orexo

A pharmaceutical and digital therapeutics company

Annual Report **2021**

Content

Communication universe

Our corporate website, www.orexo.com, is our primary communication channel. You are also welcome to follow us on our social media channels.

LinkedIn YouTube

blog.orexo.com

Orexo's formal annual report according to the Annual Accounts Act covers the pages 54–94.

We **empower** people

Our passion is to improve life for people suffering with mental illness and substance use disorders.

These are areas of great human distress and with wide social and economic implications for societies worldwide.

With innovative pharmaceuticals and evidence-based digital therapies we empower these people on their journey to a healthier and happier life.

This is Orexo

Orexo develops improved pharmaceuticals addressing unmet needs, foremost within the growing space of mental illness and substance use disorders. To achieve better treatment results and help more people, Orexo also works with evidence-based digital therapies. The products are commercialized in the US, which is the main market, or via partners worldwide.

Orexo has long experience of developing improved pharmaceuticals that have been approved on multiple international markets. The company was founded in Uppsala, Sweden, in 1995, where the research and development work still are performed.

At the launch of the lead product ZUBSOLV®, for the treatment of opioid dependence, in the US in 2013 a commercial platform was establish on the world's largest pharmaceutical market. Thanks to the success of ZUBSOLV®, investments have been made to broaden thebusiness and today it is divided in three business areas, **HQ & Pipeline, US Pharma and Digital Therapeutics.**

HQ & Pipeline[1]

Orexo develops pharmaceuticals addressing large medical needs. In the work to develop new improved drugs, well-known substances are combined with innovative proprietary Drug Delivery technologies.

amorphOX™, is Orexo's novel and scalable drug delivery platform. It possesses unique properties that support highly differentiated pharmaceuticals and amorphOX™ will form the backbone of the company's future drugs.

The development of new drugs are conducted internally or in collaboration with partners.

Read more on pages 18–19 and 21–25

US Pharma

Orexo's own sales force commercializes pharmaceuticals in the US. Today US Pharma consists of the lead product ZUBSOLV®, for the treatment of opioid dependence.

In 2023 US Pharma will expand with one product as the development project OX124, a rescue medication for overdoses, is planned to get launched.

This business area is an important cash generator and in 2021 US Pharma EBIT amounted to SEK 278 million.

Read more on pages 26–29

Digital Therapeutics

Access to qualified psychosocial support is limited for patients suffering with mental illness and substance use disorders.

Orexo's evidence-based digital therapies grounded in cognitive behavioral therapy techniques, offer better treatment access for patients and improve their outcomes. Digital therapeutics, which is a subsector to digital health, is set to become a crucial part of the future pharma landscape. The American market for digital therapeutics is in its infancy but expects to gain momentum as viable reimbursement routes are established.

Read more on pages 30–33

[1] From an accounting standpoint, costs referring to the head quarter are included, as well as royalty from out—licensed pharmaceuticals

Steady progress in a challenging business landscape

Q1

- A new patent for the leading development project OX124, an overdose rescue medication, was issued by the US Patent and Trademark Office (USPTO). The patent protects the technology until 2039.
- To capture growth opportunities and for the redemption of the former bond a new corporate bond was issued amounting to a nominal value of SEK 500 million.
- A partnership agreement was reached with Magellan Rx to test the digital therapy MODIA™ with patients and other payers in their network. Magellan Rx is the third largest payer for the treatment of opioid dependence in the US.
- A new patent protecting ZUBSOLV® until 2032 was issued by USPTO.

Q2

- ZUBSOLV's access to the Public payer segment increased from 34 to 42 percent, as Medicaid in Kentucky resolved to reimburse all buprenorphine/naloxone pharmaceuticals for the treatment of opioid dependence.
- Two additional patents protecting ZUBSOLV® until 2032 were issued by USPTO.
- A pivotal study evaluating the efficacy of MODIA™ in combination with sublingual buprenorphine/naloxone pharmaceuticals for the treatment of opioid use disorder was initiated. In total more than 400 patients will be tested and the study is expected to be finalized in mid 2022.
- A commercial agreement for the digital therapies vorvida® and deprexis® was signed with the large healthcare provider Trinity Health North Dakota.

Q3

- A commercial partnership agreement was signed with SoberGrid, the largest global social media network for people in addiction recovery, giving a large group of users' access to vorvida® and deprexis®.
- A pivotal study for the leading pharmaceutical project OX124 was initiated.
- A commercial agreement for vorvida® and deprexis® was signed with the large healthcare provider Benefis Health System.

Five-year financial overview

SEK million	2021	2020	2019	2018	2017
Net revenues	565.0	663.6[1]	844.8	783.1	643.7
whereof ZUBSOLV® US net revenue	*522.7*	*623.3*	*719.2*	*621.5*	*485.8*
Cost of goods sold	–78.9	–65.6	–105.6	–171.8	–164.4
Operating expenses	–700.2	–617.9	–508.0	–515.6	–421.9
EBIT	–214.1	–19.9	231.2	95.8	57.4
EBIT margin, %	–37.9	–3.0	27.4	12.2	8.9
US Pharma EBIT	278.2	331.2	347.1	192.8	67.4
US Pharma EBIT margin, %	53.2	53.1	48.3	31.0	13.9
EBITDA	–161.0	19.0	272.1	116.6	78.2
Earnings per share, before dilution, SEK	–6.51	–2.45	6.33	3.99	0.67
Earnings per share, after dilution, SEK	–6.51	–2.45	6.20	3.93	0.67
Cash flow from operating activities	–229.0	16.8	290.9	242.0	146.6
Cash and cash equivalents	504.1	505.3	816.8	589.8	327.9

[1] Royalty from Abstral® excl. sales in the EU and the US. The contracts for these markets ceased in late 2019, mainly as an effect of patent expiration

Q4

- MODIA™ paper published in the Journal of Medical Internet Research Mental Health.
- Positive results showed from a pivotal trial for the leading development project OX124.
- Information was provided about amorphOX™ which is a novel and inventive drug delivery platform that will be the backbone in the development of future highly differentiated products regardless active ingredients and administration routes.
- The development of a nasal adrenaline medication, OX640, based on the novel amorphOX™ platform, was initiated.
- The collaboration with the commercialization partner Accord Healthcare ramped up preparing for the launch of ZUBSOLV® in the EU.

Impact from Covid-19

The Covid-19 pandemic, with society lockdowns and social distancing, has significantly fueled the number of people suffering from mental illness and substance use disorders.

In parallel, access to treatment has not been adapted to keep up with the increased demand. This is partly attributable to a combination of patients to a greater extent were not seeking care during lockdown and that physicians were more reluctant to grow patient load. As the impact of Covid-19 diminishes, and in light of the significant rise in mental illness and substance use disorders, it's expected that these areas will be prioritized.

The Covid-19 pandemic has challenged the sales force, but as societies are opening up, access to physicians and other healthcare providers is improving, which is facilitating sales efforts.

The development chain has also been affected by the pandemic, for example, delivery and permission delays with external partners have partly influenced project timelines.

Protecting employees and ensuring business continuity has sometimes necessitated measures to reduce the spread of the Covid-19 virus.

Nikolaj Sørensen,
President and CEO

Ready to start capitalizing on a **broader business**

During 2021, we took several important steps in our work to build a broader and stronger Orexo. Our rescue medication for overdoses, OX124, developed according to plan and if approved a launch in the US is expected in late 2023. Despite the lack of viable reimbursement routes for digital therapies, we reached strategically important collaboration agreements with healthcare providers and distributors. At the end of the year, we stand on a much stronger operational foundation, well equipped to meet the increasing need for care from people who are suffering from mental illness and substance use disorders.

In many ways, 2021 was a troublesome year from a health perspective. Despite the incredibly fast development and approval of effective vaccines, Covid-19 has kept a tight grip on society with impacts way beyond viral infection. The pandemic, in combination with the restrictions, has triggered a surge in people with depression, alcohol misuse and opioid dependence.

Sustainability commitment focusing on increasing patients' access to treatment

At Orexo we are working hard to improve life for people suffering from mental illness and substance use disorders. Our ongoing transformation journey, from being a one-product company to a company offering both pharmaceuticals and clinically proven digital therapies, will enable us to help many more people in urgent need of help. A mission fully embraced by my colleagues and also manifested in our support of UN´s Sustainable Development Goals, with focus on the target 3.5 to prevent and treat substance abuse. To view our full sustainability commitment, see pages 35–51.

Strengthened position for ZUBSOLV® enabling good growth opportunities

The foundation of Orexo's expansion into new areas of mental illness treatments is our profitable business area US Pharma, driven by revenues from ZUBSOLV®, a treatment of opioid dependence. All evidence indicates the issues with opioid use disorders (OUD) accelerated in 2021 and also the physicians tell us they have seen an increased rate of relapse during the year. However, the growth in patients being treated for OUD slowed down and the market grew by only 8 percent. The explanation for this slow down, when compared to the previous year's double digit growth, is that during Covid-19 many physicians have restricted access to their clinics and reduced acceptance of new patients. As a response, Orexo has increasingly adopted virtual sales methods, and reduced the size of the field force during 2021 as a consequence of less access to the customers.

> **“At Orexo we are working hard to improve life for people suffering from mental illness and substance use disorders.**

As expected ZUBSOLV® sales declined compared to 2020, but we have seen a stabilization in the sales during the year and the negative effect from increased competition in United Health Group and Humana in 2019 has declined. We have also succeeded in strengthening the overall access to ZUBSOLV® in 2021 with reimbursement within Medicaid in Kentucky. Maintaining and improving market access is critical to ensure strong resilience of ZUBSOLV® in the face of increased competition. Together with our pipeline projects and our digital therapy MODIA™ for OUD, the excellent market access provides good growth opportunities for our US Pharma business in 2022 and the years to come.

DTx partnership strategy will open doors to the B2C segment and to employers

Our new business area, Digital Therapeutics, has entered a market with significant growth prospects, but it is also a market clearly in its infancy and still to gain momentum. Orexo's strategy is to position our digital therapies as a complement to existing healthcare, to improve the efficiency and quality of care as well as to widen access to treatments for patients. There are a wealth of applications available for mobile devices claiming different health effects on mental illness. In contrast, Orexo's partnership with GAIA AG has provided us with access to three digital therapies that have shown significant clinical evidence of their positive impacts. Each of Orexo's digital therapies is equipped with AI techniques that enable customization based on each user's individual needs.

During 2021, first vorvida® and later deprexis® were promoted directly to patients. However, due to restriction in our ability to target specific potential customers in social media, which undermine an attractive return on investment, we have phased out these activities to focus fully on sales through partnerships. One example is the partnership with SoberGrid, the largest online community for people with addiction problems.

Together with SoberGrid we are planning to expand this combination of coaching services and our digital therapies to new sales channels such as employers, labor unions and other healthcare distribution platforms. The first example is the recently announced distribution partnership with the second largest US pharmacy, Walgreen's, where our joint services will be available on their digital healthcare marketplace, FindCare®.

DTx as a complement to existing treatment programs among large healthcare providers

The main customer segment for our digital therapies is expected to be healthcare providers who leverage the digital therapies as a complement to their care as usual. This combination will provide the patients with the comfort and trust in a contact with a healthcare professional and the advantages of a digital therapy they can use when it's convenient in their everyday life. During 2021, we worked to develop this model in collaboration with Trinity Health and, later in the year, Benefis and Justmiine agreed to implement a similar model. With assimilation into existing healthcare services, the reimbursement process for the digital therapies will be managed as an integrated element of the medical billing process at the healthcare provider. This type of integration is new to the healthcare providers and without existing reimbursement codes, Orexo has worked intensively with Trinity Health to develop a model that can be leveraged by other similar healthcare providers.

> **Our new business area, Digital Therapeutics, has entered a market with significant growth prospects, but it is also a market clearly in its infancy and still to gain momentum.**

We are convinced that obtaining reimbursement and making the DTx available to patients within established health care infrastructure offer the greatest value potential, both for the payers, providers and Orexo. Even more important is that patients will benefit from being able to combine new innovative treatment options with the trust and credibility of their existing healthcare provider.

A great part of the DTx spending in 2021 refers to non-recurrent costs

Launching the DTx business area have been related to significant expenses. Also investments have been made to build the infrastructure to enable distribution, payment and reimbursement of the products, and these systems have to meet the highest data privacy requirement. In addition we have had significant expenses to build the promotional and communication platform. A lot of these expenses are non-recurring and the focus for 2022 is increasingly on expenses associated with specific customer partnership, rather than the broad investments made in 2021.

Overdose rescue medication, OX124, is approaching the US market

We are excited about our opportunity to diversify into new growth areas like digital therapeutics, but Orexo's core competence is pharmaceutical development and we have made some notable progress in 2021. Our pipeline is now addressing the rapid increase of fatal opioid overdoses with synthetic opioids through the pharmaceutical candidates OX124 and OX125, and we have expanded into a new disease area with OX640 that will treat the rapid growth of people who are at risk of serious allergic reactions.

