

SOCIAL FINANCING FRAMEWORK

February 2024



1. Introduction

Orexo in brief

Orexo AB (publ) (“**Orexo**” or the “**Company**”) is a Swedish pharmaceutical company with over 25 years of experience developing improved pharmaceuticals based on proprietary formulation technologies that meet large medical needs. On the US market, Orexo provides innovative treatment solutions for patients suffering from opioid use disorder (OUD) and adjacent diseases or conditions, such as mental illness. Products targeting other therapeutic areas are developed and commercialized worldwide via leading partners.

The opioid crisis is one of the largest health crises in the US in modern times – an epidemic with wide social and economic implications for societies. Orexo’s core commitment is to improve the life of people suffering from OUD with pioneering and holistic treatment solutions – working broadly at both federal and local level in the US to give more people access to treatment options.

Orexo’s treatments of OUD include maintenance treatment with Zubsolv®, a digital mental health program through MODIA® and soon, the opioid overdose rescue medication, OX124. OX124 contains a high dose of naloxone and is developed to revive people who have overdosed using the potent synthetic opioids, which causes a majority of all overdoses today. As the use of synthetic opioids increases, the need for more long-acting rescue medications also increases. If the market is not saturated with high dose alternatives like OX124, or need to be complemented, Orexo will advance OX125 which is a more long-acting rescue medication, compared to OX124, based on nalmefene.

Orexo’s new products are formulated based on a new nasal power technology and the drug delivery platform, AmorphOX®, developed by Orexo. AmorphOX can ensure fast effect of the medication, which is critical in life saving rescue medications, and it enhances the stability of the product which means that the products work independent on storage conditions (i.e., cold, warm). Further, the technology is also applicable on other products such as vaccines where it can help reducing the need for controlled temperature storage and refrigeration, which can help expanding the access to medication for people living in rural areas and in developing countries.

Orexo’s sustainability strategy

Orexo’s business strategy and how it is operationalized during day-to-day work is shaped by the Company’s Code of conduct. The strategy supports Agenda 2030, the Sustainable Development Goals and is aligned with international standards and well-known initiatives, including the International Labor Organization Conventions, and the UN Guiding Principles on Business and Human Rights.

Orexo has also been a participant in the UN Global Compact since 2017, and its strategy aligns with both UN principles and the SDGs. SDG target 3: “Good health and well-being”, and in particular target 3.5: “Strengthen the prevention and treatment of substance abuse, including narcotic drug abuse and harmful use of alcohol” continue to be core to Orexo’s business. Further details are shared in the Responsible business section and in each of the focus areas.

Responsible business based on trust, transparency, integrity and no tolerance for corruption is central in all Orexo’s activities and a foundation for the Company’s sustainability work

Reduce the impact on **environmental and climate change** across all activities and within the portfolio

Increase **access to healthcare** by patient support and strengthening knowledge in substance abuse and mental illness

In **all Orexo’s teams**, create a healthy working climate where inclusion and diversity are a matter of course

About the market and the unmet need

Substance use disorder and mental illness cause large human suffering and bring with it substantial social and economic consequences. Globally, 284 million people are misusing drugs, a surge of 26% since 2010.¹

By working to increase access to healthcare and offering an advancing treatment portfolio, Orexo is contributing to combating the widespread opioid crisis in the US, and via its partners in Europe. In the US around 8.9 million people are misusing opioids, 6.1 million people are dependent on opioids and 2.4 million people are undergoing medication assistant treatment.² The US opioid crisis has continued to accelerate due to the prevalence of synthetic opioids, especially illicit fentanyl. Fatal overdoses have reached record-high levels, and the number exceeds 111,000 annually.³ Overdoses caused by opioids counts for approx. 76%, of which nine out of ten involve synthetic opioids such as illicit fentanyl.⁴

The treatment of substance use disorder and mental illness has for a long time been an area that has not attracted pharmaceutical companies in the same way as the treatment of cancer, cardiovascular diseases, and diabetes, for example. For over a decade, treatment of OUD has been Orexo's main therapeutic area, which in recent years has broadened to also help patients suffering from mental illness, such as depression and alcohol misuse.

Orexo is established in the US since 2013 and develops drugs that combines well-known substances with their own developed formulation technologies. A new drug typically takes three to five years to develop, and the Company's operations are focused within the fields of mental illness and in particular, substance use disorder. To support the patients in their recovery and improve treatment results, Orexo also works with digital mental health programs.

