**Press release**

# Orexo completes 1,080 patient REZOLV study and reports on improved treatment of opioid dependent patients

**Uppsala, Sweden, September 2, 2016** – Orexo AB (publ.) announces that the REZOLV retrospective study (Retrospective Evaluation of Zubsolv® Outcomes – A Longitudinal View) has been completed as planned in August. With 1,080 patients, the study is the largest retrospective study completed in the US aimed at optimizing the treatment of opioid dependence.

The opioid epidemic in the US continues to increase, and with recent legislative changes in the US that expand access to treatment, the current annual growth of nearly 9 percent of patients treated is expected to accelerate significantly. During the past 3 years, Orexo has identified a substantial lack of real-world clinical outcome data on treatment of opioid dependence with buprenorphine-based treatments such as Zubsolv (buprenorphine and naloxone) sublingual tablet (CIII). REZOLV was undertaken as an opportunity to inform physicians, payers and patients about factors that may positively impact treatment outcomes when using Zubsolv for the treatment of opioid dependence.

Overall the study was a success, with 978 of the 1,080 patients in total confirmed as being evaluable for treatment efficacy. From the patients evaluable for treatment, 77.6 percent (n=759) were determined to have been a treatment success, defined as a patient who completed 28 days of treatment and tested negative for opiates on the last follow-up drug screen.

To enable physicians and payers to define the optimal treatment plan of each patient treated with Zubsolv, the REZOLV study offers the largest existing clinical database. The data from the REZOLV study can assist in identifying and rationalizing some of the important factors associated with successful treatment of opioid dependence. Amongst such factors identified, the REZOLV study indicated that positive treatment outcome was related to:

- Patients who were older (>50 years, n=101) had a treatment success of 88.1 percent compared 73.8 percent of patients aged 20-30 years
- Patients who had support of a spouse or a partner (n=315) had a higher treatment success of 83.5 percent, compared to 75.2 percent for patients without a partner
- Patients who were employed (n=534) showed a higher rate of treatment success compared to those who were unemployed (n=444), with rates of 81.5 percent and 73,0 percent, respectively
- Patients who were abusing heroin (n=358) had a treatment success of 69.6 percent and patients injecting opioids (n=235) showed a treatment success of 65.5 percent, indicating an increased risk of treatment failure

- Previous history of failed treatment (n=460) had a negative impact on the treatment success with 72.2 percent succeeding compared to 84.7 percent of patients with Zubsolv® as their first treatment (n=458)
- Treatment success was not impacted by the experience of the physicians or whether they were Board certified in addiction treatment.

The study results have generated an extensive amount of clinical data that Orexo will use in its dialogues with key stakeholders, including physicians, prescribers, politicians and payers, on how to advance the treatment of opioid dependence. The completion of the REZOLV study further strengthens Orexo's position as the market player with the most substantial clinical database, as a result of its substantial investments into documenting how treatment of opioid dependence may be optimized.

"The finalization of the REZOLV study is one more important milestone we have reached during the summer. In June we signed an ex-US license agreement with Mundipharma, followed by new legislation in the US with the potential to significantly improve access to treatment with Zubsolv and now we have finished the REZOLV study," says Nikolaj Sørensen, CEO and President, Orexo AB. "We have seen a positive uptake in the use of Zubsolv in the US this summer, and with the REZOLV study we strengthen our ability to engage with physicians and payers in optimizing and improving access to treatment of opioid dependence. With the extensive clinical data we can also improve education of new and existing prescribers and thereby enable them to improve their treatment programs for opioid dependence with Zubsolv," Nikolaj Sørensen continues.

**For more information please contact:**

**Orexo AB (publ.)**
Nikolaj Sørensen, CEO and President
Tel: +46 (0)18 780 88 00
Email: ir@orexo.com

**About Orexo**

Orexo is a specialty pharmaceutical company commercializing its proprietary product Zubsolv for 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 is focusing 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.

For information about Orexo please visit **www.orexo.com** or follow us on Twitter**, @orexoabpubl.**

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**About REZOLV**

The REZOLV study was a medical record review conducted to examine and characterize the impact of treatment and psychosocial factors on the early outcomes of patients who utilized Zubsolv® therapy for opioid dependence. The data was collected from 1,080 patients being treated by 134 physicians across 87 US treatment sites of which 80 were private practices and 7 were institutional sites. The data collected included a profile of the medical practice and the treating physicians at each site, in addition to the scope of addiction treatment services and treatment standards employed. Individual patient data included demographics, medical, psychosocial and drug abuse histories, along with details of the individual addiction treatment program and progress over the first 28 days of therapy with Zubsolv or up to the point of discontinuation.