The main focus in 2021 has been on our lead product candidate, OX124 and during 2021 we showed positive data from the pivotal clinical trial and completed the setup of the commercial supply chain and we are on track to apply for market authorization with the FDA in the second half of 2022.

amorphOX™ will form the backbone of future pharma products beyond current therapeutic areas

To develop OX124, we had to overcome several issues, including creating a stable product with a rapid dissolve time of a nasal powder, whilst also meeting the FDA quality requirements. As part of this process we have developed a new novel proprietary drug delivery platform, amorphOX™. This platform provides for excellent chemical and physical stability, commonly a significant problem for amorphous drug compositions and amorphOX™ will form the backbone of our future pharma products, both developed in-house or in partnership with other pharmaceutical companies.

The first example is the development of a nasal adrenaline medication, OX640, for emergency treatment of allergic reactions. The medication will provide important benefits to patients and health care systems, ensuring the correct adrenaline dose is both reliably and conveniently available when needed via a nasal formulation. We will continuously assess the best commercialization route for OX640 and consider when and where to include a partner in the development of the product.

From a future financial management perspective, a significant share of the investments in the development of OX124 are synergistic with the pipeline products based on the amorphOX™ technology platform.

Thanks to our employees – who are key for our future success

Our employees are key for our success and I would like to thank the entire team, in both Sweden and the US, for their excellent and tireless efforts during an eventful year.

Strategic milestones in neartime

- ✓ Advanced the pharma pipeline with pharmaceutical candidates that goes beyond mental illness and SUD and with positive data from the OX124 pivotal trial.
- ✓ Developed amorphOX™, a new drug delivery platform that will form the backbone of future pharmaceuticals.
- ✓ Established a new business area within a new groundbreaking product category – digital therapeutics, including three synergistic and evidence-based therapies.
- ✓ Developed a scalable distribution and reimbursement platform for digital therapies on the US market.
- ✓ Partnership established with a larger regional healthcare provider in the US to develop efficient reimbursement pathways and treatment programs for the DTx business.

> **amorphOX™ will form the backbone of our future pharma products, both developed in-house or in partnership with other pharmaceutical companies.**

Your contributions have been outstanding as we've worked together to navigate the complexities of yet another year with Covid-19. It has required an exceptional effort and reflects the strength of our company's culture.

I will also take the opportunity to thank all our shareholders for your trust while Orexo is on this transformation journey. Thanks to revenues from our lead product, ZUBSOLV®, we have the last two years been able to invest in our pipeline and establish a new business area within digital therapeutics. And as we finalize the investments and expenses required to build the necessary infrastructure the focus on profitability will increase with the ultimate goal to become a more diversified company.

Uppsala, Sweden, March 2022
Nikolaj Sørensen
President and CEO

Strategic road-map to **build a stronger and broader Orexo**

The strategy for long-term growth is built on maximizing the potential of the strong commercial platform on the US market. The lead product, ZUBSOLV®, which is an important cash generator, has paved the way for investments in novel pharmaceutical candidates and evidence-based digital therapies with the aim to build a broader and stronger company.

Strategic priorities

1. **Broadening the portfolio of commercial products to be promoted by our US Pharma and Digital Therapeutics business areas.**
2. **Maintaining ZUBSOLV® profit contribution and ensure it is sustainable and growing over time.**
3. **Establishing a new profitable business area within Digital Therapeutics and create a new platform for growth.**
4. **Enhancing the development pipeline in pharma, led by OX124, an opioid overdose rescue medication, and the novel amorphOX™ platform.**

Core competencies **creating a ground for future success**

Innovation
Proven track record in developing novel and inventive drug delivery technologies paving the way for approval of multiple drugs. Well-established partnership with GAIA AG for the development of evidence-based digital therapies.

Clinical
Successfully completed large clinical trials performed in the buprenorphine/naloxone market both for pharma and digital therapeutics. Has successfully conducted multiple pivotal trials.

Regulatory affairs
Experience from securing product approval in multiple large markets, such as the US and Europe.

Commercialization
Nationwide US sales force, directed to the treatment of mental illness and substance use disorders. Strong relations with insurance companies and healthcare providers in the US.

Supply
Established stable and flexible supply chains, among others for nasal rescue medications. Performed multiple tech-transfers to contract manufacturing organizations and has a proven ability to lower cost of goods sold.

Investment themes for **long-term growth**

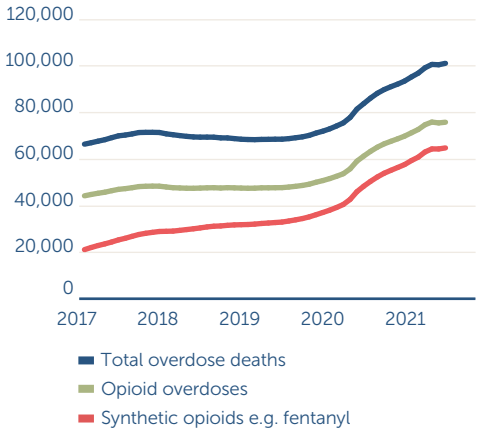
Addresses large and growing markets

The Covid-19 pandemic, with society lockdowns and social distancing, has led to significant increases in drug addiction and mental health issues globally. In the US, which is Orexo's key market, the opioid crisis is severe with overdose death tolls reaching record-highs.

Increased access to synthetic opioids, such as fentanyl, has caused a sharp rise in the number of fatal overdoses. Behind these figures there is profound human suffering and to fill the treatment gap the need for therapies that go beyond traditional regimens, such as digital therapeutics, is significant.

From an economic and societal point of view, drug addiction and mental illness are a considerable problem. In addition to loss of life and lower quality of life, large costs are associated with lower productivity and there are also increased healthcare and correctional treatment costs. To curb the accelerated opioid crisis multiple activities are ongoing on a federal and state level to increase access to treatment.

Number of fatal overdoses in the US[1]



[1] 12 months' data as of June 30, 2021

Pipeline targeting large medical needs

Illustration of an amorphous particle.

Orexo will continue to leverage on its long experience to develop improved pharmaceuticals that have been approved on markets worldwide. Development of new drugs are based on innovative drug delivery platforms targeting large medical needs within areas of mental illness and substance use disorders or other therapeutic areas where the drugs can make a large difference for patients and healthcare providers. The development process is characterized by lower clinical risk, shorter time to market and lower costs.

The novel drug delivery platform, amorphOX™, is an inventive powder technology. amorphOX™, dissolves rapidly while maintaining chemical and physical stability, overcoming a frequent challenge in the development of pharmaceuticals using substances with an amorphous structure. This technology is highly scalable as it works with different active substances, dosage forms and administration routes. amorphOX™ is used in the pharmaceutical candidates OX124, OX125 and OX640 and will form the backbone in the future development of new innovative drugs, conducted internally or along with partners.

Commercial presence in the US with comprehensive synergies

One of the most important strategic priorities for future growth is to capitalize on the strong commercial presence, including the market access network in the US. Adding additional products to the US commercial platform will significantly increase the productivity within the commercial organization.

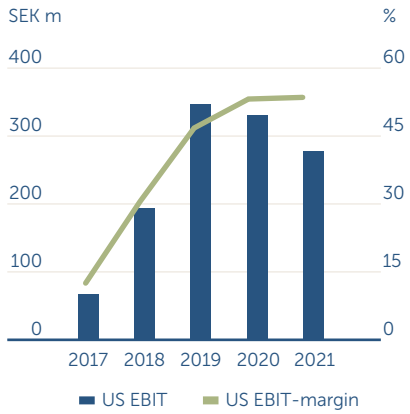
In late 2023 the most advanced development project, OX124 – a rescue medication targeting synthetic overdoses, is expected to be launched in the US. Along with ZUBSOLV® and the new digital therapy MODIA™ for opioid dependence, Orexo will have the most comprehensive range of treatment options for people suffering from opioid use disorder while the extensive synergies are expected to be achieved within the commercial platform.

Strong cash generation from US Pharma

Orexo's lead pharmaceutical ZUBSOLV® is an important cash generator. In 2019 US Pharma EBIT, which is fully related to sales from ZUBSOLV®, reached a record-high of SEK 351 million. The strong profitability has paved the way for investments in pipeline and the digital therapeutics venture.

The ZUBSOLV® demand has been negatively impacted by generic competition at the insurance companies United Health Group and Humana. This impact is declining and sales of ZUBSOLV® is expected to stabilize, with the potential to grow if the market reach pre-Covid growth rates or with new market access improvement.

US Pharma EBIT and EBIT Margin



Entered digital therapeutics, a new evidence-based frontier in patient care

The health care sector is facing enormous challenges. To handle the balancing act between supply and demand there is an increasing need for better efficiencies. Digital health is contributing to streamlining health care. Digital therapeutics, which is a sub-sector of digital health, expands access to care and improves treatment results. Mental illness and substance use disorders are areas where digital solutions are most applicable.

The market for digital therapeutics is still in its infancy, but as distinct finance structures are in place and the awareness among health care providers and patients is increasing, the market is expected to show strong growth. Orexo is one of the players that is working relentlessly to drive this change and with scientifically proven digital therapies and an established relationship among insurance companies and healthcare providers in the US, Orexo is well established to capitalize on this growth opportunity.

OUR HEROES
Marguerite

I reached a turning point when I realized I had lost everything

My problems started after a sexual encounter at the age of 5. At 15, my drug addictions began.

I've been with my boyfriend since I was 16. I was 22 when we married and began planning a family. I spent most of my twenties pregnant, and my postpartum depression was worse each time. In the end, I had to go into rehab and my sister gained control over my children. My addictions were spiralling, and my husband was misusing too. My husband and I were far apart emotionally. I felt so alone.

I stayed in rehab, and I had some suicide attempts that landed me in hospital. Crisis got involved. You have to hit that point. You have to lose everything.

That's when I started my recovery journey. I learned how to reframe things. You're not recovering from drugs – you're recovering from your old way of thinking. One day I woke up and the leaves on the tree were a lot greener than they'd ever been. I realized, I'm happy with me. It was just a switch, knowing it has to start and end with me.

I formed a relationship with God. I pray morning, noon, and night to thank God for getting me to where I am. It's been over 7 years since I took heroin and 5 years since I used stimulants. I've got my kids back. My husband and I are closer, and my sister and I are rebuilding our relationship.

You're the only one standing in your way, so if you want something better, go and get it.

Visit our Blog to read Marguerite's full story
blog.orexo.com

OUR HEROES
Elise

Turning tragedy into my life's purpose

My daughter, Giana died from a heroin overdose on January 3, 2014. As a child, Giana had asthma and several allergies, so she took up swimming. She competed at a high level in school and went to college on a Division I swimming scholarship.

After a year at college, Giana developed severe anorexia. She was hospitalized, where they diagnosed major depressive disorder and anxiety. She went back to college and graduated with a major in English and then studied to become a veterinary nurse. Giana worked in a veterinary hospital but had issues with eating and anxiety and was under the care of a psychiatrist. She started working out with some male body builders and they were injecting an opioid called nalbuphine.

I learned of her opioid dependency 19 months before she died. I had no idea how to deal with opioids, but I was determined to stand by her. For the next 18 months, Giana was in and out of treatment facilities. They didn't treat her psychiatric illness properly or integrate treatments for her mental health and opioid addiction. Thirteen months before she died, Giana made the switch to heroin and it was downhill from there.

I do what I can to help others. I've joined the Advisory Boards of the Behavioural Health Department in Philadelphia and Safehouse Inc. and I'm part of the Philadelphia Overdose Prevention Network. I've published a memoir: Even If Your Heart Would Listen: Losing My Daughter to Heroin.

As a family, we fundraised for a memorial bench and put it in a place that was special to Giana. It's somewhere I go sometimes, just to be.

Read Elise's full story at
blog.orexo.com

With our blog our mission is to shed light on lives affected by addiction and the road to recovery. The opinions expressed in this blog are solely those of the authors and do not necessarily reflect the views of Orexo. The authors have been asked not to reveal specifics around potential medically assisted treatments or other therapy used to reach recovery to Orexo or the readers.

Having a holistic treatment approach **improves treatment results**

Being addictive to drugs is a chronic disease that affects both a person's brain and their behavior resulting in a significant impact on their quality of life. People suffering from drug addiction have a higher incidence of also experiencing other mental illnesses and vice versa. Taking a holistic treatment approach to all elements of an individual's mental health can have an instrumental impact on those peoples' lives.