In addition, the Company has developed an emergency medication for allergic reactions to broaden its portfolio of rescue medications. At present there are between 26-45 million people at risk of a severe allergic attack in the US alone.⁵ Current allergic rescue products are needle-based autoinjectors that administer epinephrine to reverse life-threatening reactions (anaphylaxis). Whether self-administered or with the help of others, applying needle injections correctly is often intimidating, with the potential loss of precious life-saving minutes. Existing solutions are expensive, and devices must be replaced frequently because epinephrine rapidly degrades during storage. Orexo will strive to bring to market a needle-free, reliable and effective intranasal product, with the potential for doubling the stability and shelf-life of current solutions. Additionally, the single-dose nasal administration is easy to use, easy to teach others and easy to learn for caregivers.

There is an extensive treatment need:

➤ Opioid use disorder

8,900,000

Americans are misusing opioids²

6,100,000

are dependent on opioids²

2,400,000

are undergoing MAT treatment²

➤ Allergies

Up to 45,000,000

Americans at risk of a severe allergic attack⁵

1) Climate change and health (who.int)

2) Substance Abuse and Mental Health Services Administration 2021 NSDUH report

3,4) Center of Disease Control and Prevention

5) Prevalence and Severity of Food Allergies Among US Adults - PMC (nih.gov)

Target Group

Orexo's portfolio consists of pharmaceutical products, and digital mental health programs and the Company's development pipeline comprises rescue medications based on the AmorphOX platform. The Company's main mission is to improve the lives for people suffering with opioid dependence, but also closely related diseases or conditions such as mental health issues. Orexo also goes beyond these therapeutic areas where its formulation technologies can improve drugs, such as for the treatment of severe life-threatening allergies.

The purpose of this Social Financing Framework is to secure a high level of disclosure and transparency on the funding needed to facilitate Orexo's continuous mission to develop and launch essential life-saving medicines and treatment for their vulnerable and underserved lead target group – patients suffering from OUD.

Substance use disorders, incl. OUD, is a chronic relapsing brain disease affecting the reward, memory and motivation systems of the brain. It is caused by substances such as drugs, alcohol and nicotine. The reasons for developing an addiction are wide-ranging, but genetic factors are thought to account for a large part of a person's vulnerability to developing an addictive behaviour. Environmental factors such as exposure to drugs also plays a part.

The co-morbidity rate between mental illness and substance abuse is high, where 25% of people suffering from a serious mental illness also have a substance use disorder.⁶ Reversely, 17% of people with substance use disorder also suffers from a serious mental illness⁷, such as anxiety, depression, schizophrenia, PTSD, ADHD or bipolar disorder. A RESOLV study made by Orexo in 2016 showed that 32% of the patients with substance use disorder were also diagnosed with co-existing depressive disorder (which is just one mental illness).

For people with severe allergies, epinephrine is commonly used for the emergency treatment of allergic reactions, including anaphylaxis. Epinephrine is however an unstable active ingredient sensitive to chemical degradation, which gives them a limited shelf-life with restrictive handling and storage. Orexo has developed a powder-based nasal technology with excellent chemical and physical stability. It is therefore more flexible in how it's handled and stored, and from a social point of view it spares patients from additional pain as the treatment is needle-free. In addition, the medicine will suit very well in emerging markets as not cold chains are needed for storage.

Accessibility

The main treatment method for opioid use disorder is medication assisted treatment (MAT) which is a combination of a buprenorphine/naloxone and psychosocial support. Access to MAT is limited and Orexo is working actively to improve access through education of physicians and working with stakeholders to improve funding and reduce hurdles for physicians to offer MAT. Orexo works continuously with accessibility through a market access team, the sales force, insurance companies, private practitioners, clinics, hospitals and through partnerships.

To improve treatment results, MAT should be combined with psychosocial support. A lack of psychologists and counsellors could entail that patients do not get the opportunity to go to the root with what caused their dependence.

Orexo has therefore several digital mental health programs that can be used anywhere and 24 hours a day, to manage addiction, depression or alcohol misuse. The therapies can be taken standalone or along with medication. The programs is based on cognitive behavioural techniques and enables the provision of psychosocial support to a much broader patient group, many of which are living in rural areas.

Orexo is also collaborating with a partner to offer these programs within Veterans Affairs (VA). If successful, millions of veterans and their family members can get access to psychosocial support to help them overcome their mental health issues, including addiction, depression or alcohol misuse.

Further improved access to care

There is a long history of under-investment in treatments for substance use disorder. Clinicians sometimes do not take insurance due to burdensome paperwork and low reimbursement, leading to larger levels of unmet needs. Access to MAT has long been limited, as physicians need to undergo extensive training to be licensed to treat patients and there has been a limitation on how many one physician can treat.

