

Press Release

Orexigen and FDA Identify a Clear and Feasible Path to Approval for Contrave®

Interim Results from Outcomes Trial Would Support Resubmission of Contrave NDA

SAN DIEGO, Sept. 20, 2011 /PRNewswire via COMTEX/ -- Orexigen® Therapeutics, Inc. (Nasdaq: OREX) announced today that following a recent meeting with senior officials in FDA's Office of New Drugs (OND), the Company received written correspondence detailing OND's design requirements for a cardiovascular outcomes trial (CVOT) for Contrave® that would address the Complete Response Letter (CRL) received in January 2011. Orexigen believes that these design requirements are reasonable and feasible and provide the certainty required to reinitiate development of Contrave. Importantly, FDA stated that "if the interim analysis meets the specified criteria to exclude an unacceptable increased cardiovascular (CV) risk, the drug could be approved." Furthermore, FDA stated that "While we still plan to convene a public advisory committee meeting to discuss topics related to obesity drug development early next year, that meeting will not impact on the advice provided in this letter and the agency will honor the advice provided."

"We have been working with clinical experts, advocacy groups, and our partner, Takeda, throughout this process and are pleased with the feedback provided by FDA that identified a very clear and feasible path forward for this important therapy," said Michael Narachi, President and CEO of Orexigen.

The most important aspects of the CVOT design outlined by FDA include that the trial be powered based on an intent-to-treat analysis, along with criteria for interpreting the results at interim and final analyses that are similar to those that are applied to diabetes drugs. Specifically, FDA advised that the trial enroll a population of overweight and obese patients with an estimated background rate of 1.0-1.5% annual risk of major CV events. In this population, the upper bound of the 95% confidence interval should exclude a hazard ratio of 2.0 and 1.4 at the interim and final analyses, respectively. Both FDA and Orexigen estimate that such a study would require approximately 87 total events by the interim analysis to enable resubmission of the NDA for approval. Orexigen estimates that the entire study would require less than 10,000 patients and less than two years from study start to the interim analysis. The Company plans to meet with the review division to finalize a protocol with the objective of initiating the CVOT in the first half of 2012, with potential approval in 2014.

Based on this new feedback from FDA outlining a clear and feasible path forward for Contrave, the Company's three near-term priorities for the program are to: (1) finalize the trial protocol with FDA; (2) re-engage with parties that expressed interest in partnering the ex-North American markets for Contrave; and (3) implement the CVOT as soon as it is able.

"In my experience, Contrave demonstrated great potential for the treatment of obesity in a broad range of patients," said Ken Fujioka, MD, director of the Nutrition and Metabolic Research Center and The Center for Weight Management at the Scripps Clinic, and investigator for the Contrave Obesity Research Program. "On behalf of those working hard to address this significant unmet need, I am pleased to see that a pragmatic approach to bringing this therapy to market appears to be taking shape."

Orexigen management will host a conference call and webcast to discuss this update today at 4:30 p.m. Eastern time. The live call may be accessed by phone by calling (866) 730-5763 (domestic) or (857) 350-1587 (international), participant code 66064656. The webcast can be accessed live on the investor relations section of the Orexigen web site at <http://www.orexigen.com/> and will be archived for 14 days following the call.

About Contrave

Contrave, an investigational combination therapy of naltrexone HCl and bupropion HCl, was studied for its ability to help people with obesity initiate and sustain weight loss of at least 5 percent of their starting body weight in one year. Contrave was submitted for U.S. regulatory approval in March 2010. The original submission was based on multiple clinical trials that evaluated Contrave in more than 4500 patients. Orexigen received a Complete Response letter from FDA on January 31, 2011.

About Orexigen Therapeutics

Orexigen Therapeutics, Inc. is a biopharmaceutical company focused on the treatment of obesity. Contrave has completed Phase 3 clinical trials, and the Company's other product candidate, Empatic(TM), has completed Phase 2 clinical trials. Each of the components of the Company's product candidates has already received regulatory approval and has been commercialized previously. Further information about the Company can be found at www.orexigen.com.

Forward-Looking Statements Related to Orexigen

Orexigen cautions you that statements included in this press release and the conference call are not a description of historical facts and are forward-looking statements. Words such as "believes," "anticipates," "plans," "expects," "indicates," "will," "intends," "potential," "suggests," "assuming," "designed" 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: the study design for, and the timing and feasibility of, the CVOT; the potential for resubmission and approval of an NDA based on interim results of the CVOT; the prospects for ultimate approval of an NDA for Contrave; and the potential to complete a partnership or similar transaction for ex-North American rights to Contrave and maintain the Company's existing North American collaboration with Takeda Pharmaceuticals. 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 and the conference call due to the risk and uncertainties inherent in Orexigen's business, including, without limitation: Orexigen's ability to maintain and raise sufficient capital to fund the CVOT and maintain its other operations; the uncertainty of the FDA approval process, including requirements for additional clinical and non-clinical studies or other commitments prior to the submission and approval of an NDA for Contrave; Orexigen's ability to demonstrate that the risk of major adverse CV events in overweight and obese subjects treated with Contrave does not adversely affect the product candidate's benefit-risk profile; the potential for FDA's planned 2012 public advisory committee meeting on obesity drug development to result in additional NDA approval requirements for Contrave as well as post-approval commitments; Orexigen's dependence on Takeda Pharmaceuticals for aspects of the development and commercialization of Contrave; reliance on third parties to supply Contrave and assist with the development of Contrave and the regulatory submissions related thereto; the potential for adverse safety findings relating to Contrave; intense competition in the obesity marketplace and the potential for new products to emerge that provide different or better therapeutic alternatives for obesity and weight loss compared to Contrave; 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. Further information regarding these and other risks is included under the heading "Risk Factors" in Orexigen's Quarterly Report on Form 10-Q, which was filed with the SEC on August 8, 2011 and is available from the SEC's website (www.sec.gov) and on our website (www.orexigen.com) under the heading "Investor Relations". 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.

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