Addiction related diseases are a chronic brain disease

Substance use disorders, SUD, also named drug addiction, is a chronic relapsing brain disease affecting the reward, memory, and motivation systems of the brain. It is caused by use of substances such as drugs, alcohol and nicotine. The reasons behind developing an addiction are wide-ranging, with genetic factors thought to account for a large part of a person's vulnerability to developing addictive behavior. Environmental factors such as stress and exposure to addictive substances also play a part in developing addiction.[1] Drug and alcohol addiction often have a strong impact on patients private and professional life.

Mental illness deeply impacting day-to-day living

Mental illness applies to a wide range of mental health conditions, affecting people's mood, thinking and behavior, leading to functional impairment impacting life activities. Examples of mental illness are anxiety, depression, schizophrenia, post-traumatic stress, ADHD[2] and bipolar disorder. Mental illness is thought to be caused by a variety of factors such as genetics, brain chemistry and environmental issues.

The short road to overdose

Patients with opioid use disorder need to ensure a constant intake of opioids as otherwise they can experience withdrawal symptoms just hours after their last dose of opioids.

It is not uncommon for these patients to turn to unconventional ways of obtaining access to opioids, such as from the illegal market.

Unfortunately, efforts to limit access to prescription opioids appear to have resulted in an unintended consequence, as patients have resorted to heroin and stronger synthetic opioids, such as fentanyl, to compensate for the limited availability of prescription opioids, with often fatal outcomes.

Patients who turn to heroin or synthetic opioids have an increased risk of experiencing an overdose, and fatalities relating to opioid overdoses is one of the most common death causes among Americans under the age of 50.[3]

Mental illness can trigger a substance use disorder and vice versa

Mental illness frequently co-occurs with substance use disorders (SUD). The relationship between the two is bi-directional, meaning that people who abuse substances are more likely to suffer from mental illness, and the other way around. For example people who are depressed may drink or abuse drugs to lift their mood or escape from feelings of guilt or despair. While substances like alcohol, which is a depressant, can increase feelings of sadness or fatigue.

Studies show that 25 percent of people suffering from a serious mental illness[4] also have a SUD, while 17 percent of them with a SUD experienced a serious mental illness.[5] With respect to opioid use disorder, Orexo's own retrospective data from the RESOLV study performed in 2016, showed 32 percent of patients were diagnosed with co-existing depressive disorder to highlight just one of the co-existing mental illnesses many of these patients have.

Having a holistic treatment approach improves treatment results

Access to health care and social services capable of providing treatment and social support is key for people suffering from mental illness and addiction diseases. The treatment gap is huge and from a co-occurring perspective, only about half of individuals with comorbid mental health and drug addiction received treatment in 2018.[6]

Having a holistic treatment approach for comorbid SUD and mental illness can have an instrumental impact on those peoples lives.[7] Cognitive behavioral therapy based techniques in conjunction with traditional pharmaceutical treatments have a long history in helping treat many mental illnesses, helping to support motivation and functional recovery to improve overall treatments results.

Opioid use disorder

Treatment of opioid use disorder (OUD) is often administered over long periods of time or chronically. Medication Assisted Treatments, or MAT for short, is the combination of a pharmacological treatment indicated for OUD along with behavioral based therapy. The most common treatments are based on buprenorphine, methadone or naltrexone. Buprenorphine is often combined with the antagonist naloxone to help prevent misuse. The most frequently used medication as part of a MAT program in the US is buprenorphine/naloxone which can be taken under the tongue as a tablet or film. Methadone is most commonly administered orally in a supervised setting while naltrexone is most frequently given as a monthly injection.

People where misuse of opioids has turned to illicit drug use face a large risk of suffering life-threatening overdoses where rescue medications such as naloxone are often required.

Alcohol abuse

Alcohol abuse and alcohol use is a growing challenge. Treatment may involve individual or group therapy, outpatient programs, or a residential inpatient stay where for example cognitive behavioral therapy is often used to coach patients to change behavior. Currently, there are only a few medications approved by the FDA for the treatment of alcohol abuse and alcohol dependence. These medications are largely targeted to those who have already stopped drinking and are trying to maintain abstinence.[8] There remains a significant gap in helping individuals manage their drinking behavior.

Depression

Depression is a leading cause of disability around the world and contributes greatly to the global burden of mental illness. There are many approaches to the management of depression with pharmacological and behavioral therapies being the cornerstone of many of these management approaches.

32%

share of patients with opioid dependence who also were diagnosed with depression, according to Orexo's RESOLV study.

Treatment of opioid use disorder

is often administered over long periods of time or chronically.

[1] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3898681/
[2] Attention Deficit Hyperactivity Disorder
[3] Drug Policy Alliance
[4] According to SAMHSA (Substance Abuse and Mental Health Service Administration) serious mental illness refers to depression, schizophrenia, biopolar disorder and other mental disorders causing serious impairment
[5] SAMHSA, Center for Behavioral Health Statistics and Quality, National Survey on Drug Use and Health, Mental Health, Detailed Tables available at: https://www.samhsa.gov/data/population-data-nsduh.
[6] SAMHSA
[7] Kelly TM, Daley DC. Integrated Treatment of Substance Use and Psychiatric Disorders. Soc Work. Mueser KT, Gingerich S. Treatment of co-occurring psychotic and substance use disorders. Soc Work Public Health. 2013;28(3-4):424-439. doi:10.1080/19371918.2013.774676. Torrens M, Rossi PC, Martinez-Riera R, Martinez-Sanvisens D, Bulbena A. Psychiatric comorbidity and substance use disorders: treatment in parallel systems or in one integrated system? Subst Use Misuse. 2012;47(8-9):1005-1014. doi:10.3109/10826084.2012.663296. Kelly TM, Daley DC, Douaihy AB. Treatment of substance abusing patients with comorbid psychiatric disorders. Addict Behav. 2012;37(1):11-24. doi:10.1016/j.addbeh.2011.09.010. Public Health. 2013;28(0):388-406. doi:10.1080/19371918.2013.774673
[8] Winslow BT, Onysko M, Hebert M. Medications for alcohol use disorder. Am Fam Physician. 2016;93(6):457-465

amorphOX™ – a **novel and inventive** drug delivery platform

Orexo has successfully developed a drug delivery platform, amorphOX™, which is a novel and inventive powder-based technology, that is very rapidly dissolving and stable. As amorphOX™ works with different APIs, dosage forms and administration routes it is a versatile platform with significant potential.

Amorphous solids are non-crystalline solids, and possess no long-range order, giving them unique and highly sought-after properties, such as very rapid dissolution in water. These properties enable formulation of drugs in a manner that allows for a faster onset and a higher bioavailability.

Historically however, amorphous drug compositions were found to be both chemically and physically unstable and therefore to degrade during storage. Orexo has a solution to this problem with the development of a drug delivery platform. The platform, named amorphOX™, is a powder-based technology that is both chemically and physically stable when stored in even elevated temperatures, while still being rapidly dissolving.

A versatile drug delivery platform

The powder-based technology is made up of particles that are built using a unique combination of a drug, carrier materials and, optionally, other excipients such as a permeability enhancer. The particles are presented as an amorphous composite of the various ingredients providing for excellent chemical and physical stability. The surface structure can be tuned for optimal process ability, and the size of the particle can be tailored to suit different administration routes.

Orexo is in the process of developing an aspect of the amorphOX™ platform to formulate and administer naloxone (OX124) and nalmefene (OX125) to reverse opioid overdoses. The number of deaths from opioid overdoses has grown in recent years, particularly in the US, creating a need for new and improved rescue medications, particularly for overdoses caused by synthetic opioids such as fentanyl.

Validated in humans

Both OX124 and OX125 are administered nasally and have shown very promising results in human clinical trials. Besides being well tolerated, the amorphOX™ platform provided higher exposure, faster onset and lower variability in comparison with the market leading products. In 2021, the pivotal clinical study for OX124 was successfully performed. OX124 shows almost instant dissolution in a minimal amount of liquid as well as remarkable chemical and physical stability, even under accelerated conditions.

These properties make it ideal for a nasally administered emergency medication to reverse opioid overdoses. First, it needs to be storable so that it works when it is needed. Second, it needs to be easy to administer and have a very rapid onset as an overdose from an opioid progresses rapidly.

Wide applicability

The amorphOX™ platform has also shown good results in accelerated stability studies when used with numerous other APIs with very different chemical structures. The technology also supports various dosage forms and administration routes and the properties of the powder can be tailored to meet specific needs such as particle size, dissolution, and mucosal retention. This makes it a versatile technology with broad applicability in pharmaceutical development across multiple therapeutic areas.

amorphOX™ is a novel and inventive drug delivery platform with significant potential.

Robust patent strategy

For Orexo, as an innovative company, a strong patent portfolio that covers all existing products and pipeline projects is central for the business. The patent strategy involves having the proper protection in place on the relevant markets for any given product. Product specific patents are important assets, whether the company chooses to sell a product via a commercial partner, or bring it to the market by Orexo's own commercial team. As a pharmaceutical company present on the US market, having enforceable patents listed in FDA's 'Orange Book' for the company's drug products is a very important part of the strategy.

Orexo has an in-house IP department that work in close collaboration with innovators and the development team, as well as with external counsel, to ascertain that all aspects of the innovative process are covered, laying the foundation for the patents in the portfolio. Orexo's global experience of patent enforcement is an invaluable asset in shaping the patent strategy.

Business areas

Orexo's operational organization is divided in three business areas[1], HQ & Pipeline, US Pharma and Digital Therapeutics. However, as a small company the three areas share many resources and benefit significantly from a high degree of interaction and collaboration to reach the company's overarching business objectives and the objectives of each business segment.

Lorem ipsum bildtext

[1] Also called segment in the financial reporting

HQ & Pipeline

Expanded pipeline **targeting large unmet needs**

By combining well-known and well-documented substances with our own innovative formulation technologies, Orexo is developing improved drugs that meet significant medical needs. In our innovative work environment, new ideas and concepts are highly valued. This underpins our work of developing new, improved drugs that make a big difference to patients and healthcare providers.

Orexo has developed multiple drugs, from idea to approval in markets around the world. The developments are based on innovations made possible by the interactions between skilled researchers and experts with different scientific backgrounds. High transparency and multi-functional collaborations make the innovation culture to flourish.

When evaluating and prioritizing ideas, medical needs, technical implementation, intellectual property rights and commercial potential are all considered. The ambition is to initiate all product developments internally and to maintain full control throughout the entire development process. If necessary, external expertise is added and collaborations are made with external partners, such as contract manufacturing organizations and academia.

Development of drugs targeting major medical needs

The development work is mainly focused on formulating drugs that prevent and treat mental illness and substance use disorders. These are all therapeutic areas that are growing globally, but are particularly prevalent in the US, which is Orexo's prioritized market. Based on clinical experience and good relationships with US healthcare providers, knowledge and insights can be transformed into opportunities to provide innovative solutions that meet major unmet medical needs.

An example is the opioid crisis that has accelerated in the wake of Covid-19. The widespread use of powerful synthetic opioids, such as fentanyl, has caused a record number of Americans to overdose. Overdose is one of the most common cause of deaths if you live in the US and are under 50 years of age. The need for life-saving drugs that quickly and effectively resuscitate these people has never been greater.

3 questions to Robert Rönn, SVP and Head of R&D

How would you summarize the development in 2021?

It has been an intensive and fruitful year where we have made important progress in several areas. Our commitment to help patients in the addiction field continues and our naloxone product for the treatment of opioid overdose, OX124, passed a significant milestone with the successful completion of a pivotal clinical study. In parallel, our focus on the development of innovative drug delivery solutions has resulted in amorphOX™, yet another important technology platform for Orexo. With amorphOX™, I see significant opportunities even beyond the addiction field and it has already enabled us to further progress our pharma pipeline with the addition of OX640, a nasal adrenaline product for the treatment of allergic reactions.

What are your priorities in 2022?

Our main priority is to complete the development of OX124 and file for approval in the US. We will also advance the development of OX640 and perform the first human clinical study. Furthermore, the development of OX125, our nalmefene product for opioid overdoses will continue.

What would you like to achieve in a 5 year horizon?

My vision is to develop several new drugs based on the amorphOX™ platform. In five years' time, Orexo has initiated and led the development of multiple new pharma products approaching the market and we have a wide pipeline of development programs in various phases.

Overdose rescue medications pave the way for an expanded pipeline

To meet the need for overdose rescue medications that are effective against synthetic opioids, the pharmaceutical candidates OX124 and OX125 are being developed. Both contain different substances that meet unique needs and the drugs are aimed at multiple target groups in the market. Alongside OX124 and OX125, a new drug delivery platform has been developed, amorphOX™.

