

OREXIGEN(TM) Therapeutics Reports a Summary of Results from the Phase Iib Trial of Contrave(TM) to Treat Obesity

Orexigen Therapeutics

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Orexigen (TM) Therapeutics, Inc. (NASDAQ: OREX), a biopharmaceutical company focused on the treatment of central nervous system (CNS) disorders including obesity, announced a summary of Contrave (TM) results at The Obesity Society's Annual Scientific Meeting (NAASO) being held in New Orleans, October 20-24, 2007.* The Company presented both consolidated weight loss results from its Contrave Phase Iib trial and the first release of key secondary endpoint data. Contrave is one of the company's two late-stage obesity drug candidates.

"We believe the results of this trial have again confirmed the clinically meaningful bupropion-naltrexone synergy on extended weight loss," said Orexigen President and CEO, Gary Tollefson, M.D., Ph.D. "Additionally, this synergism may be associated with an improvement in markers of both cardiovascular and diabetic risk."

The Phase Iib trial was a 24 week, double-blind, placebo-controlled, multi-center trial with a 24-week extension that randomized 419 healthy obese patients to either: placebo, bupropion sustained release (SR) 400mg, naltrexone immediate release (IR) 48mg or a combination of bupropion SR 400mg and naltrexone IR 16mg, 32mg or 48mg daily. A subset of patients also had a dual X-ray absorptometry (DEXA) scan (75 randomized patients) to measure body fat and a multislice abdominal CAT scan (73 randomized patients) to measure visceral fat at baseline and at week 24.

The previously reported efficacy results at 48 weeks for weight loss from baseline body weight across the three Contrave dosage groups ranged from 5.0% to 6.6% (last observation carried forward analysis) and from 8.0% to 10.7% (completer analysis). The Company also reported that 24 week Contrave clinical responders continued to lose additional weight through 48 weeks.

Among the newly released secondary outcome measures were improvements in both serum lipids and glycemic indices at week 24, the primary trial endpoint. In this trial, the optimal treatment results were observed in the Contrave 32/400mg dose group. This group demonstrated statistically significantly greater improvement when compared to either the placebo and monotherapy groups on measures of fasting glucose and insulin resistance (log (HOMA) and the insulin check index (QUICKI)). Significant improvements were also observed when compared with at least one of the control groups in waist circumference, insulin, triglycerides, and homeostatic model assessment of insulin resistance (HOMA). The chart below summarizes these secondary endpoint data. LS Mean Change from Baseline (+/- SE) Week 24 Completer Population Placebo Nal48 Bup NB32 Weight (% -1.1 +/- -1.7 +/- -3.1 +/- -7.1 +/- 0.7 change) 1 0.6*** 0.9*** 0.7*** DEXA Fat -4.0 +/- -3.2 +/- -4.1 +/- 2.9* -12.0 +/- 1.7 Mass (% 2.0** 2.5** change) 2 CT Measured -4.6 +/- 2.7* -0.1 +/- -2.3 +/- 4.3* -14.0 +/- 2.4 Visceral Fat 3.6** (% change) 2 Waist (cm) 1 -1.0 +/- -3.8 +/- 12.7 -2.9 +/- 6.0 -5.4 +/- 7.6 5.4** Fasting 1.9 +/- 1.3* 3.4 +/- 1.7* 3.5 +/- 1.5* -2.0 +/- 1.5 Glucose (mg/dL) 1 Insulin (mu 0.9 +/- 0.9** 1.7 +/- 1.3** -0.5 +/- 1.1 -3.0 +/- 1.1 U/mL) 1 Triglyceride -15.0 +/- -17.6 +/- -18.4 +/- -43.6 +/- 8.8 (mg/dL) 1 7.7* 10.4 9.0* HOMA 1 0.3 +/- 0.2** 0.5 +/- 0.3** -0.1 +/- 0.3 -0.8 +/- 0.3 Log (HOMA) 1 0.023 +/- 0.037 +/- -0.004 +/- -0.141 +/- 0.029** 0.039** 0.034* 0.033 QUICKI 1 -0.002 +/- -0.003 +/- -0.000 +/- 0.017 +/- 0.003*** 0.004** 0.004** 0.004 Comparisons with NB32: *P-value = 0.05; **P-value = 0.01; ***P-value = 0.001. 1 24 Week Completer Population from overall NB-201 study 2 24 Week Subset Completer Population

In a subset of patients who had a DEXA scan or an abdominal CAT scan at baseline and week 24, the mean reduction in visceral fat ranged from 13.7% to 16.7% across the Contrave groups compared to a 0.1% to 4.6% mean reduction for patients receiving either of the monotherapies or placebo. Visceral fat is located inside the abdominal cavity and surrounds vital organs such as the liver. Visceral fat accumulation, as

opposed to subcutaneous fat which is found just underneath the skin, is associated with increased risk of heart disease and Type II diabetes. These results suggest that weight loss associated with Contrave therapy results primarily from fat tissue loss, including a loss of visceral fat.

There were no serious adverse events related to treatment with Contrave. Overall the 32/400mg group experienced the lowest rate of discontinuation due to adverse events at just under 16 percent. Nausea was the most common adverse event reported in the trial. It typically occurred on initial drug exposure and was transient and mild. Discontinuations due to nausea through 24 weeks were substantially lower in the 32/400mg group (7.9%) than in the higher dose 48/400mg group (18.0%). Other adverse events included headache, dizziness and insomnia. There was no indication of meaningful adverse effects of Contrave therapy on vital signs including blood pressure and pulse, ECG intervals, laboratory evaluations or on a scale evaluating depression.

Contrave employs a proprietary formulation of two CNS molecules, bupropion and naltrexone, that have been independently approved by the US Food and Drug Administration in other indications. Orexigen has developed its own proprietary SR version of naltrexone to further improve drug tolerability and has it in the Company's ongoing phase III Contrave program. Bupropion and naltrexone target pathways in the hypothalamus that mediate appetite, energy expenditure, and food craving. The unique combination of these molecules is designed to provide clinically meaningful weight loss for patients by both initiating weight loss and then sustaining it over a longer period of time.

About Orexigen Therapeutics

Orexigen Therapeutics, Inc. is a biopharmaceutical company focused on the development of pharmaceutical product candidates for the treatment of central nervous system disorders including obesity. Orexigen's lead combination product candidates targeted for obesity are Contrave (TM), which is in Phase III clinical trials, and Empatic (TM), which is in the later stages of Phase II development. Both product candidates are designed to take advantage of the Company's understanding of how the brain appears to regulate appetite and energy expenditure, as well as the mechanisms that come into play to limit weight loss over time. Each product candidate is designed to act on a specific group of neurons in the central nervous system with the goal of achieving appetite suppression and sustained weight loss. Further information about the Company can be found at <http://www.Orexigen.com>.