion of the night in which the patient population studied suffered the greatest impairment. These data are consistent with data from the prior Phase III study (VP-VEC-162-3101), in which 20mg and 50mg of tasimelteon significantly improved LPS (by 21.5 to 26.3 minutes compared to placebo), WASO (by 24.7 to 33.7 minutes compared to placebo), and TST (by 33.7 to 47.9 minutes compared to placebo) in a model of transient insomnia. Taken together, the results of both of these studies demonstrate the versatility of tasimelteon to treat the symptoms of insomnia acutely and chronically both in a model of transient insomnia and in patients with chronic primary insomnia.

These results suggest that circadian misalignment may play an important role in the pathophysiology of chronic primary insomnia in many patients, especially those who have difficulty falling asleep, said Charles A. Czeisler, PhD, MD, FRCP, Chairman of Vanda's Scientific Advisory Board.

This study also demonstrated that tasimelteon was well-tolerated and exhibited a safety profile generally similar to placebo.

#### About Tasimelteon

Tasimelteon, (VEC-162), is Vanda's novel melatonin agonist in development for the treatment of insomnia and circadian rhythm sleep disorders (CRSD). Researchers believe that the interplay between the MT-1 and MT-2 pathways and environmental signals such as external light-dark cues results in the drive for wakefulness during daytime hours and sleepiness during night-time hours.(1) In patients with insomnia or CRSD, the regulation of the sleep/wake cycle is disrupted.(2) By binding to both the MT-1 and MT-2 receptors in a balanced fashion, tasimelteon helps modulate the patient's circadian rhythm, re-setting the sleep/wake cycle and providing simultaneous, immediate sleep- promoting benefits.(1)

#### About Insomnia and Circadian Rhythm Sleep Disorders

Insomnia, the most common sleep disorder, affects approximately 50-70 million American adults.(3,4) It is characterized by difficulty falling asleep, waking frequently during the night, waking too early and not

being able to return to sleep, or waking up and not feeling refreshed.(5)

CRSD, another type of sleep disorder defined as the inability to sleep at usual or customary times, affects millions of Americans in a number of forms, including Shift Work Disorder, which affects 10% of Americans who are shift workers; Delayed Sleep Phase Disorder, which affects 5-10% of chronic insomnia patients; and Jet Lag Disorder, which typically affects air travelers crossing five or more time zones.(6-8)

#### Conference Call

The company has scheduled a conference call for today, Thursday, June 26, 2008 at 10:00 AM ET. During the call, Mihael H. Polymeropoulos, M.D., Vanda's President and CEO, will discuss the trial results.

Investors can call 1-866-831-6162 (domestic) and 1-617-213-8852 (international) prior to the 10:00 AM start time and ask for the Vanda Pharmaceuticals conference call hosted by Dr. Polymeropoulos. A replay of the call will be available Thursday, June 26, 2008, at 12:30 PM ET and will be accessible until Thursday, July 3, 2008, at 5:00 PM ET. The replay call-in number is 1-888-286-8010 for domestic callers and 1-617-801-6888 for international callers. The access number is 27175887.

The conference call will be broadcast simultaneously on the company's Web site, <http://www.vandapharma.com>. Investors should click on the Investor Relations tab and are advised to go to the Web site at least 15 minutes early to register, download, and install any necessary software. The call will also be archived on the Vanda Web site for a period of 30 days, through July 26, 2008.

#### About Vanda Pharmaceuticals Inc.

Vanda Pharmaceuticals Inc. is a biopharmaceutical company focused on the development and commercialization of clinical-stage product candidates for central nervous system disorders. The company has three product candidates. Vanda's lead product candidate, iloperidone, is a compound for the treatment of schizophrenia for which Vanda submitted a New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA) in September 2007. The FDA accepted Vanda's iloperidone NDA for filing in November 2007 and Vanda expects a decision from the FDA on or about July 27, 2008. Vanda's second product candidate, tasimelteon (VEC-162), is a compound for the treatment of sleep and mood disorders, which is currently in Phase III for chronic primary insomnia. Vanda's third product candidate, VSF-173, is a compound for the treatment of excessive sleepiness in Phase II. For more on Vanda Pharmaceuticals Inc., please visit <http://www.vandapharma.com>.

#### Cautionary Note Regarding Forward-Looking Statements

Various statements in this release are forward-looking statements under the securities laws. Words such as, but not limited to, believe, expect, anticipate, estimate, intend, plan, targets, likely, will, would, and could, and similar expressions or words, identify forward-looking statements. Forward-looking statements are based upon current expectations that involve risks, changes in circumstances, assumptions and uncertainties. Vanda is at an early stage of development and may not ever have any products that

generate significant revenue. Important factors that could cause actual results to differ materially from those reflected in the company's forward-looking statements include, among others: delays in the completion of Vanda's clinical trials; a failure of Vanda's product candidates to be demonstrably safe and effective; Vanda's failure to obtain regulatory approval for its products or to comply with ongoing regulatory requirements; a lack of acceptance of Vanda's product candidates in the marketplace, or a failure to become or remain profitable; Vanda's inability to obtain the capital necessary to fund its research and development activities; Vanda's failure to identify or obtain rights to new product candidates; Vanda's failure to develop or obtain sales, marketing and distribution resources and expertise or to otherwise manage its growth; a loss of any of Vanda's key scientists or management personnel; losses incurred from product liability claims made against Vanda; a loss of rights to develop and commercialize Vanda's products under its license and sublicense agreements and other factors that are described in the Risk Factors section (Part II, Item 1A) of Vanda's quarterly report on Form 10-Q for the quarter ended March 31, 2008 (File No. 000-51863). In addition to the risks described above and in Part II, Item 1A of Vanda's quarterly report 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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