

OREXIGEN™ THERAPEUTICS REPORTS POSITIVE PHASE II RESULTS FOR CONTRAVE™ COMBINATION-THERAPY TO TREAT OBESITY

--Top-Line Positive Data Presented at American Diabetes Association

Scientific Sessions --

--Data Include First Public Disclosure of the Contrave Ingredients--

San Diego, CA, and Washington, DC, June 10, 2006 – OREXIGEN™ Therapeutics, Inc., a privately held clinical-stage neuroscience company developing a novel strategic approach to the treatment of obesity, today announced that the company's lead program, Contrave™, a combination of two centrally-acting medications, demonstrated greater sustained weight loss in a six month Phase II clinical study than either monotherapies or placebo. The findings showed that in the subjects using Contrave more than half of those who completed the trial demonstrated 5% weight loss over 24 weeks, 18% demonstrated 10% weight loss, and the trajectory of these weight loss curves showed no evidence of a plateau. These top line Phase II data for Contrave were presented at the 66th annual Scientific Sessions of the American Diabetes Association (ADA) in Washington, DC.

"These results show the greater potential for weight loss that can be achieved by combining therapies," said Louis Aronne, M.D., Clinical Professor of Medicine at Weill Cornell University Medical College and director of the Comprehensive Weight Control Program at New York Presbyterian Hospital-Weill Cornell Medical Center, who addressed the findings as part of a plenary session, at the ADA meeting." Dr. Aronne continued: "Thirty percent of American adults are obese and at significant health risk and it is clear that properly-designed medical interventions can help treat this epidemic."

Contrave is a rationally formulated combination of CNS products designed to achieve weight loss and then to off-set the body's natural compensatory mechanisms to avoid the typical weight loss plateau. The company disclosed for the first time that Contrave is a proprietary formulation of naltrexone, used to treat narcotic and alcohol dependency, and bupropion, a dopamine and norepinephrine reuptake inhibitor. Though neither of these individual products has been approved for weight loss by the FDA, several million patients have received these medications for other uses over the last twenty years. The company is further refining the formulation and optimal dose ratio of the two agents as part of its ongoing Phase III clinical program.

"This naltrexone/bupropion combination derives from our identification of specific neuronal systems in the brain that balance energy expenditure and appetite to regulate body weight," said Gary Tollefson, M.D., Ph.D., OREXIGEN president and CEO. "We believe that the positive findings we report today offer proof of concept for our Contrave clinical program."

The Contrave combination is based on in vitro studies that show naltrexone acts synergistically with bupropion to stimulate the proopiomelanocortin (POMC) system in the brain to release alpha-MSH, a hormone that increases energy expenditure and reduces hunger. Naltrexone also blocks autoinhibition of POMC by the body's natural opiate beta-endorphin. Orexigen scientists believe that blocking this autoinhibition is an important element in preventing the typical plateau and weight regain observed with most obesity interventions.

The multi-center study was conducted at 8 US academic centers and evaluated 206 obese subjects with a body mass index of 30 to 40 with each of the monotherapies, the combination and placebo along with a minimal diet and exercise program. The Phase II findings were presented at the ADA by the study's principal investigator, Frank Greenway, M.D., chief of the Clinical Obesity Laboratory and Outpatient Research Clinic at the Pennington Biomedical Research Center.

A companion product now in Phase II testing, Excalia™, is believed to be working via a distinctly different approach within appetite and energy pathways with a goal of providing a more substantial weight loss profile. More information about the company and its programs is available at this website.