New legislation passed in December 2022 has the potential of making a huge difference for this underserved patient group, as the cap for how many patients a physician can treat is eliminated. To push boundaries to unlock the accessibility to medications, regardless of who is making them, Orexo also works along with policy makers, advocates, and other stakeholders at federal and state levels, including local community groups.

Affordability

In general, the buprenorphine/naloxone market in the US grew by 4% in 2023. The growth primarily took place in the largest payer segment, the **Public payer segment**, where care is financed by the State and Federal payers such as Managed Medicaid, FFS Medicaid and Medicare Part D. Care. Treatment financed by private insurance companies (**Commercial payer segment**), often signed by employers, showed a slower growth rate by comparison. The market is dominated by generic medications with buprenorphine/naloxone and is characterized by high price sensitivity.

Within the Commercial payer segment, 98% of patients will receive reimbursement if they get Zubsolv prescribed by their physician.

For the Public payer segment, the corresponding figure is 50%, an increase from 30% a few years ago. In recent years, the Company has increased its focus on the Public segment. As a result, the share of patients under the Medicaid plans who can get Zubsolv reimbursed has increased and sales towards patient with a Medicaid insurance plan (public insurance) has also increased.

Orexo has financial patient support programs in place for the financially vulnerable patients for Zubsolv and intends to expand this program to cover digital mental health programs and future pharmaceuticals (such as OX124). The existing three financial patient support programs includes:

The **first** is offered to people living below three times the US federal poverty level without any other financial coverage of their medication. The program will cover the full cost of Zubsolv for six months and can be extended if the patient still meet the inclusion criteria after six months.

The **second** is the Zubsolv Co-pay assistance program which saves patients significant costs for Zubsolv. This program is intended for patients without insurance or with a private health insurance and will cover up to USD 225 of the price per prescription.

The **third** is Zubsolv's 15 tablet voucher program which is a program that provides up to two free 15 tablet vouchers. The program is available for all patients and is intended to cover the time between the patient is diagnosed and the insurance company has approved the patient is eligible for reimbursement.

With regards to OX124, Orexo will have financial support programs in place to reduce the out-of-pocket cost for eligible patients, including the most financially vulnerable people. The Company will also conduct volunteering through community organizations, which among others include harm reduction organizations.

Similar to Zubsolv, the main cost of OX124 for patients will be dependent on access to reimbursement of OX124 by the public- and private insurance companies. Orexo will work intensively to ensure that all patients have access to reimbursement for OX124, independent of their health insurance.

Moreover, Orexo's digital mental health programs will also be covered by patient support programs. In addition, this product category might also become reimbursed by insurance companies which would potentially make a large impact. Orexo is working along with policymakers to establish viable reimbursement routes for digital mental health programs.

For the projects based on the AmorphOX platform that goes beyond Orexo's key therapeutic areas, e.g., OX640, the Company will seek partnerships to reach a broader target population and thereby increase the potential to make a difference for patients and communities. In these discussions, Orexo will raise the importance of affordability. During implementation, however, it is Orexo's internal processes regarding affordability that will reflect how and to which extent the medications will reach a broad group of patients.

Alignment with UN Sustainable Development Goals

Responsible business

Responsible business based on trust, transparency, integrity and no tolerance for corruption is central to all our activities and a foundation for our sustainability work



Sustainable employees

In all our teams, create a healthy working climate where inclusion and diversity are a matter of course



Access to healthcare

Increase access to healthcare by patient support and strengthening knowledge of substance abuse and mental illness



Environment and Climate change

Our ambition is to reduce our impact on environment and climate change across all our activities and our products



Sustainability management and policy

Orexo's Code of Conduct, also known as the Business Compliance and Ethics Code, serves as an umbrella for all Orexo's policies and guidelines. It is based on corporate values, legislation, and internationally recognized standards, such as the Universal Declaration of Human Rights, the Helsinki Declaration⁸, and the Ten Principles of UN Global Compact. Orexo's Code of Conduct underpins the business and describes expectations and requirements in the areas of human rights, personnel and labor law, environment, and anti-corruption. It also describes ethical research and development expectations,

as well as patient safety requirements.

The sustainability topics identified as the most important for Orexo and Orexo's stakeholders in their materiality assessment include responsible manufacturing and transport, increased access to products, ethical business, climate change, responsible procurement and employee well-being.

