Ambien CR® Improved Insomnia and Daily Functioning in Patients with Co-Morbid Major Depressive Disorder

- Ambien CR® (zolpidem tartrate extended-release) CIV tablets 12.5 mg significantly improved sleep onset, sleep maintenance and total sleep time compared to placebo -

Paris, France, June 10, 2008 – Sanofi-aventis announced today the results from a new study that showed Ambien CR® (zolpidem tartrate extended-release) CIV tablets 12.5 mg provided significant improvement in sleep onset, sleep maintenance and total sleep time over 8 weeks in patients with co-morbid insomnia and major depressive disorder (MDD) who were administered a Selective Serotonin Reuptake Inhibitor (SSRI) for depression. Ambien CR® also improved sleep-related next-day functioning measures. This data was presented at the SLEEP 2008 22nd Annual Meeting of the Associated Professional Sleep Societies (APSS).

“The results of this study demonstrate that Ambien CR® can be considered a viable treatment option for the insomnia MDD patients experience and help them get the good night’s sleep they need to improve their next-day functioning” declared Thomas Roth, PhD, director of the Sleep Disorders and Research Center at Henry Ford Hospital, Detroit, Michigan.

Ambien CR® Improved Sleep Quality and Sleep Impact on Daily Activities in MDD Patients

Total sleep time was increased in the Ambien CR® group throughout the study. At Week eight, patients reporting sleeping an average of 101 minutes more than baseline compared to placebo-treated patients who reported sleeping an average 64 minutes more (P<0.0001). On average, Ambien CR®-treated patients reported falling asleep sooner and exhibited improved sleep maintenance based upon fewer nighttime awakenings and decreased wake time after sleep onset compared to placebo-treated patients (P<0.0001). In addition, patients reported improvements in secondary measures related to daytime functioning, including morning energy, morning concentration and sleep impact on daily activities.

Treatment-emergent adverse events occurred in 72.9 % of the patients treated with Ambien CR® and 66.3% of the patients treated with placebo. The most frequent adverse events experienced by Ambien CR® and placebo were headache (14.1%; 17.9%) and nausea (10.9%; 8.4%). These adverse events have been reported in previous studies of both Ambien CR® and SSRIs and are known to be part of the safety profile of both treatments.

“Current therapies for MDD effectively treat depression symptoms, but may not sufficiently address the sleep difficulties frequently associated with the disorder, which are primarily difficulty falling asleep and staying asleep. The extended release formulation of zolpidem tartrate was found to be an effective adjunctive treatment option that helped patients fall asleep and stay asleep in this study, but may also have a positive effect on some secondary symptoms such as fatigue and lack of motivation,” says Maurizio Fava, MD, Professor of Psychiatry at Harvard Medical School and Executive Vice Chair of the Department of Psychiatry at Massachusetts General Hospital.
Similar improvements in sleep onset, maintenance and total sleep time and related next-day function were also demonstrated in an earlier study of Ambien CR® in patients with insomnia and co-morbid general anxiety disorder (GAD). It was the third largest, recently-completed clinical study of Ambien CR® that demonstrated improved measurements of next-day function as related to improving sleep induction and sleep maintenance symptoms of insomnia.  

**About the Study**

This was a multi-center, double-blind, parallel-group, randomized, placebo controlled study in 383 adults ages 21 to 64 with co-morbid insomnia and MDD. The study evaluated the overall improvement of insomnia, as measured by total sleep time and in patients treated with Ambien CR® and the antidepressant escitalopram (Lexapro®) 10 mg compared to treatment with placebo and escitalopram. Patients received Ambien CR® 12.5 mg (n=193) or placebo (n=192) each night and 10 mg of escitalopram each day during the 24-week study.  

Researchers assessed treatment efficacy through daily patient-reported Morning Sleep Questionnaires (MSQ) and during bi-weekly visits for eight weeks and every fourth week if the patients (depression responders) were part of an additional 16–week treatment period. The MSQ measured the primary efficacy outcome of total sleep time in addition to secondary measurements of sleep onset latency, wake time after sleep onset, number of awakenings, quality of sleep and sleep-related next-day functioning.  

**About Insomnia**

Insomnia - difficulty falling asleep, staying asleep or waking too early and not being able to get back to sleep – is one of the most common sleep problems. Approximately 50 to 70 million Americans are affected by insomnia each year, which can lead to a range of overall health and medical implications.  

**About Ambien CR® (zolpidem tartrate extended-release) CIV tablets**

Ambien CR® is indicated for the treatment of insomnia, characterized by difficulties with sleep onset and/or sleep maintenance (as measured by wake time after sleep onset). Ambien CR® is not indicated for the treatment of MDD or GAD.  

**Important Safety Information**

Ambien CR® is indicated for the treatment of insomnia. Ambien CR® is not indicated for the treatment of MDD or GAD. Due to its rapid onset of action, patients should take Ambien CR® right before going to bed and when ready for sleep. Patients should not take Ambien CR® unless they are prepared to get a full night’s sleep (7 to 8 hours) to avoid residual effects. Until they know how it will affect their physical or mental performance upon awakening, patients should not drive or operate hazardous machinery after taking Ambien CR® or any other sleep medication. Complex behaviors such as somnambulism, including driving or eating while not fully awake, with amnesia for the event, have been reported in patients who have taken a sedative hypnotic. Discontinuation of Ambien CR® should be strongly considered for patients reporting such complex behaviors. Rare cases of angioedema have been reported in patients after taking sedative hypnotics. Patients who develop angioedema should not be rechallenged. Sedative/hypnotic drugs should be administered with caution to patients exhibiting signs or symptoms of depression. Suicidal tendencies may be present in such patients and protective measures may be required. Intentional overdosage is more common in this group of patients; therefore, the least amount of drug that is feasible should be prescribed for the patient at any one time. The most commonly observed adverse effects in controlled clinical trials were headache, somnolence and dizziness.  

For full prescribing information, please visit [www.AmbienCR.com](http://www.AmbienCR.com)
About sanofi-aventis
Sanofi-aventis, a leading global pharmaceutical company, discovers, develops and distributes therapeutic solutions to improve the lives of everyone. Sanofi-aventis is listed in Paris (EURONEXT : SAN) and in New York (NYSE : SNY).

Forward Looking Statements
This press release contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended. Forward-looking statements are statements that are not historical facts. These statements include financial projections and estimates and their underlying assumptions, statements regarding plans, objectives, intentions and expectations with respect to future events, operations, products and services, and statements regarding future performance. Forward-looking statements are generally identified by the words "expects," "anticipates," "believes," "intends," "estimates," "plans" and similar expressions. Although sanofi-aventis’ management believes that the expectations reflected in such forward-looking statements are reasonable, investors are cautioned that forward-looking information and statements are subject to various risks and uncertainties, many of which are difficult to predict and generally beyond the control of sanofi-aventis, that could cause actual results and developments to differ materially from those expressed in, or implied or projected by, the forward-looking information and statements. These risks and uncertainties include those discussed or identified in the public filings with the SEC and the AMF made by sanofi-aventis, including those listed under “Risk Factors” and “Cautionary Statement Regarding Forward-Looking Statements” in sanofi-aventis’ annual report on Form 20-F for the year ended December 31, 2007. Other than as required by applicable law, sanofi-aventis does not undertake any obligation to update or revise any forward-looking information or statements.

2 Ibid.
3 Ibid.
7 Ibid.