



Press release

Positive results from human PK study assessing Orexo's intranasal nalmefene formulations for opioid overdose reversal

- *Preliminary data indicate extensive and rapid absorption of OX125 across all formulations*
- *Positive results underline the applicability of Orexo's novel intranasal drug delivery platform*

Uppsala, Sweden - June 30, 2020 - Orexo AB (publ.), (**STO:ORX**) (**OTCQX:ORXOY**), today announces positive results from its human pharmacokinetic (PK) study of OX125. The study was a cross-over, comparative bioavailability study in healthy volunteers to assess nalmefene absorption from three development formulations of OX125, Orexo's wholly-owned nasal nalmefene product, compared to a nalmefene intramuscular injection. Preliminary results indicate extensive and rapid absorption across all three OX125 formulations as well as good tolerability, supporting the viability of OX125 as a rescue medication for opioid overdose.

Highly potent synthetic opioids, such as fentanyl, have become the leading cause of death following drug overdoses in the US with over 31,000 fatalities in 2018.¹ Like naloxone, nalmefene is an opioid antagonist that acts by blocking the effects of opioids at the opioid receptors. Nalmefene also has a longer half-life than naloxone, giving an extended duration of the opioid blockade. Therefore, nalmefene could be an effective response to the increased use of potent, long-acting synthetic opioids such as fentanyl. The longer-acting properties of nalmefene may also be of particular value to protect against renarcotization (second overdose), as the antagonist wears off.

Robert Rönn, VP and Head of R&D, at Orexo, said: "I am pleased with the results from this important clinical study as well as the timely delivery from Orexo's R&D team. This is not only a proof-of-concept for our wholly-owned OX125 product, but also a demonstration of the value of our novel nasal technology platform. We will now set forth to engage with US Food and Drug Administration, FDA, to identify the optimal route to market."

"As the US heroin crisis has developed to a fentanyl crisis, the medical need for novel and more powerful opioid rescue medications is vast. The need has also escalated further due to the COVID-19 pandemic as the consequences of social distancing and economic weakness are expected to lead to a significant increase in mental health issues and substance use disorders. Alongside OX124, our naloxone rescue project, OX125 will be an important lifesaving addition in our commitment to helping patients suffering from opioid addiction in all phases. I am encouraged by the results from our R&D team and look forward to the continued development of this pharmaceutical product." **said Nikolaj Sørensen, President and CEO.**

¹ National Institute of Drug Abuse



The addressable market for OX125 and OX124 is large and growing as demand for easy to use, potent overdose reversal medication increases, not only for emergency staff and first responders, but also for opioid dependent patients, and as co-prescription for high-dose opioid pain patients. According to Orexo's estimates, greater levels of co-prescriptions and expanding access for opioid dependent patients may increase the market size from today's USD 300-500 million to USD 1.5-2 billion. The combined estimated sales potential for OX125 and OX124 amounts to USD 110-170 million five years post launch, where the majority refers to OX124.

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About Orexo

Develops improved pharmaceuticals and digital therapies addressing unmet needs within the growing space of substance use disorders and mental health. The products are commercialized by Orexo in the US or via partners worldwide. The main market today is the American market for buprenorphine/naloxone products, where Orexo commercialize its lead product Zubsolv® for treatment of opioid use disorder. Total net sales for 2019 amounted to SEK 844,8 million and the number of employees was 127. Orexo is listed on the Nasdaq Stockholm Mid Cap (ORX) and is available as ADRs on OTCQX (ORXOY) in the US. The head office, where research and development is also performed, is situated in Uppsala, Sweden.

For more information about Orexo please visit, www.orexo.com. You can also follow Orexo on Twitter, [@orexoabpubl](https://twitter.com/orexoabpubl), LinkedIn and YouTube.

About OX125

OX125 is a nasal nalmefene rescue medication under development by Orexo. The substance is a full opioid receptor antagonist that reverses the effects of opioid agonists, including the life threatening respiratory depressant effects occurring in an opioid overdose. Nalmefene is a more potent and longer acting antagonist compared with naloxone that may increase the possibility of survival for specific target groups. OX125 is based on Orexo's nasal technology platform developed to provide rapid and effective absorption of drug substances through the nasal mucosa.



About OX124

OX124 is based on a novel and unique technology developed to provide a rapidly acting naloxone rescue medication with the aim to provide differentiated profile compared to currently marketed products and other products under development. Naloxone is a full opioid receptor antagonist which reverses the effects of opioid agonists, including the life threatening respiratory depressant effects occurring in an opioid overdose.

Results from the exploratory PK-study in healthy volunteers showed substantially higher plasma concentrations of naloxone, sustained duration of elevated plasma concentrations, and equivalent or superior onset time, when compared to the market leading product.

The information was submitted for publication, through the agency of the contact persons set out above, at 8.00 am CET on June 30, 2020.