The platform is very scalable and can be used to develop highly differentiated drugs. The broad potential of amorphOX™ opens up new, exciting development projects that can meet major medical needs in areas beyond mental illness and substance use disorders. The first example is OX640, where the goal is to develop a differentiated drug for the treatment of allergic reactions.

amorphOX™

Short facts – HQ & Pipeline

Royalty 2021	SEK 41 m
EBIT 2021	SEK –243 m[1]
EBIT margin	N.A.
Ongoing developments projects	See pages 23–25

Out-licenced pharmaceuticals developed by Orexo

All are based on Orexo's sublingual drug delivery platform.

Abstral® for breakthrough cancer pain. Commercialized by Orexo' partner Kyowa Kirin who has all rights to markets ex-US and the EU. Patent protection on RoW markets until 2024.

KYOWA KIRIN

Edluar®, for insomnia. Orexo's partner, Mylan, has all rights to markets worldwide. Patent protection in the US until 2031 and in the EU until 2025.

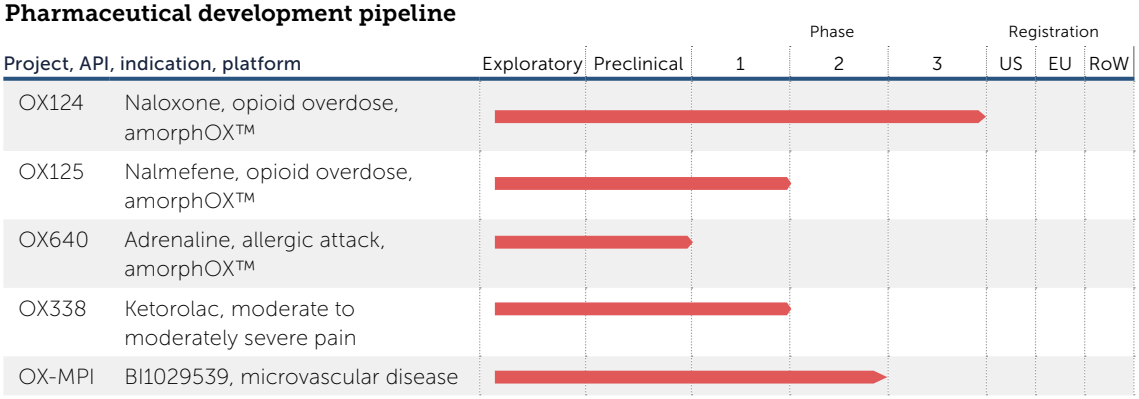
Mylan

ZUBSOLV®, for the treatment of opioid use disorder. Accord Healthcare owns the rights to the EU market including 29 countries. Patent protection until 2032.

accord
Make it better

[1] Both direct and indirect expenses have impacted EBIT

Pharmaceutical development pipeline



OX124

API	Naloxone
Technology	AmorphOX™
Indication	Opioid overdose
Development phase	Ongoing stability and validation studies
Registration with the FDA	Expected H2 2022
In-house development or via partnership	In-house
Commercialization	In the US, late 2023. Markets ex-US are evaluated.
Patent	Patent protection until 2039

Unmet need

With a significant rise among people in the US that are overdosing, due to increased misuse of highly potent synthetic opioids, such as fentanyl, the need for new and more powerful rescue medications has never been greater.

Our aim

Based on Orexo's novel drug delivery platform, amorphOX™, the aim has been to develop a rescue medication that is faster and longer-acting, and thus effective in reversing overdoses caused by synthetic opioids. This aim was fulfilled in 2021, following the finalization of a successful pivotal study.

Differentiation[1]

In clinical studies OX124 shown more rapid absorption, substantially higher plasma concentrations of naloxone, and sustained duration of elevated plasma concentrations when compared to the current market leader.

[1] 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

OX125

API	Nalmefene
Technology	AmorphOX™
Indication	Opioid overdose
Development phase	Finalized exploratory human PK study
Registration with the FDA	–
In-house development or via partnership	In-house
Commercialization	Planned for the US and along with partners in the EU/RoW
Patent	Patent protection until 2039

Unmet need
The widespread use of synthetic opioids, such as fentanyl, also increases the need for rescue medicines that are effective in rural areas where distance to emergency units require more potent and longer lasting overdose treatment.

Our aim
To develop an overdose rescue medication for situations where powerful, rapidly and long-lasting effects are required.

Differentiation
As nalmefene has a longer half-life than naloxone, OX125 has the potential to be an even more effective response to the increased use of highly potent, long-acting synthetic opioids. Results from the first exploratory human PK study in healthy volunteers showed extensive and rapid absorption of nalmefene across three different formulations of OX125.

OX640

API	Adrenaline
Technology	AmorphOX™
Indication	Allergic reactions
Development phase	Preparations for the first human phase 1 study ongoing
Registration with the FDA	–
In-house development or via partnership	Currently in-house, but partnership is planned to be initiated during the development and for commercialization
Commercialization	Planned for the US and along with partners in the EU/RoW
Patent	Pending patent applications extending into 2042

Unmet need
Today, allergic rescue products are needle-based auto injectors that administer adrenaline 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. Current solutions are costly and devices must be replaced frequently because adrenaline rapidly degrades during storage.

Our aim
With decades of no innovation, products like EpiPen dominates the market. Orexo will strive to bring to market a more fast-acting intranasal product, which is key in life-saving situations. Additionally, the single-dose nasal administration is easy to use and easy to teach others and easy to learn for caregivers.

Differentiation
Built on our amorphOX™ platform, OX640's dry-powder, single-use, intranasal delivery will provide rapid and extensive absorption with the potential of doubling the stability and shelf-life of current solutions. Moreover, OX640 is preservative-free with no sodium metabisulfite or other stability agents currently needed in today's devices. These preservatives can in itself cause allergic reactions.

OX338

API	Ketorolac
Technology	Oral
Indication	Moderate to moderately severe pain
Development phase	Finalized exploratory human PK study
Registration with the FDA	–
In-house development or via partnership	In-house
Commercialization	Planned for the US and along with partners in the EU/RoW
Patent	Pending patent applications extending into 2041

Unmet need
Opioids are still used unnecessarily for pain refief in many situations, further fueling the opioid crisis.

Our aim
Based on Orexo's novel oral formulation technology, the aim is to develop an opioid-level pain relief treatment for short-term pain (up to 5 days) without the risk of addiction.

Differentiation
Results from the exploratory PK study in healthy volunteers showed significantly better PK profile, such as faster uptake and higher peak, when compared to nasal spray available on the market.

OX-MPI

API	BI1029539
Technology	Oral
Indication	Microvascular disease
Development phase	Phase 2 study
Registration on various markets	–
In-house development or via partnership	Managed by Orexo's partner GESYNTA
Commercialization	–
Patent	–

Unmet need
Several severe microvascular complications currently have few or no approved pharmacological treatment options.

Our aim
Gesynta Pharma AB, who owns all the rights to OX-MPI (GS248), aims to develop a treatment for microvascular diseases in chronic inflammatory conditions.

Differentiation
More effective and/or safer than currently approved treatments.

US Pharma

Covid-19 **fuels the need** for Orexo's **treatments on the US market**

In the wake of Covid-19, societal lockdowns and social distancing have exacerbated the opioid crisis in the US. In 2021 a record-high number of Americans died of an overdose and treatment needs have never been greater. Orexo is established in the US since 2013, with an own sales force and on a daily basis sales representatives visits physicians, medical clinics and minor hospitals treating patients suffering from opioid dependence.

Significant need for treatment options
The use of drugs is growing globally. Approximately 300 million people are using drugs.[1] Opioids continue to cause the most harm and are the reason for the majority of drug-related deaths.[2] The problem with opioid misuse is by far the greatest in the US where about a fifth of those dependent on opioids live.[3] A sharp increase in prescription for opioid painkillers during two decades is the primary reason that today there are an estimated 10 million people abusing opioids in the US.[4] Approximately 4 million are considered to be in need of treatment.[5] Of these, approximately 1.5 million receive so-called Medication Assisted Treatment, MAT,[6] where the most common form of treatment is buprenorphine/naloxone.

Fentanyl is prevalent and causing the surge in fatal overdoses
The Covid-19 pandemic, with society lockdowns and social distancing, have fuelled the opioid crisis in the US. According to latest available annual data the number of fatal overdoses surpassed 100,000,[7] and overdose is today one of the most common cause of death for people under 50 years. 76 percent of the fatal overdoses were related to the misuse of opioids, foremost synthetic opioids, such as fentanyl.[8] Fentanyl supply is accelerating in the US due to a significant increase of illegal manufacturing in Mexico.

Large economic burden on the US society
From an economic point of view the misuse of opioids is a considerable problem. In addition to loss of life and lower quality of life, large costs are associated with lower productivity, increased healthcare and correctional treatment costs. The opioid epidemic cost the US society a tremendous amount. Additionally the costs continue to rise which can be explained by the growing death toll in recent years and as it includes a broader societal cost of premature death.

Opioid use disorder can be treated
Opioid use disorder is a treatable condition. As a result of its chronic nature and long-time repercussions, the effectiveness of treatment varies among patients, and treatment is often administered over long periods of time or chronically. The gold standard for MAT in the US is buprenorphine/naloxone which can be taken under the tongue as a tablet or film. Other treatment options are methadone which is most commonly administered orally under supervision and treatment using buprenorphine

>100,000
Record-high number of Americans who die of an overdose on an annual basis.[7]

10 million
Estimated number of Americans who are misusing opioids.

[1] World Drug Report
[2] World Health Organization
[3] World Drug Report
[4] Substance Abuse and Mental Health Services Administraton
[5] Clarion Healthcare
[6] Substance Abuse and Mental Health Services Administraton
[7] Center of Disease Control, predicted numbers as of June 2021
[8] Center of Disease Control, predicted numbers as of June 2021

3 questions to Robert DeLuca, President of Orexo US Inc.

How would you summarize the development in 2021?
Despite the impact of the pandemic on market growth and reduction of face to face interactions with our customer base especially MDs/HCPs, I am quite pleased with the stability and resilience of ZUBSOLV® and the US team. The US Pharma business delivered in its 8th full year a strong profit and sustainable cash enabling continued investments in the pipeline and in digital therapeutics.

What are your priorities in 2022?
To continue to deliver solid pharma profits and cash flows while building on the launch and sales of the digital portfolio, which has strong synergies with our sales force, and also preparing for the launch of OX124 in 2023.

In addition, with MODIA™ available we will increase our efforts to improve the availability of MAT for OUD patients. I also continue to seek business development opportunities to further strengthen our product portfolio.

What would you like to achieve in a 5 year horizon?
The US organization is consistently outperforming its prior years internal revenue targets by driving sales to a much higher level where the company becomes less dependent on ZUBSOLV® revenue through sales from pharma generated from the pipeline, the digital therapies and newly acquired products. Additionally, we have a pipeline of development projects to fuel the organization in the following 5 years.

standalone in a monthly injection. To reach improved overall treatment result MAT should be provided in combination with behavioral counselling and psychological support. In the US, treatment usually takes place in private practices or at specialist medical clinics, and more rarely in hospitals.

The buprenorphine/naloxone market in the US

The market for treatment of opioid dependence using buprenorphine/naloxone grew 8 percent in 2021. A slowdown from the record-high 15 percent in 2020. A progress explained by high comparison numbers in 2020 as an effect of Covid-19, but is also attributable to a combination of patients to a greater extent were not seeking care during continued lockdown and that physicians were more reluctant to grow patient load. The growth predominantly took place in the largest payer segment, the Public segment, where care is financed by the public sector payers, such as Managed Medicaid, FFS Medicaid and Medicare Part D. Care financed by private insurance companies, often signed by employers, comprised by the Commercial payer segment, showed a lower growth pace compared to the Public segment.

Generics part of the market continue to be dominant which mainly refers to the public financed care which is characterized by high price sensitivity.[1]

ZUBSOLV® is an important cash generator

Despite great generic competition and price pressure ZUBSOLV® continued to show strong profitability with an EBIT margin of 53 percent. EBIT amounted to SEK 278 million for the full year. This is a decrease from previous year, reflecting lower net revenues of SEK 523 million (623) due to lower demand, albeit with a significantly lower decline pace, at the insurance companies United Health Group and Humana. In 2019, these insurance companies added generics to their formulary lists resulting in ZUBSOLV® moving from being exclusively reimbursed to reimbursed. Meanwhile the demand increased on multiple formulary lists, foremost within Medicaid, but also in parts of the Commercial payer segment.

278 million

US Pharma EBIT in 2021, corresponding to an EBIT margin of 53%.