91%

Of the Orexo's total revenues refers to UN SDG goal 3.5 – Prevent and treat substance abuse

8) A number of recognized ethical principles for medical research involving humans, developed by the World Medical Association (WMA)

2. The Social Financing Framework

As part of Orexo’s social commitment, this social financing framework (the “**Framework**”) has been developed to be in line with both ICMA Social Bond Principles 2023 (“**SBP**”) as well as the APLMA/LMA/LSTA Social Loan Principles 2023 (“**SLP**”). This Framework is applicable for the issuance of social bonds, social loans, and other type of debt instruments (collectively, the “**Social Financing Instruments**”)

Further, Orexo intends to follow the best practices in relation to Social Financing Instruments and as market

standards develop, this Framework may be amended and/or updated to reflect changes in market praxis.

Orexo will be transparent and disclose information according to the key components of the SBP and SLP, set out below:

1. Use of Proceeds
2. Process for Project Evaluation and Selection
3. Management of Proceeds
4. Reporting



3. Use of proceeds

Definition of eligible projects and target population

This Framework has been established by Orexo and will be applicable under the issuance of any Social Financing Instrument where the net proceeds will exclusively be applied towards financing and/or refinancing of social investments that are aligned with the SBP – and SLP Social Project Categories and falls within the Eligible Projects as defined in the

table 1 below. Orexo intends to, by investing in these Eligible Projects, continue its development, manufacturing, and commercialization of new medicines with the purpose to give people in medically vulnerable areas increased access to essential healthcare (i.e., to treat opioid-dependent patients, to prevent opioid overdoses with OX124 and/or OX125, and provide treatment of life-threatening allergy reactions OX640).

Table 1. Social project category, eligible projects, and target population

SBP/SLP Project Category	Selected Eligible Projects	Target Population	UN SDGs
Access to essential services (i.e., healthcare)	<p>New investments</p> <ul style="list-style-type: none"> • Development, manufacturing and commercialization of OX124 and, if there is a market need, also advance OX125 a nalmefene based opioid overdose rescue medication • Collaboration projects with key stakeholders to make OUD treatment solutions available to vulnerable patients • Continued development of OX640 for treatment of life-threatening allergy reaction • Development of other projects based on the AmorphOX platform improving stability and accessibility of medications <p>Refinancing of previous investments</p> <ul style="list-style-type: none"> • As described on following page and Table 2 (with identical target population as for new investments) 	<ul style="list-style-type: none"> • Foremost people/patients in economically or medically vulnerable areas suffering from substance (i.e., opioid) use disorder, adjacent diseases/ conditions, and mental illness • People suffering from life-threatening and severe allergies • Healthcare systems and patients in developing countries or other regions/countries where there is a need for medicines that do not require cold chains to ensure reliability and efficacy 	 

New financing of social investments

The net proceeds from any new Social Financing Instrument will continue to be invested in projects and activities to support patients suffering from OUD including adjacent diseases/conditions and to expand the use of the drug delivery platform AmorphOX. The primary project will be to make OX124, available to patients. This includes financing of the manufacturing and commercialization of the product.

In addition, proceeds will be used for the development of other products, that goes beyond the OUD space, while still based on AmorphOX, and where Orexo can help other companies to reach extended shelf-life, improved temperature resistance (no need for cold chain) and an innovative delivery technology to increase bio-availability of their product.

For instance, Orexo currently develops an emergency treatment (under the AmorphOX platform) targeting people suffering from life-threatening severe allergies.

Refinancing of social investments

In 2014, Orexo issued a four-year senior unsecured bond of SEK 500 million (the “**Initial Bond**”). The net proceeds from the Initial Bond was primarily applied towards expanding the commercialization of Zubsolv in the US and financing of the ongoing clinical trial program.

In 2017 and 2021, Orexo refinanced the Initial Bond where the proceeds, apart from refinancing the initial Bond, has been used to finance a continued development of the Company’s product OX124 – a *high-dose rescue medication for opioid overdose with naloxone* – and the associated drug delivery platform AmorphOX. In addition, Orexo has also invested in digital therapies, as a tool to expand access to treatment and support patients with OUD, alcohol misuse and depression.

