CLOSER LOOK

MEMORANDUM

Orexigen announces termination of recently initiated CVOT for Contrave (naltrexone/bupropion extended-release), CONVENE trial - April 18, 2016

Executive Highlights

- Last Friday, Orexigen released a Form 8-K, announcing that the company has terminated its recently initiated CVOT for Contrave (naltrexone/bupropion extended-release), the CONVENE trial. The company also received a letter from Nasdaq notifying that the company's common stock has fallen below $1.00 per share for 30 consecutive trading days.

Last Friday, Orexigen released a Form 8-K, announcing that the company has terminated its recently initiated CVOT for Contrave (naltrexone/bupropion extended-release), the CONVENE trial. This expected news follows Takeda's departure from the partnership in mid-March, as Orexigen stated that "the transfer of the recently-initiated, multi-year CONVENE cardiovascular outcomes trial from Takeda to the Company would involve substantial complexity due to the scope, size, and nature of the trial." The Form 8-K noted that the termination is the best route forward following "careful assessment," as the company "determined that the transfer of current clinical trial operations and systems may result in a significant interruption to study conduct and possibly data integrity." Orexigen stated that it notified the FDA of these changes and "specifically reaffirmed its commitment to meeting the post-marketing requirements for Contrave," including completion of a CVOT with a study report due to the Agency by January 2022. Moving forward, the company has stated that it will confer with the FDA and finalize a revised protocol and plans to start a new CVOT under its IND. Orexigen reported that it has notified the clinical trial sites of the termination decision and as of April 6, 2016, 13 of the 500 planned sites had randomized 58 participants (out of the planned 8,800) - a very small number.

As a reminder, this news marks the second CVOT Orexigen has terminated prematurely, after the Light Study ended early due to data integrity concerns after the release of interim data, while this most recent termination was driven by company politics between Orexigen and Takeda. We are not particularly surprised by this recent development, Orexigen is in a very challenging position with huge financial burdens surrounding the post-approval development costs.

- **Dr. Steven Nissen (Cleveland Clinic, OH) has shared that he is not optimistic about Orexigen fulfilling the FDA's post-marketing requirements anytime soon.** In addition, while the company terminated the trial relatively early on in the patient enrollment, Dr. Nissen criticized the time wasted on all the pre-trial efforts. This latest termination reminds us of the complexity of involving corporate interests in such regulatory activities - in our eyes, this second CVOT fallout is the ultimate result of a domino effect from Orexigen's prior interim data disclosure and ongoing tension with former partner Takeda regarding the trial as well as a challenging commercial enviornment.
- **While Orexigen has expressed confidence in starting a new CVOT, we feel that extreme modifications and compromises with the FDA will need to be made to fit within the company's current limitations.** With this recent development, the CVOT landscape for obesity drugs overall does not look promising, as Vivus' CVOT ACQLAIM for Qsymia (phentermine/topiramate extended-release) is also awaiting redesign conversations with the FDA. As we believe that obesity drugs are critical pieces of the obesity management toolkit, we very much hope that the FDA can address this post-marketing requirement with the appropriate regulatory oversight without removing patient-access to these treatment options for obesity.

- **On April 11, 2016, Orexigen also received a letter from Nasdaq notifying the Company that the company's common stock has fallen below $1.00 per share for 30 consecutive trading days**, and is therefore not in compliance with the minimum bid price requirement to be listed on Nasdaq. Things look challenging moving ahead, that is for certain.

-- by Melissa An, Sarah Odeh, and Kelly Close