Short facts – US Pharma

Net revenues 2021	SEK 523 m
EBIT 2021	SEK 278 m[2]
EBIT margin	53%
Pharmaceuticals	ZUBSOLV®, for the treatment of opioid use disorder. For improved treatment results it should be used along with psychosocial support. ZUBSOLV® is based on Orexo's sublingual drug delivery platform. Patent protection until 2032. Accord Healthcare owns the rights to the EU market.
Target group	Insurance companies, private practices, specialist medical clinics, and minor hospitals.
Distribution channels	Orexo's own sales force, incl. 30–40 employees. The sales force also commercializes Orexo's digital therapies, focusing on MODIA™.
Key market	The buprenorfine/naloxone market
Key market growth in 2021	8%
Competition landscape	Suboxone® Film, generics on Suboxone® Film and Subutex®/ Suboxone® tablets
Percentage number of patients who can get the treatment reimbursed	The Commercial payer segment, 98% of the patients. The Public payer segment, 42% of the patients.

[1] Generics of Suboxone® Film and tablets and also of Subutex® tablets
[2] Both direct and indirect operating expenses have impacted EBIT

On the market, ZUBSOLV® is the only pharmaceutical that is actively marketed towards healthcare providers and during the year the sales force activities continued to be impacted by Covid-19. In the autumn, the sales force was trained in MODIA™, the new digital therapy for opioid dependence. MODIA™ in combination with MAT, such as ZUBSOLV®, presents exciting opportunities for increasing treatment results and, in the latter part of the year, a campaign was initiated to increase awareness and knowledge among physicians. The aim is to accelerate the launch of MODIA™ in combination with ZUBSOLV® during 2022.

In 2021, access to ZUBSOLV® in the Public payer segment increased 8 percentage points, from 34 to 42 percent, while it decreased from 99 to 98 percent in the Commercial payer segment.

Multiple drivers for future growth

- Covid-19 effects are expected to diminish, improving patient access to care and Orexo's access to customers.
- Multiple comprehensive activities on-going on federal and state levels will increase access to treatment.
- Capitalizing on the overall market access improvements for ZUBSOLV® with Public payer access at 42 percent and the continued strong access in Commercial at 98 percent (99).
- The MODIA™ launch is building on the ZUBSOLV® successes and provides opportunities to open new market segments.

Digital Therapeutics

Digital therapeutics on the way to playing **a vital role in the future** healthcare landscape

In an effort to broaden the business, Orexo has started to work with evidence-based digital therapies. The trigger was the development of MODIA™, which addresses a large unmet need for psychosocial counselling in the medical treatment of opioid dependent patients. The market for digital therapeutics is in its infancy and during 2021 several important steps were taken to facilitate reimbursement of these new and pioneering treatment tools.

Digital therapies increase access to psychosocial support

Digital therapeutics are a new and innovative form of treatment. With the use of digital therapeutics it is possible to prevent and manage, and in some cases also treat, clinical disorders and chronic diseases. Orexo's digital therapies will help patients suffering from mental illness and substance use disorders. Support from a therapist or psychologist is becoming an increasingly common element to improve treatment results. As more and more people seek treatment, the lack of psychosocial support increases. Digital therapies, which have a proven clinical effect, not only relieve healthcare services but also enable significantly more people to have access to qualified therapeutic treatments.

Mental illness increases significantly in the wake of Covid-19

In the US, mental illness is sharply increasing in all age groups. The development is predominantly driven by Covid-19, and in a study conducted during the pandemic by the Center of Disease Control, data shows a surge in the number of people suffering from depression and stress symptoms, trauma and addiction.[1] Many have sought care during the pandemic, but access to care has been limited. Nearly 18 million Americans who sought care for mental illness in 2020 have experienced delayed or cancelled care visits.[2] At the same time, digital healthcare increased significantly and in 2020, as many as 26 million Americans received help through telemedicine, which primarily meant on-line prescriptions but also digital meetings with healthcare providers.[3]

Digital therapies with clinically proven efficacy

Orexo's digital therapies are developed by or alongside GAIA AG, which has considerable experience of developing evidence-based digital therapies within various therapeutic areas. The therapies are developed in consultation with psychologists, physicians and patients and are based on cognitive behavioural therapy techniques. As the program is supported by artificial intelligence the therapies, to some extent, can be customized based on patients' needs. The therapies are available for patients 24/7 and can be used as standalone treatments or alongside traditional pharmaceuticals. Studies prove consistently positive clinical effects among patients and improved retention rates with ongoing combined medical treatments.

18 million

The amount of Americans who sought care for mental illness during Covid-19 in 2020 and experienced delayed or cancelled care visits.

[1] https://www.cdc.gov/mmwr/volumes/69/wr/mm6932a1.htm
[2] https://www.nami.org/mhstats
[3] https://www.nami.org/mhstats

3 questions to Dennis Urbaniak, EVP Digital Therapeutics

How would you summarize the development in 2021?
Our pipeline of new commercial opportunities was greatly accelerated through new partnerships, such as SoberGrid, Trinity Health, Justmine, and also with Walgreens, who we signed a collaboration with at the beginning of January 2022. These complementary platforms have created significant new qualified sales opportunities to pull through in 2022.

What are your priorities in 2022?
- Drive growing, sustainable demand in the areas that we have secured billable product access.
- Expand the overall number of users and market access for all three DTx therapies.
- Successfully scale our MODIA™ launch that began in late Q4, 2021.
- Leverage our learnings from 2020–2021 to optimize our investments and improve long term ROI.

What would you like to achieve in a 5 year horizon?
I would like Orexo to be seen as the industry leader in tangible DTx commercialization, delivering real world outcomes for patients while also ensuring DTx becomes a significant contributor to Orexo's revenue growth and profitability.

Market in its infancy but viable reimbursement routes will drive short-term growth

Digital health means digitization of services to prevent and manage clinical disorders and diseases more effectively. Supported by digital technology, patients' results can be improved and health care costs greatly reduced. The sector has grown significantly in recent years, and Covid-19 has further accelerated these developments. Digital therapeutics are a part of Digital health and the market for the treatment of mental illness and substance use disorders with these new innovative solutions is in an early phase.

With increased product knowledge and awareness, along with viable reimbursement routes, the market is predicted to show strong growth. In 2021 several important milestones were reached which will, as of the beginning of 2023 facilitate insurance companies and healthcare programs, such as Medicaid and Medicare, to reimburse digital therapies within the mental illness space. The global market for digital therapeutics, which includes all therapeutic areas, is expected to show an average annual growth of 30 percent and amount to USD 13 billion in 2026.[1]

View also underlying drivers that are expected to fuel long-term growth. See below.

Progress during the year

During the year, the sales force increased its focus on entering agreements with large healthcare providers as well as initiating partnership's to reach out to employers and patients directly. The most extensive collaboration is with Trinity Health in North Dakota, which is one of the major healthcare providers in the state. By adding the digital therapies to an already existing treatment program, the products can get reimbursed. However, before the physicians can start prescribing the therapies, Trinity Health needs to get certain administrative processes in place and that work, along with a new pandemic wave, has delayed full implementation until 2022. This reimbursement model has paved the way for collaboration with other major care providers such as Benefis Health System and Justmiine. A strategically important partnership was launched with SoberGrid, which is the largest digital network for people with addiction disorders. The collaboration is an important and cost-effective channel for reaching patients directly, and in early 2022 the collaboration reached an important milestone when vorvida® and deprexis® along with Sober Grid's complimentary therapeutic support, were added to Walgreen's digital marketplace for healthcare services, FindCare®.

The launch of MODIA™ was triggered by a campaign to raise knowledge and awareness among physicians who are prescribing ZUBSOLV®. Additionally a comprehensive clinical trial was initiated for MODIA™, which along with real world evidence collaborations with payers, such as the MAT analysis published with Magellan in 2021, will be critical for the long term commercialization of MODIA™.

Did you know this about DTx?

- Subsection of digital health
- Evidence-based therapeutic intervention
- Prevent, manage, or treat a medical disorder or disease
- Particularly applicable in the mental illness & addiction space
- Standalone or along with pharma treatment
- Available 24/7.

Underlying drivers to fuel future long-term growth

1 Aging population and sky-rocketing costs are forcing the healthcare providers to rethink how to deliver healthcare to increase efficiency and value.

2 Patients want to be seen as consumers and requires holistic and customized treatments with access 24/7.

3 Covid-19 has further pushed forward the ongoing tech revolution and the use of telemedicine is pervasive.

4 Providers will be rewarded based on the ability to add patient value. Analyzing RWE data pave the way for efficient allocation of resources.

[1] https://www.marketsandmarkets.com/Market-Reports/digital-therapeutics-market-51646724.html?gclid=Cj0KCQiAgP6PBhDmARIsAPWMq6lxh2pUz7zySH2_jL94UXWQU89DoqrCvuIUgvNP3J11jhgjZVYvCwAaAlcLEALw_wcB

Brief facts Digital Therapeutics

Net Revenues 2021	SEK 1.1 m
EBIT 2021	SEK –250 m[1]
Gross margin	N.A.
Therapeutics	**MODIA™** 6 months therapy for opioid dependence, should be used along with medical treatment. Extensive clinical trial ongoing. **deprexis®** 3 months evidence-based therapy to manage symptoms of depression. **vorvida®** 6 months evidence-based therapy, to reduce alcohol consumption among adults with problematic drinking behaviors. **MODIA™** and **vorvida®** launched in the US through the EUA and **deprexis®** is being marketed under enforcement discretion aligned with an earlier dialogue that GAIA AG had with the FDA.

Target groups	Insurance companies, larger health-care providers, other target groups such as, employers, organizations and consumers are reached through partnerships.
Distribution channels	Sales force shared with US Pharma, incl. 30–40 sales representatives, and through partnerships.
Key market	Digital therapeutics for the treatment of mental illness and SUD. A market in a very early phase due to lack of viable reimbursement routes.
Key market growth 2021	N.A.
Competitiors	Among others Pear Therapeutics, Hello Better, Happify Health and Silvercloud.
Percentage of patients who can get the therapies reimbursed	Reimbursement routes are not yet fully established.

[1] Both direct and indirect operating expenses have impacted EBIT

Sustainability report

Orexo **improves the lives** of people

People staying healthy, being able to work and take care of their loved ones is Orexo's ultimate goal and our biggest contribution as a company to a sustainable society. On the way to achieving this, Orexo will carry out its work in a way that as far as possible minimizes our environmental impact. Through a clear sustainability agenda that permeates the entire business, we will contribute to a more sustainable world.

Sustainability has been important for Orexo for many years and a responsible business is central to all our activities and a foundation for our sustainability work. Orexo's sustainability work is managed by the Sustainability group and the team includes representation from the management team and other relevant functions creating the ability to influence the company's strategies and policies. The sustainability goals are achieved by integrating our ambitions and sustainability values in our policies and procedures and by communication with our employees and business partners.

In 2020, Orexo refined its sustainability agenda by defining four focus areas. These were updated in 2021: a) Innovation and partnership, b) Sustainable people, c) Sustainable supply chain, and d) Environment and climate change.

In 2021, we initiated a process to evaluate, analyze and further develop the agenda. It started with an analysis of the present situation to identify important sustainability topics. This was followed by a stakeholder analysis and stakeholder dialogue. In 2022, the stakeholder dialogue will be followed by a materiality analysis. The process ensures that Orexo identifies material topics, involvement of the whole organization and eventually a more powerful sustainability agenda.

Frameworks are guiding our employees

Orexo's policies and procedures guide managers and employees in their day-to-day work and are aligned with international standards and well-known initiatives, such as the ILO conventions and the UN Guiding Principles on

Statement by the CEO

Orexo's Sustainability Report is prepared in accordance with the Swedish Annual Accounts Act and it also act as our Communication on Progress according to the reporting guidelines of the UN Global Compact. I am pleased to reaffirm Orexo's support of the Ten Principles in the areas of Human Rights, Labor, Environment and Anti-Corruption.

Yours sincerely

Nikolaj Sorensen
President and CEO

Business and Human Rights. Orexo is also a participant in the UN Global Compact. The Swedish head office, where we carry out research and development, is responsible for developing and maintaining corporate governance both for the Swedish parent company and its US subsidiary, Orexo US, Inc. The majority of the commercial activities are run by Orexo US, Inc., which also manages a number of guidelines adapted to local expectations and conditions in the US. Further details regarding governance and guidelines are described under Responsible business and each of the four focus areas.

Orexo contributes to the UN Sustainable Development Goals

Orexo supports Agenda 2030 and the Sustainable Development Goals (SDGs). In 2021, Orexo participated in the UN Global Compact's program "SDG Ambition Accelerator", a program that challenges participating companies to set more ambitious and clear goals in line with the SDGs. Our focus continuous to be on Goal 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." Target 3.5 connects directly to our business' ambition to prevent and treat mental illness and addictive diseases. The SDGs will play an important part in our continued work to set a robust and material sustainability agenda. Further, the supply chain and the use of contract manufacturing plays an important part in the company's contribution to the SDGs.

Responsible business

Orexo operates in a market and industry where ethics and transparency are instrumental. Our overall corporate governance promotes the transparency to combat corruption and safeguard human rights.