Of the 1,080 total patients from which information was gathered, 978 were confirmed to be evaluable for treatment. Evaluable patients were defined as those who had completed 28 days of Zubsolv treatment and had a follow-up drug screen, or completed less than 28 days of treatment due to non-compliance, had requested a change in medication, or required a higher level of care. From the patients evaluable for treatment, 77.6 percent (n=759) were determined to have been a treatment success, defined by an evaluable patient who completed 28 days of treatment and tested negative for opiates on the last follow-up drug screen.

**About Zubsolv in the US**

Zubsolv (buprenorphine and naloxone) sublingual tablet (CIII) is indicated for the 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. Keep Zubsolv sublingual tablets 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.

To read more about Zubsolv in the US, please visit: **www.zubsolv.com** and **www.outthemonster.com**.

**Important Safety Information, Zubsolv® in the US**

Keep Zubsolv in a secure place away from children. If a child accidentally takes Zubsolv, this is a medical emergency and can result in death. Get emergency help right away.
Zubsolv can cause serious and life-threatening breathing problems. Call your doctor right away or get emergency help if (a) you feel faint, dizzy, or confused; (b) your breathing gets much slower than is normal for you; (c) you feel sleepy and uncoordinated; (d) you have blurred vision; (e) you have slurred speech; (f) you cannot think well or clearly; or (g) you have slowed reflexes and breathing. In an emergency, have family members tell the emergency department staff that you are physically dependent on an opioid and are being treated with Zubsolv.

The most common side effects of Zubsolv include: headache, drug withdrawal syndrome, nausea, decrease in sleep (insomnia), vomiting, pain, increased sweating, swelling of the extremities, and constipation. Tell your doctor about any side effect that bothers you or that does not go away
Do not switch from Zubsolv to other medicines that contain buprenorphine without talking with your doctor. The amount of buprenorphine in a dose of Zubsolv is not the same as the amount of buprenorphine in other medicines that contain buprenorphine. Your doctor will prescribe a starting dose of buprenorphine that may be different than other buprenorphine-containing medicines you may have been taking.

Zubsolv contains an opioid that can cause physical dependence. Do not stop taking Zubsolv without talking to your doctor. You could become sick with uncomfortable withdrawal signs and symptoms because your body has become used to this medicine. Physical dependence is not the same as drug addiction. Zubsolv is not for occasional or "as needed" use.

An overdose, and even death, can happen if you take benzodiazepines, sedatives, tranquilizers, or alcohol while using Zubsolv. Ask your doctor what you should do if you are taking one of these. You should not drink alcohol while taking Zubsolv, as this can lead to loss of consciousness or even death.

Do not inject ("shoot-up") Zubsolv. Injecting Zubsolv may cause life-threatening infections and other serious health problems. Injecting Zubsolv may cause serious withdrawal symptoms such as pain, cramps, vomiting, diarrhea, anxiety, sleep problems, and cravings

Before taking Zubsolv, tell your doctor about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements

Before taking Zubsolv, tell your doctor if you are pregnant or plan to become pregnant. It is not known if Zubsolv will harm your unborn baby. If you take Zubsolv while pregnant, your baby may have symptoms of withdrawal at birth. Talk to your doctor if you are pregnant or plan to become pregnant

Before taking Zubsolv®, tell your doctor if you are breastfeeding or plan to breastfeed. Zubsolv can pass into your breast milk and may harm the baby. Talk to your doctor about the best way to feed your baby if you take Zubsolv. Monitor your baby for increased sleepiness and breathing problems

Do not drive, operate heavy machinery, or perform any other dangerous activities until you know how Zubsolv affects you. Buprenorphine can cause drowsiness and slow reaction times. This may happen more often in the first few weeks of treatment when your dose is being changed, but can also happen if you drink alcohol or take other sedative drugs when you take Zubsolv.

Zubsolv is a controlled substance (CIII) because it contains buprenorphine, which can be a target for people who abuse prescription medicines or street drugs. Keep your Zubsolv in a safe place to protect it from theft. Never give your Zubsolv to anyone else; it can cause death or harm them. Selling or giving away this medicine is against the law.

To report negative side effects associated with taking Zubsolv, please call 1-888-982-7658. You are encouraged to report negative side effects of prescription drugs to the FDA.
Visit **www.fda.gov/medwatch** or call 1-800-FDA-1088.

Please see full **Prescribing Information** and **Medication Guide** for Zubsolv**.**

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