Press release

Orexo's flagship pharmaceutical pipeline asset OX124 enters pivotal trial

- **The first cohort of healthy volunteers has been dosed. New Drug Application (NDA) filing expected in the second half of 2022.**
- **OX124 is designed to reverse the effect of overdoses caused by the most powerful synthetic opioids that today are behind the vast majority of fatal overdoses in the US**
- **Upon approval Orexo will along with ZUBSOLV® and modia™ have the most comprehensive range of treatment options for people suffering from opioid use disorder on the US market**

Uppsala, Sweden – July 16, 2021 – Orexo AB (publ.), **(STO:ORX) (OTCQX:ORXOY)** today announces that the company has successfully initiated the pivotal trial (OX124-002) for its lead pharmaceutical pipeline asset, OX124. The first cohort of healthy volunteers has been dosed on July 15, 2021.

OX124 is a powerful naloxone rescue medication, designed to reverse opioid overdoses, including those from highly potent synthetic opioids, such as fentanyl. To meet the target profile for more potent rescue medications, Orexo has developed a novel and unique intranasal formulation technology that allows for rapid and efficient delivery of active ingredients through the intranasal route.

The use of synthetic opioids is the leading cause of death in fatal overdoses in the US, a trend that has seen further acceleration in the wake of the Covid-19 pandemic. For the full year of 2020, the number of overdose deaths surpassed 92,000 for the first time in history, an increase of 30 percent versus the previous year. Approximately 75 percent of these deaths were caused by opioids, and within the opioid-related deaths, synthetic opioids accounted for the vast majority,[1] underlining the need for more powerful and faster-acting rescue medications.[2]

The pivotal trial OX124-002 is a 4-period cross-over, comparative bioavailability study in healthy volunteers, comparing two dose regimens of OX124 to two dose regimens of an injection reference product. The study is intended to be the primary support for the OX124 New Drug Application in the US. Initial study results are expected in Q4 2021, and if successful, Orexo is expecting to file OX124 with the US Food and Drug Administration in the second half of 2022.

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[1] All numbers are taken from https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm

[2] N Volkow "Scientific Solutions for the Opioid Crisis" (2018) https://www.nichd.nih.gov/sites/default/files/2018-01/201801_volkow_nichd_opioids.pdf

In a previous exploratory clinical study (OX124-001) in healthy volunteers, OX124 showed more rapid absorption, substantially higher plasma concentrations of naloxone, and sustained duration of elevated plasma concentrations when compared to the current market leader.[3]

Nikolaj Sørensen, President and CEO of Orexo AB, said: *"The initiation of our pivotal trial for OX124 is an important milestone and I am looking forward to making this life-saving medication available to millions of patients in need as swiftly as possible. Together with ZUBSOLV® and our new digital therapy modia™ for opioid use disorder, Orexo will soon be the company offering the most comprehensive range of treatment options for patients suffering from opioid addiction in the US and continue to be at the forefront of fighting this devastating disease."*

The addressable market for 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. If the project progresses according to the current plan, the US launch can take place in 2023. If approved, OX124 is estimated to have a sales potential of USD 70 - 110 million.

Costs related to the final development and which apply to the current financial year are included in the company´s OPEX guidance for 2021.

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About Orexo

Orexo develops improved pharmaceuticals and digital therapies addressing unmet needs within the growing space of substance use disorders and mental illness. The products are commercialized by Orexo in the US or via partners worldwide. The main market today is the US market for buprenorphine/naloxone products, where Orexo commercializes its lead product, ZUBSOLV®, for treatment of opioid use disorder. Total net sales for Orexo in 2020 amounted to SEK 664 million and the number of employees was 138. Orexo is listed on the Nasdaq Stockholm Mid Cap (ORX) and is available as ADRs on OTCQX (ORXOY) in the US. The company is headquartered in Uppsala, Sweden, where research and development activities are performed.

[3] https://orexo.com/investors/regulatory-press-releases/2019-01-07-positive-results-from-human-pk-study-assessing-orexo-s-new-intranasal-naloxone-formulations-for-opioid-overdose-reversal

For more information about Orexo please visit, **www.orexo.com**. You can also follow Orexo on Twitter, @orexoabpubl, LinkedIn and YouTube.

The information was submitted for publication at 8.00 am CET, on July 16, 2021.