Innovation and partnership

Our ambition is to become a leading player within the large and growing space of mental illness and substance use disorders and to improve access to treatment.

- New innovations
- Establish partnerships to develop and increase access to treatment
- Continuing collaborations with universities

Sustainable People

Our ambition is to offer a safe and healthy workplace where everyone feels valued and respected.

- Good health and well-being for our employees and a safe working environment
  - An equal and non-discriminatory work culture

Sustainable Supply Chain

Our ambition is to ensure good management of social, ethical and environmental impacts throughout the supply chain.

- Sustainable procurement
- Responsibility throughout our supply chain

Environment and Climate Change

Our ambition is to to operate efficiently and to reduce the climate and the environmental impact of all activities.

- Reduction of greenhouse gas emissions
- Improve or resources usage and and reduce amounts of waste

Frameworks

UN Agenda 2030
The UN Sustainable Development Goals sets an ambitious and necessary agenda to lead the world towards more sustainable development. Orexo's operations has a direct and indirect impact on several of the goals. Orexo has the greatest impact on the sustainability goal number 3 "Good health and well-being".

UN Global Compact
The organizations that participate in the UN Global Compact commit themselves to living up to ten principles regarding human rights, working conditions, environmental impact and anti-corruption, and respect these throughout their value chain. As a participant in the UN Global Compact, Orexo's sustainability agenda builds on and follows these principles. The principles give the company the long-term focus and the direction required to create a positive change in the business.

ILO core conventions
Orexo complies with the International Labor Organization's (ILO) eight core conventions, which constitute a minimum standard for working conditions, all over the world. It is about basic human rights in working life.

UN Guiding Principles on Business and Human Rights
Orexo follows the UN's Guiding Principles on Business and Human Rights. These principles were adopted in 2011 and mean that an activity should not contribute to human rights violations and that companies should act to prevent such.

3 questions to Cecilia Coupland

SVP and Head of Operation, management representative in Orexo Sustainability Group

How would you summarize sustainability for 2021?
Mental illness and substance use disorders are growing issues that have increased substantially during the pandemic. I am proud of the progress we made during 2021 in our research projects and in our collaborations with partners. These developments are creating opportunities to both bring new, improved products to the market and enabling our existing products to reach more people who are struggling.

The many challenges addressed by the Sustainable Development Goals continues and our participation in the UN Global Compact program SDG Ambition Accelerator has given us valuable insights into where our biggest impacts are. We have also taken further strides in our understanding of our current situation and what is important for us, by performing an internal and external stakeholder analysis. This will serve as great base for our future sustainability efforts.

What are your sustainability priorities for 2022?
Our main priority is to finalize our materiality analysis and use this as a basis for setting a sustainability plan for coming years. The plan will include the whole of Orexo, both the Swedish R&D operations and our sales organization in the US. Furthermore, we will accelerate our efforts in understanding the sustainability impact of our external suppliers, which are a crucial part of our value chain.

What would you like to achieve in a 5 year horizon?
My vision is that in five years we will have a full understanding of our sustainability impact through our operations and value chain and that we will have executed our sustainability plan. Also, that we will be recognized as a responsible company that goes beyond our legal obligations for sustainability.

Responsible business

Orexo operates in the pharmaceutical industry, marketing a controlled substance. This sector of the industry has a history of unethical business conduct, hence business practices for companies like ours receive heavy scrutiny by law enforcement and legislative bodies. For us at Orexo, responsible business practices are a top priority and we have no tolerance for non-compliance.

Ethical practice underpins all Orexo's business operations. Orexo operates in markets that offer good business opportunities, but operations can also be in high-risk markets with exposure to serious risks such as bribery and corruption. Orexo has no tolerance for this.

Orexo's Code of Conduct "Business Compliance and Ethics Code" serves as an umbrella for all other policies and guidelines in the company and is based on corporate values, legislation and internationally recognized standards, such as the Universal Declaration of Human Rights, the Helsinki Declaration[1] and the Ten Principles of UN Global Compact. Orexo's Code of Conduct is the basis of our business and it describes expectations and requirements in the areas of human rights, personnel and labour law, environment and anti-corruption. It also describes ethical expectations of research and development as well as requirements regarding patient safety.

The Code of Conduct must be followed by all board members, employees and temporary staff at Orexo AB and its subsidiaries. To ensure legal compliance, manage risks and to achieve set sustainability ambitions, Orexo has several policies and guidelines linked to the Code of Conduct.

To ensure good business ethics, and compliance with laws, regulations and Orexo's values, all board members, personnel and temporary staff are required to read and understand Orexo's Code of Conduct. In Sweden this is done at least biannually by reviewing and reaffirming their understanding and compliance with the Business Compliance and Ethics Code. Correspondingly in the US, the US Code of Business Conduct and Ethics is reviewed and reaffirmed annually.

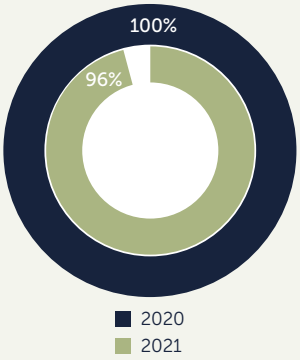
Supporting Orexo's Code of Conduct there is a Comprehensive Compliance Program. This consists of policies and procedures structured to mitigate the legal, regulatory and ethical risks associated with research and development, quality control and the US commercial pharmaceutical operations.

Orexo's management systems assist personnel in accessing and tracking the policies and procedures relevant to their role. Policies and procedures are reviewed on an ongoing basis as business needs evolve and at least once every two years. All new employees receive comprehensive introductory training including the Orexo Code of Conduct, role-specific compliance requirements, and the Safety, Health and Environment framework.

Business Compliance and Ethics Code			
Supplier Code of Conduct	US Comprehensive Compliance Policies	Safety, Health and Environment Policies	Human Resources Policies

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

Implementation of Code of Conduct



All data can be found in the Sustainability Data Summary.

Whistleblower system where everyone can make their voice heard

Orexo must be a transparent, healthy and open organization that complies with laws, regulations and the company's Code of Conduct. The Code of Conduct urges individuals to pay attention to and report suspected business ethics violations or unethical conduct, without retaliation or any threat of retaliation.

If someone suspects that a serious violation has occurred, it is important that this is reported and that the reporting can be done anonymously. In 2021, a new process and tool for anonymous reporting, WhistleB, was introduced for the Swedish operations. In the US, the whistle blower system, Ethics Point, has been in use since many years. In 2021, no reports were made.

Marketing and sales

For businesses within the healthcare sector, one recognized risk is unethical business and compliance violations in interactions with healthcare professionals, healthcare organizations and government officials. Orexo's Code of Conduct therefore sets requirements and expectations and supports employees in their daily work.

Orexo has its main market in the USA, where the subsidiary Orexo US, Inc. is responsible for product commercialization. The subsidiary operates in accordance with laws and regulations established at the federal and state levels. The guidelines, collectively referred to as "US Comprehensive Compliance Policies", describe accepted marketing practices and activities related to drug sales, including the reporting of marketing expenses and interaction with government authorities and healthcare representatives. All employees in the US are trained in these, both through teacher-led training and virtual training.

All new sales representatives receive specific training held at the Orexo office in New Jersey. The training lasts for a week covering sales and product training as well as all promotional policies, federal laws and regulations related to pharmaceutical sales and ethics, and their role as a sales representative, including interacting with physicians. At the end of the training, everyone takes a test to show that they have understood the material and the expectations and requirements. After this, there are periodic reminders and refreshers, during which sales representatives are given opportunities to discuss examples of field interactions in the context of compliance requirements to test the policy content, in addition to regular requests to read and acknowledge understanding of the policies and procedures. During 2021, eight new sales representatives were trained and 100 percent of read and acknowledged requests were completed within the allotted 30 days. In addition, during 2021, the entire sales team was trained in preparation for the MODIA™ launch, including an in-person compliance module.

Subpoena

On June 14, 2020, Orexo US, Inc. received a subpoena requesting the provision of certain information to US authorities linked to ZUBSOLV® and other buprenorphine products. Orexo has no knowledge of the reason for this subpoena. Orexo has engaged legal counsel to assist in the event of further requests for information or other activities related to this. No further information was received in 2021.

Innovation and **partnership**

Orexo's sustainable development is based on innovations made possible by the interaction between skilled researchers and experts with different scientific backgrounds. Innovation is at the core of the continued development of new formulation technologies and early development projects, enabling us to offer better medicines to patients globally. We recognize the importance of access to good healthcare and we are working closely with a number of partners to enable our drugs and digital therapies to reach more patients.

Our ambition is to become a leading player within the large and growing space of mental illness and substance use disorders and to improve access to treatment.

Important questions

- New innovations to prevent and treat substance use disorders and mental illness.
- Establishing partnerships to develop and increase access to treatment.
- Continuing collaborations with universities to strengthen pharmaceutical development.

Highlights 2021

- Pivotal trials for OX124 completed with positive results – a drug that will help reversing overdoses caused by synthetic opioids.
- New drug delivery platform amorphOX™ giving new possibilities for new drug development.
- Completion of EU ZUBSOLV® supply chain and approval for launch in H1 2022.

Innovation is at the core of Orexo's business and drives our ambition of becoming a leading player in the treatment of mental illness and substance use disorders. To alleviate suffering and improve people's quality of life, equitable access to treatment is critical. To lead the way through offering novel and improved treatments, Orexo has been investing in several areas. These include the pipeline of pharmaceutical candidates, a new business area - digital therapeutics, and in university research projects. On the market Orexo is working with various players, such as lobbyists, authorities, policy makers, universities and industrial organizations, to increase access to treatment as well as to create awareness and knowledge about digital therapies that have the potential to give access to therapeutic support. The relationships and knowledge from these collaborations add great value to our research and development of future innovations and new products. We also work to reach more patients through partnerships, collaborations and financial assistance programs.

Innovations for improved treatment and reduced environmental impact

Overdoses from opioid misuse continue to cause many deaths. During 2021, Orexo continued to focus on the development project OX124. The OX124 product is based on Orexo's new drug delivery platform amorphOX™ and is designed to counteract overdoses caused by the most powerful synthetic opioids that is currently behind the vast majority of overdose fatalities in the US. The pivotal trial, completed in 2021, showed strong clinical data (see page 23).

As described on page 18, Orexo has developed the new drug delivery platform amorphOX™. This platform offers new opportunities to develop drugs with good chemical and physical stability which dissolve rapidly in small amounts of liquid. The delivery platform works for a broad scope of different active ingredients and its properties make it ideal for the development of emergency drugs. We also see

opportunities for environmental benefits having a platform which supports the development of pharmaceutical products with a longer shelf life.

Orexo's new pharmaceutical candidate OX640, a nasal adrenaline product for the emergency treatment of allergic reactions, is also based on the amorphOX™ platform. Adrenaline is a very unstable active ingredient sensitive to chemical degradation and today's commercially available adrenaline products have a limited shelf life. OX640 shows promising chemical and physical stability data and could provide a needle-free alternative with greater flexibility in its handling and storage. Further, OX640 does not contain any preservatives which are common among today's treatment solutions and can trigger allergic reactions.

University collaborations

Orexo participates in SweDeliver, an interdisciplinary collaboration between academia and industry, founded in 2020 with financial support from Vinnova, Sweden's innovation agency. The Faculty of Pharmacy at Uppsala University is the academic hub of the center. The scientific focus is on important research challenges in parenteral, oral and pulmonary drug delivery. In addition to this, young researchers are given the opportunity for education and career development. The goal of the center is for research to lead to the development of new and improved drug treatments. Orexo provides financial support, scientific expertise, an industrial perspective, and mentorship to young researchers. In 2021, SweDeliver launched a new initiative where motivated students were offered the opportunity to pursue a six-week research project at an industrial partner. Orexo had one of the six internship openings and during the summer of 2021 we had a student adding value to one of our important research projects.

In addition to the specific internship program, Orexo continuously provides university students with thesis project opportunities. In 2021, we had one student working with us. In addition, we have study visits from the university and we are also invited to give lectures as part of university courses. These collaborations aim to strengthen the development of future pharmaceutical researchers.

Increased access to ZUBSOLV®

Helping to remove financial barriers that impede access to our products remains a priority. To enable greater access to ZUBSOLV®, we are currently running two programs that help to reduce out- of-pocket costs. The ZUBSOLV® Co-pay assistance program saves patients significant amounts of out-of-pocket costs when they pick up their ZUBSOLV® prescription and use the co-pay card. The ZUBSOLV® 15 tablet voucher program provides up to two free 15 tablet vouchers (30 tablets in total). Additionally, the ZUBSOLV® Patient Assistance Program provides free products to those patients that meet the US poverty level requirements.

