



OREXIGEN™

## Orexigen(R) Therapeutics Announces That Contrave(R) May Reverse the Incidence of Metabolic Syndrome

### Shows Potential to Reduce Risks for Diabetes and Heart Disease

SAN FRANCISCO & SAN DIEGO, Jun 07, 2008 (BUSINESS WIRE) -- Orexigen(R) Therapeutics, Inc. (Nasdaq: OREX), a biopharmaceutical company focused on the treatment of central nervous system disorders, including obesity, today announced that based on a review of data from its Contrave(R) Phase IIb trial, patients assigned to Contrave dosage groups demonstrated a 50% reduction in the prevalence of metabolic syndrome. Metabolic syndrome is a group of risk factors associated with obesity that may increase the risk of developing diabetes or cardiovascular disease. According to the American Heart Association, metabolic syndrome affects an estimated 47 million Americans.

Orexigen conducted a retrospective evaluation on the baseline prevalence of metabolic syndrome, as it is defined by the Adult Treatment Panel (ATP) III Guidelines. The data revealed that among Contrave patients who completed 24 weeks of treatment, the percentage of subjects with metabolic syndrome decreased from 31% to 15% (p less than 0.05). Among patients on placebo, the prevalence of metabolic syndrome decreased by a smaller percentage, from 38% to 30%. Improvements were also evident in key markers of metabolic and cardiovascular disease. The findings can be found in ADA abstract number 2735-PO.

Of the three Contrave dosages evaluated, the NB-32 dosage (32 mg naltrexone IR / 400 mg bupropion SR) demonstrated the best overall risk-to-benefit ratio with a decrease in the percentage of patients with metabolic syndrome from 30% to 14% using a conservative intent-to-treat analysis (p less than 0.05). Improvements among Contrave patients were seen in triglycerides (0.6% increase for placebo, 33.6% decrease for NB-32, p less than 0.01), waist circumference (1.8% decrease for placebo, 6.4% decrease for NB-32, p=0.06) and HDL cholesterol (0.3% increase for placebo, 15.1% increase for NB-32, p less than 0.01). These findings are consistent with synergistic reductions in percentage change from baseline in total body weight and visceral fat previously shown with Contrave.

"These results are especially important because they suggest that obesity-related morbidity, including diabetes and cardiovascular risk, may be improved with Contrave-associated weight loss," said Orexigen President and CEO, Gary Tollefson, M.D., Ph.D. "The present findings are consistent with a recent paper which also demonstrated that even a moderate decrease in weight resulted in significant reductions in the prevalence of metabolic syndrome (Phelan et al, 2007). Especially noteworthy in our results was the increase in HDL cholesterol since the literature also indicates that a 1 mg/dl increase in HDL cholesterol may lead to a reduction in cardiovascular risk of approximately 2-3% (Hausenloy & Yellon, 2008). These results may be especially meaningful to patients, physicians and payers."

Contrave is a proprietary formulation of bupropion and naltrexone in varying dose ratios being developed by Orexigen for the treatment of obesity. Contrave is currently being studied in four Phase III clinical trials, with results anticipated in late 2008 or early 2009 and the filing of a New Drug Application (NDA) with the FDA projected for late 2009. Bupropion and naltrexone were selected as the components of Contrave based on preclinical studies that showed their ability to both initiate and sustain weight loss when used together. In the NB-201 trial, Contrave, in the absence of a significant diet or exercise regimen, demonstrated weight loss at 48 weeks ranging from 8.0% to 10.7% across the three dosage groups among patients who completed the trial.

#### About Orexigen Therapeutics

Orexigen(R) Therapeutics, Inc. is a biopharmaceutical company focused on the development of pharmaceutical product candidates for the treatment of central nervous system disorders, including obesity. The Company's lead combination product candidates targeted for obesity are Contrave(R), which is in Phase III clinical trials, and Empatic(TM), which is in the later stages of Phase II clinical 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>.

#### Forward-Looking Statements

Orexigen cautions you that statements included in this press release that are not a description of historical facts are forward-

looking statements. Words such as "believes," "anticipates," "plans," "expects," "indicates," "will," "intends," "potential," "suggests," "assuming," "designed," "projects" and similar expressions are intended to identify forward-looking statements. These statements are based on the Company's current beliefs and expectations. These forward-looking statements include statements regarding enrollment, timing, execution and completion of clinical trials of Contrave, the timing of an NDA submission with the FDA for Contrave, the efficacy and safety of Contrave, the potential to obtain regulatory approval for, and effectively treat obesity with, Contrave, and the ability of Contrave to reduce obesity-related morbidity, including cardiovascular or diabetes risk. The inclusion of forward-looking statements should not be regarded as a representation by Orexigen that any of its plans will be achieved. Actual results may differ from those set forth in this release due to the risk and uncertainties inherent in the Company's business, including, without limitation: the progress and timing of the Company's Contrave clinical trials or the development of Contrave; the potential that earlier clinical trials may not be predictive of future results; the potential for adverse safety findings relating to Contrave to delay or prevent regulatory approval or commercialization, or result in product liability claims; Orexigen or its licensors may not be able to obtain, maintain and successfully enforce adequate patent and other intellectual property protection of its product candidates; and other risks described in the Company's filings with the Securities and Exchange Commission (SEC). You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof, and Orexigen undertakes no obligation to revise or update this news release to reflect events or circumstances after the date hereof. All forward-looking statements are qualified in their entirety by this cautionary statement. This caution is made under the safe harbor provisions of Section 21E of the Private Securities Litigation Reform Act of 1995.

SOURCE: Orexigen Therapeutics, Inc.

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