Table 2. Refinancing of social investments (past 36 months)

- Development of OX124, including the drug delivery platform AmorphOX, establishment of a supply chain for the new technology and application of approval with the FDA. OX124 is targeting the US market with the potential to revive individuals who have got an overdose caused by potent illicit synthetic opioids, such as fentanyl
- First clinical trial for OX125, high-dose rescue medication for opioid overdose with nalmefene, targeting the US market predominantly individuals and lay-people living in rural areas
- First clinical trial for OX640, a nasal epinephrine rescue medication for allergic reactions, targeting a global market through partnerships
- Testing of the new drug delivery platform, AmorphOX, in multiple different molecules including large biological molecules such as vaccines
- Investment in digital mental health programs including three digital programs for the management of OUD, alcohol misuse, and depression

4. Process for project evaluation and selection

The management team and the board of directors take overall responsibility for Orexo's sustainability strategy and have, in connection to the establishment of this Framework, appointed a Social Financing Committee which is a subgroup to Orexo's sustainability committee (OSC). OSC is well established in Orexo and has a cross functional representation from both the headquarter in Sweden and the US organization. The team is led by Cecilia Coupland, SVP and Head of Operations and member of the Company's management team. OSC meet frequently and will assess the projects twice per year and report to the management team and board of directors.

The primary objectives and responsibilities for the OSC in terms of the Social Financial Framework are to:

- Evaluating the compliance of proposed Eligible Projects with the eligibility criteria outlined in the Use of Proceeds section
- Assess and monitor progress of each project based on Social Financial Framework KPIs for each project and report to the management team and board of directors

- Ensuring that the pool of Eligible Projects is aligned with the categories and criteria, as specified in the Use of Proceeds section.
- Replacing investments that no longer meet the eligibility criteria
- Approving the Social Financing Investor Report

A main responsible for evaluating and selecting Eligible Projects that are in line with the criteria set out in table 1 in section 3. Use of Proceeds. The list of Eligible Projects is monitored on a continuous basis and the OSC is responsible for replacing investments e.g., following divestments, liquidation, and concerns regarding alignment of underlying activity with eligibility criteria).

5. Management of proceeds

An amount equal to the net proceeds from the issuance of any Social Financing Instrument will be credited to an earmarked account that will support the funding of Orexo's investments in Eligible Projects. As long as any Social Financing Instrument is outstanding, and the earmarked account has a positive balance, funds may be deducted from the earmarked account and added to Orexo's lending pool in an amount up to all disbursements from that pool made in respect of Eligible Projects. The earmarked account will ensure prudent monitoring and track the Eligible

Projects, under the responsibility of Orexo's finance department. If, for any reason, an Eligible Project ceases to comply with the requirements set out in this Framework, such a project will be removed from the pool of Eligible Projects.

Proceeds not yet allocated towards Eligible Projects will be placed in the liquidity reserves and managed as such.

6. Reporting



Orexo will on an annual basis, until full allocation, and in the event of any material development, provide investors with detailed information regarding the allocation of the net proceeds from any Social Financing Instrument, which will be publicly available on the Company's website.

Orexo will disclose the following information related to allocation of proceeds:

1. A description of the Eligible Projects approved by the OSC
2. Type and amount of each Social Financing Instrument issued under this Framework, including proceeds utilised and any unallocated positive balance held on the earmarked account
3. Information and split on new financing and refinancing

Further, Orexo will disclose the social impact of the Eligible Projects financed under this Framework. The output and impact assessment will, if applicable, be based on the Key Performance Indicators (KPIs) presented in the table below.

Table 3. Impact reporting and example of selected impact indicators aligned with the selected SBP/SLP Project Category

SBP/SLP Project Category	Example of selected impact indicators	UN SDGs
<p>Access to essential services (i.e., healthcare)</p>	<p>Output:</p> <ul style="list-style-type: none"> • Total number of patients and to the extent possible vulnerable patients reached by Orexo's OUD treatment solutions related to the Eligible Projects • Number of products offering patient assistant programs and reach of these programs • Number of medicines based on the AmorphOX drug delivery platform <p>Impact:</p> <ul style="list-style-type: none"> • Improved quality of life for OUD patients through improved access to treatment and treatment support • Reduced morbidity from opioid overdose through access to Orexo's OUD treatment solutions • New medications with improved bioavailability and/or stability, reducing the need for cold storage and thereby improve access to medication in areas where controlled storage facilities are sparse 	 <p>3 GOOD HEALTH AND WELL-BEING</p>  <p>TARGET 3-5</p> <p>PREVENT AND TREAT SUBSTANCE ABUSE</p>

7. External review

Second party opinion

Orexo has retained Sustainalytics to review Orexo's Social Financing Framework and provide a second party opinion to attest alignment with the ICMA Social Bond Principles and Social Loan Principles, the relevant UN SDGs and market practice. Sustainalytics evaluation of this Framework and second opinion has verified the credibility, impact, and alignment with the ICMA SBP and SLP.

The Framework together with Sustainalytics' second party opinion will be made available at Orexo's website at: <https://orexo.com/investors/>