These programs were launched in 2013 and have provided financial assistance to many patients. In 2021, 145 patients received help through the ZUBSOLV® Patient Assistance Program, while more than 81,000 co-pay cards and

5,300 tablet vouchers were redeemed. There has been a reduction in the programs over the last years and this is explained by the erosion of Orexo's market share to generics, the loss of contract exclusivity with one of our key insurance plans and the sales representatives reduced ability to make in-person sales calls due to shutdowns during the pandemic.

In 2020, Orexo entered into a licensing and delivery agreement with Accord Healthcare to make ZUBSOLV® available on the European market. There are estimated to be 1.3 million high-risk opioid users in Europe[1], yet treatment rates are low. Only around 50 percent of people with opioid dependence are receiving some form of substitution treatment across Europe, although this varies greatly between countries.[2]

In 2021, all the permissions and equipment were finalized for the supply chain in Europe, preparing for launch in H1 2022. Orexo is responsible for product supply and Accord Healthcare has in-licensed the rights from Orexo. With the commercialization in Europe, people in up to 29 additional countries will have access to ZUBSOLV®.

The need for therapeutic support

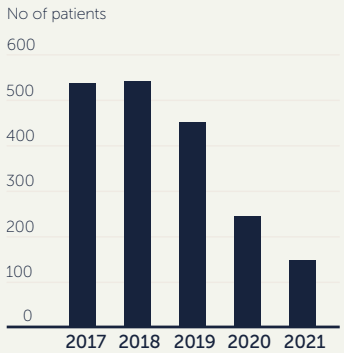
To address the lack of psychosocial counseling in the treatment of opioid-dependent patients, Orexo entered a partnership with GAIA in 2019 to develop a digital therapy for opioid use disorder, MODIA™. In addition to MODIA™, Orexo acquired the evidence-based digital therapies vorvida® (for problematic drinking) and deprexis® (for depression) in 2019 and 2020 respectively. During the pandemic, mental illness and substance use disorders have increased substantially. Orexo is working to increase awareness and knowledge about our new, pioneering treatments and is collaborating with various players to open up viable reimbursement routes, which are critical giving more patients access to the right treatment.

In 2021, Orexo continued to donate vorvida® and deprexis® to front-line healthcare professionals. Through our partnerships with the Texas Nurses Association[3] and Trinity Health in North Dakota[4], we provided all partner employees access to deprexis® and vorvida® free of charge. The use of these therapies is voluntary and completely anonymous. To date, 190 unique logins have been distributed to staff as part of these programs. In addition, we initiated a program with St. Louis University School of Medicine in November 2021, to provide front line workers, including all interns, residents and fellows with free access to deprexis® and vorvida® .

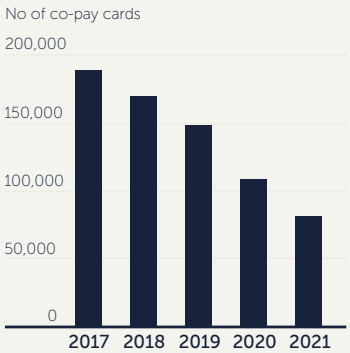
In addition to external partnerships, we continued to provide all our employees and their families with access to our digital therapies free of charge.

ZUBSOLV® patient programs

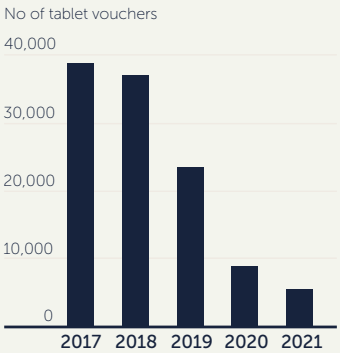
Patient assistant program



Co-pay assistance program



Tablet voucher program



All data can be found in the Sustainability Data Summary

[1] European Monitoring Centre for Drugs and Drug Addiction (EMCDDA)
[2] EMCDDA – Tackling Opioid Dependence
[3] https://www.texasnurses.org/news/544391/Deprexis-Free-Digital-Therapy-for-Nurses.htm
[4] https://www.trinityhealth.org/digital-therapies-help-frontline-workers-cope-2/

Sustainable **people**

Our people are our strength. We value one another's contributions and understand that our joint efforts are the key to our success. Our workplaces must be safe and healthy environments where every employee feels respected and has the same opportunities. We believe in an open-minded culture that sparks creativity and new ideas.

Our ambition is to offer a safe and healthy workplace where everyone feels valued and respected.

Important questions	Highlights 2021
• Good health and well-being for our employees and a safe working environment.	• High scores in employee satisfaction regardless of the pandemic. • Cooperation with IMR in Sweden and a wellness program in the US to promote work out. • No major incidents or accidents.
• An equal and non-discriminatory work culture.	• No unreasonable pay differences in salary survey. • Development of a more flexible working solutions for a better work-life-balance.

Our success is based on our commitment to the well-being of every employee. We have employee recognition programs and encourage everyone to acknowledge their colleagues' contributions. Attracting and keeping the best individuals means offering them mutually respectful workplaces where people are valued for who they are as well as their professional capabilities. Orexo enables new ideas and creativity through cross-functional cooperation. To encourage learning and new thinking we have individual development programs for our employees and funds earmarked for training. We also try to encourage our employees to make suggestions to improve processes and innovations.

The importance of wellness and health is governed by the company's overall Code of Conduct. In connection to this there are policies and procedures structured to mitigate the risks associated with the work environment. This includes governance of safety, health, recruitment, equal treatment, gender equality, discrimination and conflicts of interest as well as health insurance and other employment benefits.

Safety and health of our employees

Annual health and safety targets and activities are based on risk assessments and specific issues raised in the organization, such as employee surveys. The greatest risks identified are linked to mental health, due to a high workload, but there are also risks linked to the handling of active pharmaceutical ingredients and other hazardous substances. The handling of hazardous substances are well mitigated through risk assessments and routines. A key factor to promote physical and mental wellbeing is daily physical exercise. To encourage this, we have had a collaboration with IMR, the Institute for People in Motion, during the year where all our employees in Sweden have worked on their own health journey. Similarly in the US, we offer our employees wellness benefits, one of which is a paid subscription to a wellness program which offers virtual fitness classes in addition to mental health and other employee support resources. The company also offers an Employee Assistance Program (EAP) to support employees with issues impacting mental and emotional well-being. For our field-based salesforce in the US, driving is considered a significant risk, and one important activity during the year has been to update the fleet cars to safer vehicles. Overall, no major incidents or accidents happened connected to Orexo's operations in Sweden and US during 2021. No major incidents or accidents has occurred the last 5 years.

To ensure we continuously improve the work environment, Orexo in Sweden are using monthly surveys to monitor the well-being of employees with questions regarding their work situation, well-being, communication and participation. These surveys measure the situation for each department and group and can assist managers with creating and engaging in dialogue with individuals and teams.

Furthermore, to investigate the overall work situation for our employees we conduct an annual employee survey[1]. The results are followed up and evaluated by management but are primarily used as a tool at the group and department level to take concrete actions to improve the work environment. In 2021, we were happy to see that more than 4 out of 5 employees reported satisfaction with working at Orexo.

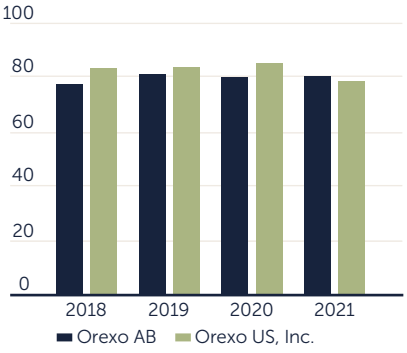
During 2021, the second year of the Covid-19 pandemic, Orexo continued to have different measures in place to reduce the spread of infection. Our sales representatives have adapted a hybrid sales model, visiting healthcare professional offices in person when they can and conducting some calls virtually if needed, depending on the state and local restrictions. We have continued to provide Personal Protective Equipment to all our employees to maintain safety and protection from Covid-19 in the workplace. Working remotely has continued to be the way of working for many employees both in Sweden and the US. While the pandemic has been challenging, we are glad the employee survey shows good results regarding psychosocial health. Employees have indicated that they feel their job provides them with a great deal of meaning and purpose and that they truly enjoy the people and teams they work with. Areas in the annual employee survey that need further development throughout 2022 are goal orientation in Sweden and professional development in the US.

Diversity and gender equality

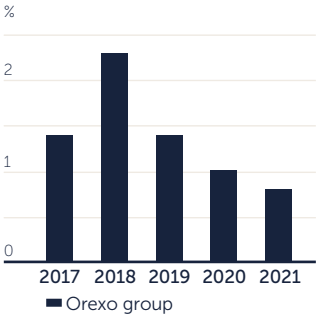
We are convinced that employees of different ages, genders, backgrounds, and experiences contribute to new thinking and innovative solutions. Diversity and gender equality are therefore important for us to achieve our goals and ambitions. Orexo is committed to diversity in hiring and conducts diversity training to ensure the organization's employment practices are in line with these objectives.

To further our work with equal rights and opportunities, we have a plan in Sweden with different focus areas. One focus area is work-life balance and one action during the year was to create a more flexible solution for when employees need to be at the office. Another focus is equal pay and every year in Sweden we conduct a salary survey. This year's survey discovered no unreasonable salary differences. In 2022, we will continue to work on the plan. In the US, our focus is more on training our employees to avoid discrimination and harassment.

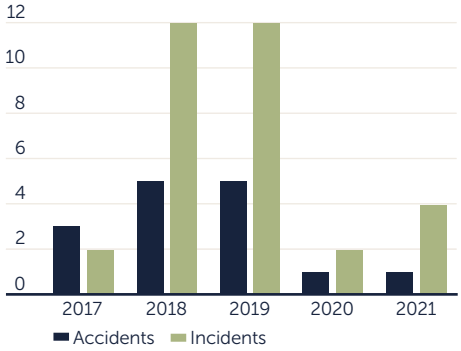
Employee satisfaction (%)



Absence due to illness (%)

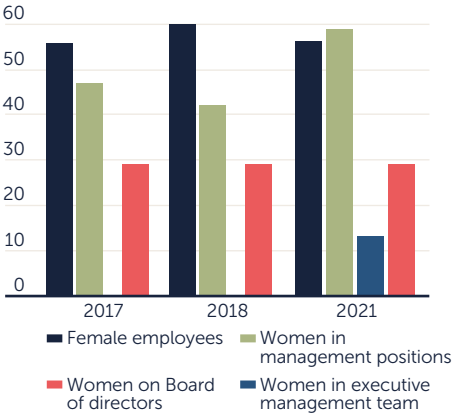


Accidents and incidents (rate)



No major accidents or incidents have occured 2017–2021.

Women in management position (%)



[1] Springlife employee survey Orexo AB, DecisionWise Orexo US, Inc.

All data can be found in the Sustainability Data Summary.

Sustainable **supply chain**

As we have a largely outsourced supply chain, we rely on these partners to produce, pack and supply our products to the market. We have great confidence in our suppliers, but we are still accountable for understanding the impact of our supply chain and to ensure it is sustainable.

Our ambition is to ensure good management of social, ethical and environmental impacts throughout the supply chain.

Important questions

- Sustainable procurement to ensure decisions and relationships reflect company values.
- Responsibility throughout our supply chain to ensure sustainability in all production steps.

Highlights 2021

- Further development of the Code of Conduct for Suppliers.
- Improvement of the responsible sourcing program with clear and improved requirements for suppliers.
- All important Tier A & Tier B suppliers evaluated. In 2021, Orexo began the process of re-evaluating suppliers.

Working towards a sustainable supply chain means that purchasing decisions and relationships that are formed must align with the company's principles and values for business ethics, work environment, human rights and the environment.

There are risks around several aspects of our suppliers. Although Orexo's direct suppliers are located in countries with strong environmental, health, safety and labour legislation, there are risks connected to these aspects. Subcontractors[1] may be found in many different parts of the world and it is therefore important to ensure that all direct suppliers have good governance and processes. Orexo is committed to complying with the UN Guiding Principles on Business and Human Rights, and it is along the supply chain that we see the greatest risks linked to human rights.

It is the ambition of Orexo to prevent, remedy and improve sustainability work throughout the supply chain. It is by putting requirements on direct suppliers and building their awareness of sustainability issues, and their role, that we jointly contribute to sustainable development.

