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Press release

New 24-week clinical study strengthens the evidence of the therapeutic value of Zubsolv® (buprenorphine/naloxone) sublingual tablet for maintenance treatment of opioid dependence

Uppsala, Sweden – April 22, 2015 - Orexo AB today announced data from a 24-week clinical trial assessing the long-term safety and efficacy of Zubsolv® (buprenorphine/naloxone) sublingual tablet (CIII) for the maintenance treatment of opioid dependence. The results establish that Zubsolv is effective, well tolerated and demonstrated a safety profile consistent with the product labeling for sublingual buprenorphine products. In addition less than 1% of the patients exited the study due to treatment failure, which further underpins the medical value of Zubsolv. The results also demonstrated an increase of 15% in employment by the patients participating in the study, which further strengthen the evidence of the value of effective treatment of opioid dependence for the society.

"This study reinforces and further highlights the safety and effectiveness of Zubsolv. Over the course of six months, the safety profile of Zubsolv was consistent with previous buprenorphine studies and patient symptoms continued to improve. In addition, we were able to observe the benefits of long-term treatment with Zubsolv on work productivity. As patients continued on their path to recovery, they experienced positive gains for employment status, hours of work missed, number of hours patients were able to work, productivity, and impairment of daily activities", said Michael Sumner, Chief Medical Officer of Orexo.

Benefits of long-term treatment for patients on their journey to recovery

The primary objective of study OX219-008 was to assess the safety and tolerability of Zubsolv after an additional 24 weeks of treatment. The results from Study OX219-008, a multi-center, open-label, 24-week, follow-up study (N=665), establish that Zubsolv is well tolerated and effective for opioid dependent patients following six months of treatment. The safety profile was consistent with the product labeling for sublingual buprenorphine products.

The most common AE was constipation (2.9%) and no individual events were reported in ≥5% of patients. There was one serious adverse event (SAE) that was considered treatment-related (depression that started on Day 19 and ceased on Day 27) and 6 patients discontinued the study with AEs that were considered by the investigator to be possibly related to treatment.

Retention rates at Week 24 (end of study) were consistent with previous long-term clinical trials with buprenorphine. The retention rates at Weeks 4, 8, 12, 16, 20, and 24 (EOS) were 84.7%, 72.6%, 63.9%, 57.6%, 50.1%, and 43.9%, respectively. Opioid cravings were assessed on a 100 point

VAS where 0 represented “no cravings” and 100 represented “the most intensive craving” the patient had ever had. Craving scores continued to improve during the extension study. At baseline of the parent studies before treatment was initiated, the mean opioid craving score was 70.8 and, by Week 24, the mean score had been improved to 10.9 in patients who completed the study.

Health Economic Outcomes were assessed using the Work Productivity and Activity Impairment Questionnaire: Specific Health Problem assessment (WPAI:SHP). The WPAI:SHP assessed 7 items related to work productivity and impairment associated with opioid dependence. By the end of the study in week 24, 15% more patients were currently employed as compared to the parent study baseline. In addition, patients reported missing 4.8 fewer hours of work per week on average due to their opioid dependence. Mean hours actually worked per week increased by 4.6 hours per week from baseline. Patients also reported improvements in the degree to which their opioid dependence affected their productivity and daily activities.

Study OX219-008 was an extension of the ISTART (Study 006) and Study 007. Results from both of the parent studies have previously been released and can be found under the following **link**. The ISTART study showed Zubsolv was as effective as Suboxone® Film and more than 70 percent preferred Zubsolv after being exposed to both Zubsolv and Suboxone Film.

“The results of this extension study represent another addition to the already robust evidence base supporting Zubsolv as an effective and well tolerated maintenance treatment for patients struggling with opioid dependence. Zubsolv treatment supports opioid addicted patients in gaining control over their life and improves their ability to function in society, as evidenced by the higher employment rates at the end of the observation period concurrent with the demonstrated reduction in opioid cravings. Orexo’s investments in this follow-up study, and in planned future studies, demonstrate our continued commitment to advancing the treatment of opioid dependence for the patients suffering from this disease and providing effective and well tolerated therapies for physicians who treat them”, said Nikolaj Sørensen, Chief Executive Officer of Orexo.

