

OREXIGEN(TM) THERAPEUTICS REPORTS POSITIVE 24-WEEK RESULTS FOR CONTRAVE(TM) PHASE III OBESITY TREATMENT STUDY

Orexigen Therapeutics

PR Newswire Europe, September 27, 2006

OREXIGEN(TM) Therapeutics, Inc., a privately held clinical-stage neuroscience company developing novel strategic approaches to the treatment of obesity, today announced that top line results for the company's lead obesity compound, Contrave(TM), demonstrated significant advantages in weight loss in a 24-week multi-center, placebo-controlled phase III trial; the trial will continue unblinded for an additional 24 weeks.

Contrave is a proprietary combination of bupropion, a dopamine and norepinephrine reuptake inhibitor, with one of several different doses of naltrexone, an opioid antagonist used to treat various addictive disorders. The bupropion/naltrexone combination is based on the company's underlying research into the brain's regulation of appetite and energy expenditure, which suggests that combining these two central nervous system drugs may improve the ability to initiate weight loss, and importantly, to continue weight loss by blocking the body's attempts to compensate for weight loss during the treatment. The trial is testing three different dosages of naltrexone combined with the same dosage of bupropion. In what may become the preferred dose pairing based on performance and tolerability, patients completing the 24-week trial using Contrave experienced on average an excess of 7% weight loss from baseline compared to approximately 1% weight loss from baseline on average for patients using the placebo. In addition, the Contrave combination outperformed either naltrexone or bupropion given alone, and the Contrave-associated weight loss trajectory showed no indication of reaching a plateau at the conclusion of 24 weeks of blinded therapy. These findings for Contrave are consistent with an earlier phase II proof of concept study presented at the annual meeting of the American Diabetes Association in June.

OREXIGEN(TM) Therapeutics, Inc.

"These clinical findings are indicative of a therapeutic synergy when combining naltrexone with bupropion for weight loss. We believe Contrave represents a unique approach to successful long-term weight loss with a very acceptable safety profile," said Gary Tollefson, M.D., Ph.D., OREXIGEN president and CEO.

"Contrave is designed to activate a hypothalamic center in the brain associated with reduced appetite, while blocking beta-endorphin, which may be responsible for limiting weight loss. We are also studying the effects of Contrave on related central pathways associated with the rewarding nature of select high calorie foods. OREXIGEN is developing Contrave to provide a steady, manageable weight loss over time. We are also developing a second compound, Excalia(TM), which is designed to provide a more pronounced weight loss trajectory and which is presently being evaluated in a large, double-blinded, phase IIb clinical trial."

The Contrave phase III trial involves more than 250 patients at 14 clinical sites, and was blinded for the first 24 weeks. A second 24 weeks of open-label treatment is currently underway. The three doses of naltrexone were selected based on OREXIGEN's innovative use of Positron Emission Tomography (PET) imaging of the opioid receptors in the human brain.

* Patients completing the 24-week trial who received Contrave with the highest test dose of naltrexone lost an average of 7.52% weight from baseline as compared to an average of 1.03% weight loss from baseline experienced by patients using the placebo. This treatment group also was more likely to have experienced nausea early in the course of their treatment.

* Patients completing the 24-week trial and receiving Contrave with the middle dose of naltrexone, the dose previously mentioned as a possible preferred dose, lost on average an excess of 7% weight from baseline, suggesting that this middle dose provides the best combination of tolerability and efficacy.

* Patients completing the 24-week trial and receiving Contrave with the lowest dose of naltrexone also experienced weight loss with improved tolerability.

No serious adverse events attributed to Contrave were reported by the study's investigators at any of the three dosages tested.

Dr. Tollefson continued: "As we review these 24-week findings we believe it is important to continue evaluating Contrave dosing in order to identify those formulations with the greatest clinical benefit coupled with a patient and regulatory view on an acceptable side effect profile."