Press release

Orexo announces data from the MODIA® study evaluating impact on use of illicit opioids

- The six-month randomized controlled trial (RCT) enrolled 437 participants at 36 sites across the US
- The study demonstrated no statistically significant difference between treatment arms in any pre-specified endpoint
- Both treatment arms had unexpectedly high rates of treatment response, with no adverse events associated with the use of MODIA
- A post hoc analysis found that patients completing all 24 modules of MODIA had a significantly higher treatment response than those who did not complete the entire program
- Orexo will continue to commercialize MODIA as a mobile medical device subject to FDA enforcement discretion

Uppsala, Sweden – **October 11, 2023** – Orexo AB (publ.), **(STO:ORX) (OTCQX:ORXOY)**, today reports top line results after having completed a study evaluating the efficacy of MODIA in combination with sublingual buprenorphine/ naloxone for the treatment of opioid use disorder (OUD) and reduction in use of illicit opioids. The study had unexpectedly high treatment response rates for both treatment arms, with no statistically significant difference in treatment response in the full population. No adverse events associated with the use of MODIA were reported.
An exploratory analysis of patients randomized to MODIA found that those who completed all 24 modules had a significantly higher rate of treatment response than those who did not complete the entire program.

A comprehensive Medication-Assisted Treatment (MAT) approach that combines medications for OUD with psychosocial support is recommended for optimal outcomes. Education of patients with OUD is critical to help them understand their disease, their treatment, and strategies to support their recovery.[1] As a browser-based digital program that can be accessed remotely at any time, MODIA provides flexible access to educational content and exercises that are based on cognitive behavioral therapy principles.

The study was a randomized, open-label, parallel-group study, enrolling patients aged 18 to 65 across the US who voluntarily sought treatment for documented moderate to severe OUD. Participants were inducted and stabilized on buprenorphine/naloxone during a brief screening

[1] American Society of Addiction Medicine*: J Addict Med*. 2020 Mar/Apr;14(2S Suppl 1):1-91. doi: 10.1097/ADM.0000000000000633.

period, then evaluated during weekly visits over the course of 24 weeks, with a primary endpoint defined as the subject having ≥80 percent of urine drug tests negative for illicit opioids and negative self-reports for illicit opioid use during the final 20 weeks of the study. Patients were randomized to receive weekly medication management i.e., background study care (BSC), or BSC in addition to MODIA. Subjects were compensated for attending study visits.

The study enrolled 437 patients at 36 centers across the US. Study completion rates were similar (55% BSC, 52% MODIA), as were treatment response rates (32% BSC, 31% MODIA). There was no statistically significant difference between treatment arms in any pre-specified endpoint of the study. These unexpectedly high treatment response rates exceeded those of similarly designed trials of long-acting injectable buprenorphine, which had 18 and 24 study visits (17% and 29%, respectively)[2,3].

An exploratory analysis of the 219 patients randomized to MODIA who subsequently completed the entire study (n=114), found that the 61 patients that completed all 24 modules of MODIA had a significantly higher treatment response rate of 61% than those that did not complete the entire program (n=53), who had a treatment response rate of 38% (p=0.0146). The difference in treatment response rate emerged after completion of 12 modules. In addition, the study showed indications of improved psychosocial outcome for those who completed MODIA which will be explored further in continued post hoc analysis.

MODIA is designed to educate patients on behavioral changes that can support their recovery journey, and to empower them with techniques to help them cope with the challenges of everyday life. To support the patients' healthy recovery, adherence to the program is important and Orexo will work with the developer of MODIA, GAIA AG to add functionality to MODIA to further improve adherence.

In the study 38% of patients reported at least one adverse event. Overall reporting of adverse events was similar between treatment arms, and no adverse events associated with the use MODIA were reported.

Nikolaj Sørensen, President and CEO of Orexo AB, said:
"Addressing the unmet need for psychosocial support in the treatment of OUD patients is part of our commitment to the treatment community. This study had a surprisingly positive treatment outcome in both arms compared to previous studies with similar designs and care as usual. To meet the requirements of the authorities of weekly tests for illicit drugs, our study compensated patients for attending weekly visits, which does not reflect typical care for OUD. Both frequent medication visits and compensation to patients can improve treatment response rates[4,5]. For MODIA we saw

[2] Lofwall MR et al, *JAMA Intern Med*. 2018;178(6):764-773. doi:10.1001/jamainternmed.2018.1052
[3] Haight BR et al, *Lancet.* 2019:393:778-790. doi:10.1016/S0140-6736(18)32259-1
[4] Carroll KM et al. *Am J Psychiatry* 2017;174:738-747. doi:10.1176/appi.ajp.2016.16070792
[5] Galanter M et al, *Am J Addictions* 2020;29:271-278

indications that the benefits from the therapy increased with completion of the entire program, and we remain enthusiastic about the potential for MODIA to support patients with OUD in their recovery journey."

The company will continue to commercialize MODIA with limited changes as a mobile medical device subject to FDA enforcement discretion following the expected expiration of the COVID Public Health Emergency Guidance in November 2023. Under enforcement discretion MODIA will be positioned as a supportive resource for patients undergoing a clinician-directed treatment, rather than as a physician-prescribed treatment regimen. The study results indicate there is high value in the combination of high frequency interactions with health care providers and completion of the MODIA program, as well as MODIA's strong safety profile. The company is continuing to analyze the study data and will continue to collect data to show the value of MODIA in supporting the patients with OUD to get their lives back.

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About MODIA
MODIA is a web-based software program intended to help OUD patients develop behavioral coping skills and provide educational information, reminders, and motivational guidance. MODIA is intended for use by patients engaged in a clinician directed Medication-Assisted Treatment (MAT) plan for OUD. In addition, MODIA supports users as they work with their clinician on a recovery plan based on the responses collected from the exercises throughout the program. Orexo owns the global commercial rights to MODIA.

About Orexo
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 American market for buprenorphine/naloxone products is the largest, where Orexo commercializes its lead product ZUBSOLV® (buprenorphine and naloxone) sublingual tablets (CIII) for treatment of opioid use disorder. Total net sales for 2022 amounted to SEK 624 million and the number of employees was 126. Orexo is listed on the Nasdaq Stockholm Main Market (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.

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

The information in the press release is information that Orexo is obliged to make public pursuant to the EU Market Abuse Regulation. The information was sent for publication, through the agency of the contact person set out above, on October 11, 2023, at 8 am CET.