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About Study OX219-008
Study OX219-008 was a multi-center, open-label, extension study in opioid dependent patients who had completed studies OX219-006 (ISTART) or OX219-007 to assess safety and efficacy for maintenance treatment of opioid dependence with Zubsolv. The primary objective was to assess the safety and tolerability of Zubsolv. Secondary objectives included retention in treatment, treatment effect on opioid withdrawal symptoms and opioid cravings, quality of life (QoL) and health economic outcomes (HEOs). Six hundred and sixty five patients entered the extension study (475 from the ISTART trial, 190 from Study 007).

The total study period for each patient was up to approximately 24 weeks from the Day 1 visit to the Week 24 (end of study [EOS]) visit. All patients included in this extension study had previously received at least 22 days of buprenorphine therapy in the parent studies. No treatment adjuncts were mandated during the study (e.g. counseling, psychosocial support, participation in 12‑step programs). Study 008 included 7 treatment visits where the first visit was the same day as the last study day in the parent studies (ISTART and OX219-007) with follow-up study visits every 4 weeks. Patients were maintained on the same dose of Zubsolv used in the previous studies. Patients who received Suboxone® Film on day 22 in the ISTART trial were switched to a corresponding dose of Zubsolv on Day 1. Zubsolv was individually titrated between 5.7/1.4 mg and 17.1/4.2 mg to a dose that relieved cravings and opioid withdrawal symptoms with minimal side effects. Dose adjustments were performed throughout the study as needed.

About the ISTART Trial

The ISTART Trial was a randomized, non-inferiority, multicenter study to assess early treatment efficacy of Zubsolv tablet versus Suboxone Film and to explore switching between treatments. The primary endpoints were retention in treatment at Day 15 and Day 3. Secondary efficacy assessments included scores on the COWS and SOWS, and opioid cravings VAS, CGI and PGI improvement from baseline, and switching between Zubsolv tablet and Suboxone Film. Seven hundred and fifty eight opioid dependent adult subjects were randomized. On days 1 and 2, patients received a blinded, fixed dose of Zubsolv (5.7/1.4 mg and 5.7/1.4 or 11.4/2.8 mg, respectively) or generic buprenorphine monotherapy (8 mg and 8 or 16 mg, respectively). On Day 3, the patients on generic buprenorphine were switched to Suboxone Film and patients in the Zubsolv tablet arm continued to receive Zubsolv. Stabilization doses were titrated to a maximum daily dose of 17.1/4.2 mg and 24/6 mg for Zubsolv tablet and Suboxone Film, respectively, based upon clinical symptoms.

About Zubsolv

Zubsolv (buprenorphine/naloxone) sublingual tablet (CIII) was approved by the U.S. Food and Drug Administration (FDA) on July 3, 2013, for maintenance treatment of opioid dependence and should be used as part of a comprehensive treatment plan, which includes counseling and psychosocial support. Treatment should be initiated under the direction of physicians who are certified under the Drug Addiction Treatment Act of 2000, and who have been assigned a unique identification number (“X” number).

Zubsolv sublingual tablets can be abused in a manner similar to other opioids, legal or illicit. Clinical monitoring appropriate to the patient’s level of stability is essential. Liver function tests should be monitored before and during treatment. Children who take Zubsolv sublingual tablets can have severe, possibly fatal, respiratory depression. Emergency medical care is critical. Zubsolv sublingual tablets should be kept out of the sight and reach of children.

Adverse events commonly observed with the sublingual administration of buprenorphine/ naloxone sublingual tablets during clinical trials and post-marketing experience are headache,

nausea, vomiting, hyperhidrosis, constipation, signs and symptoms of withdrawal, insomnia, pain and peripheral edema.

Further information on Zubsolv can be found at **www.zubsolv.com**.

Suboxone is a registered trademark of Reckitt Benckiser Healthcare (UK) Ltd.

About Orexo
Orexo is a specialty pharmaceutical company commercializing its proprietary product Zubsolv® for maintenance treatment of opioid dependence in the US. Zubsolv is an advanced formulation of buprenorphine and naloxone using Orexo's unique knowledge and expertise in sublingual drug delivery. R&D focuses on reformulation of known substances to new improved products that meet great unmet medical needs by using its patented proprietary technologies. Orexo's share is listed on Nasdaq Stockholm Exchange Mid Cap (STO: ORX) and is available as ADRs on OTCQX (ORXOY) in the US. Orexo's global headquarters and R&D are based in Uppsala, Sweden. **www.orexo.com**

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