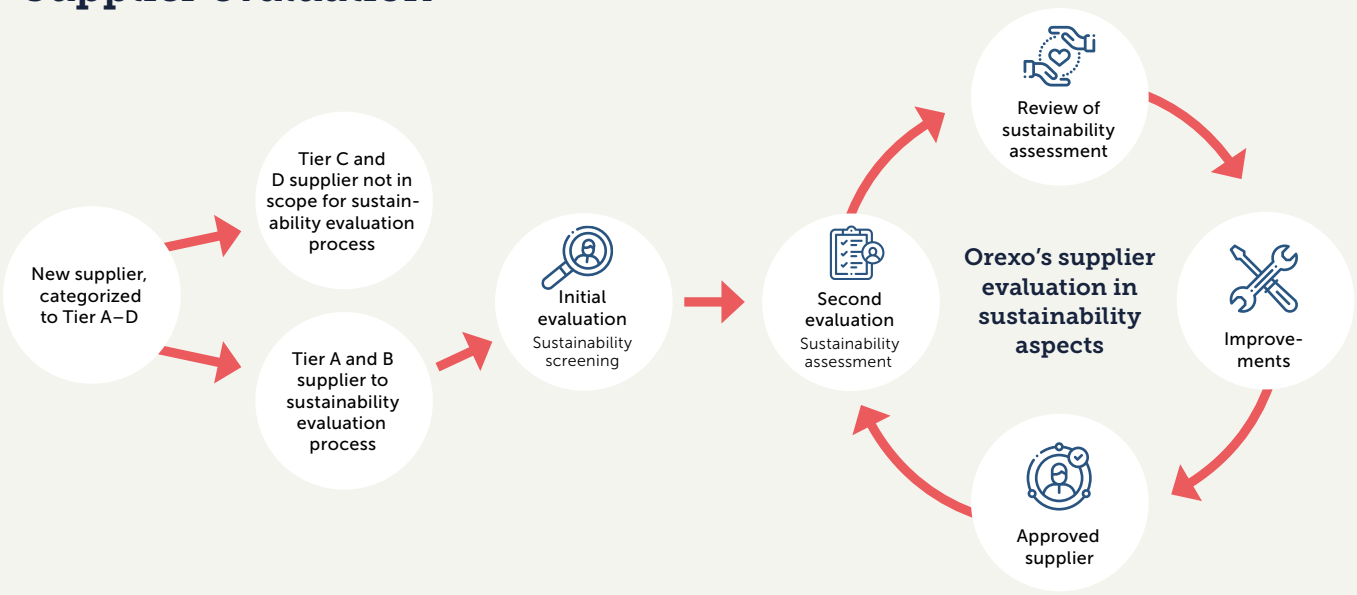
Governance and guidelines

During 2021 we improved our Responsible Sourcing Program to ensure our Supplier Code of Conduct (SCoC) is implemented throughout the supply chain. In addition, our SCoC was reviewed and updated to further clarify our expectations. It sets out minimum requirements for suppliers, including legal compliance, human rights, business ethics, safety, health and environmental expectations. To monitor and improve compliance with the SCoC, our processes and approaches aim to ensure risks regarding patient safety, product quality and sustainability are acceptable. These processes and approaches also ensure that applicable commercial aspects, such as security, financial stability and other commercial risks in the supply chain are adequately investigated.

Through the supplier evaluation process, Orexo evaluates sustainability aspects of strategically important suppliers. All suppliers are divided into Tiers A-D, where Tier A are the strategically most important. Tier A suppliers include raw materials suppliers and contracted manufacturers

[1] Delivering chemicals and intermediates to our suppliers for the Orexo production

Supplier evaluation

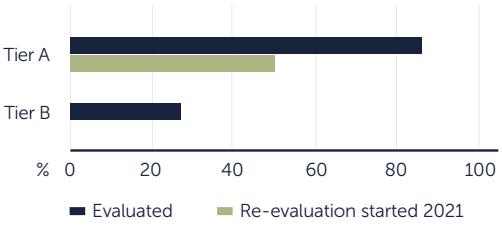


(API-production, formulation, packaging and distribution) of products on the market. Tier B-suppliers are other strategically important suppliers, such as suppliers to development projects or suppliers of systems. Tiers C and D are not prioritized for evaluation. The supplier evaluation covers legal compliance, as well as compliance with human rights, business ethics, safety, health and environmental impact. It is carried out through evaluation forms, supplier interviews and, if necessary, site visits. Supplier sustainability status is continuously monitored through supplier management.

All Tier A suppliers and many important Tier B suppliers are evaluated. With clear and improved requirements Orexo also started the process to re-evaluate all Tier A and important Tier B suppliers. In the beginning of 2022, we plan to include re-evaluation of all Tier A and previously evaluated Tier B suppliers, including additional Tier B suppliers.

Further, in 2021 we developed a screening checklist to be used early in development projects to make a first evaluation of suppliers. This is to show the suppliers the importance of having sound and systematic sustainability work and to help us with decision making.

Evaluation of suppliers



All data can be found in the Sustainability Data Summary

Environment and **climate change**

A sustainable future requires joint responsibility for the environment. All human activity depends on ecosystems and their services, such as access to clean air, clean water, and natural resources. Climate change affects both the ecosystems and people's health. Action is urgently needed! To contribute to a more sustainable world, Orexo conducts activities that reduce our impact on climate change and improve our resource efficiencies.

Our ambition is to operate efficiently and to reduce the climate and the environmental impact of all activities.

Important questions

- Reduction of greenhouse gas emissions.
- Improve our resource usage and reduce amounts of waste.

Highlights 2021

- Improved corporation for energy efficiency, with "green agreements" and ENERGY STAR certificate, with our property owners.
- Improved use of digital working methods and increased awareness of travel habits to maintain new ways of working and reduce flight travel.
- Improved efficiency of waste sorting and campaigns with less printed material.

The overall environmental work at Orexo is governed by the company's environmental policy and guidelines. An environmental action plan is set annually, based on the overall sustainability goals. The most significant environmental aspects for Orexo are waste and CO_2 emissions.

Orexo's manufacturing of products, packing and supply to market are performed by contracted manufacturers. We have not yet quantified the total environmental impact of our supply chain. However, we believe that it is in the supply chain that we find our most significant environmental impacts. We are convinced that through reviewing and putting requirements on our suppliers, we can make environmental improvements. Our work for better supplier sustainability is described earlier in this report.

Despite having an outsourced supply chain, we see the importance of reducing our direct environmental impact from our operations in Sweden and the US.

In 2021, our goals have been to continue collecting data to identify which key performance indicators are most important. This work will continue in 2022.

Climate impact

Orexos direct carbon emissions mainly relates to travel and energy usage. The R&D facilities and offices are rented and shared with other tenants. We have a "green agreement" with the property owner for the Swedish facilities. This sets out an expectation of cooperation to reduce the environmental footprint through joint work. The majority of the reported energy usage (heating, cooling and electricity) is calculated based on the size of the used premises. In the absence of individual measurements, it is not possible to see direct effects of energy reduction measures taken by any single tenant. For selected equipment, individual measurements of electricity consumption are done and in cooperation with the landlord we aim to introduce additional individual measurements on our equipment. Currently, the premises are heated with climate compensated district heating and cooled with district cooling and the electricity purchased is from renewable resources. In cooperation with the landlord, our goal is to find opportunities to reduce the overall consumption through improvements in our facilities.

The offices in the US are ENERGY STAR certificated, a third-party reviewed certification that ensure that the building is energy efficient.

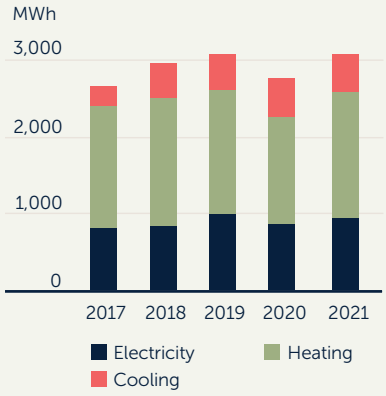
Orexo's main commercial market is in the US. The contracted manufacturers for ZUBSOLV® and several of the raw material suppliers are based in the US, as well as our own sales and marketing organization. This has historically necessitated a certain amount of business travel between the US and Sweden which changed drastically during 2020 and 2021, mainly due to Covid-19. While we see the need for travel continuing in the future, we are refining our use of digital working methods and strengthening our assessments to determine the necessity of any travel requirements.

Waste and recycling

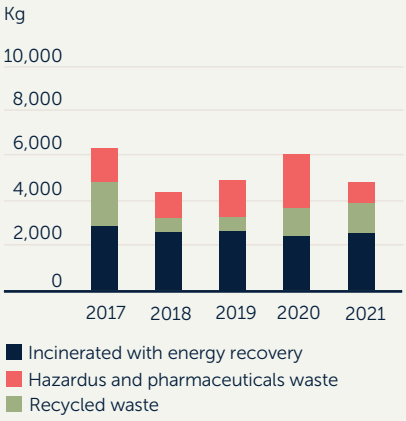
The ambition for waste is to reuse and recycle in favor of waste for incineration (with energy recovery). In our R&D facilities and offices in Sweden we have not identified any waste stream where a single effort would lead to a substantial reduction of waste to incineration or landfill. An ongoing dialogue with the waste vendor aims to give us access to improved statistics and analysis of our mixed waste for incineration. During 2021, we got access to better statistics, however, an analysis of the mixed waste still needs to be completed. Further, in 2021 we improved our waste sorting possibilities in the common areas and updated information on correct sorting. In the US, printed material is identified as the single biggest waste contribution and we work to reduce this by introducing digital information materials.

Further, better resource handling at our contract manufacturers is part of our supplier evaluation program.

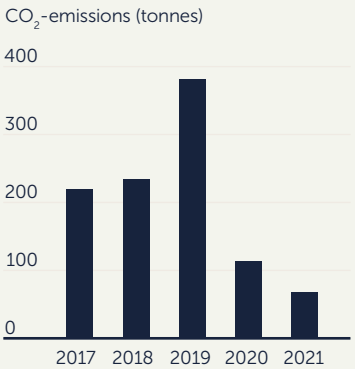
Energy[1]



Waste[1]



Flight travel[2]



All data can be found in the Sustainability Data Summary.
[1] Data cover Orexo AB
[2] Data cover Orexo AB 2017–2018 and Orexo group from 2019

Sustainability **data summary**

Responsible Business

	2017			2018			2019			2020			2021		
	Orexo AB	Orexo US, Inc.	Orexo group	Orexo AB	Orexo US, Inc.	Orexo group	Orexo AB	Orexo US, Inc.	Orexo group	Orexo AB	Orexo US, Inc.	Orexo group	Orexo AB	Orexo US, Inc.	Orexo group
Completed Code of Conduct %	81	100	89	85	100	94	83	100	93	100	100	100	94	100	96

Sustainable people

	2017			2018			2019			2020			2021		
	Orexo AB	Orexo US, Inc.	Orexo group	Orexo AB	Orexo US, Inc.	Orexo group	Orexo AB	Orexo US, Inc.	Orexo group	Orexo AB	Orexo US, Inc.	Orexo group	Orexo AB	Orexo US, Inc.	Orexo group
Employment															
Number of employees	53	37	90	55	74	129	54	73	127	53	85	138	54	67	121
employees with permanent contract %	98	100	99	98	100	99	100	100	100	98	100	99	96	100	98
employees with temporary contract %	2	0	1	2	0	1	0	0	0	2	0	1	4	0	2
Staff turnover %	–	–	–	9	–	–	17	–	–	<1	–	–	11	–	–
Number of employees + consultants	59	73	132	63	77	140	64	79	143	79	89	168	72	73	145
Consultants %	10	49	32	13	4	8	15	8	11	33	4	18	25	8	17
Gender equality															
Female employees %	51	62	56	55	64	60	54	47	50	55	62	59	57	57	56
women in management positions %	44	50	47	33	50	42	38	50	44	33	54	43	44	75	59
women in excec. management team %	–	–	0	–	–	0	–	–	13	–	–	13	–	–	13
Women on board of directors %	–	–	29	–	–	29	–	–	29	–	–	38	–	–	29
Health															
Employee satisfaction index %	–	–	–	78	83	–	81	83	–	80	85	–	80	79	–
Employee absence due to illness %	2.2	0.2	1.4	3.9	1.1	2.3	1.7	1.2	1.4	1.8	0.5	1.0	0.9	0.7	0.8

Data cover Orexo group.

Safety

	2017	2018	2019	2020	2021
Major accidents	0	0	0	0	0
Accidents	3	5	5	1	1
Major incidents	0	0	0	0	0
Incidents	2	12	12	2	4

Data cover Orexo AB.

Innovation and partnership

Improved access to ZUBSOLV®	2017	2018	2019	2020	2021
ZUBSOLV® Patient assistant program (number of patients)	539	542	451	243	145
ZUBSOLV® Co-pay assistance program (number of co-pay cards)	189,217	170,232	150,452	108,826	81,225
ZUBSOLV® Tablet voucher program (number of tablet vouchers)	38,756	36,957	23,420	8,957	5,325

Data cover Orexo group.

Environment and climate change

Energy	2017	2018	2019	2020	2021
Electricity (MWh)	805	830	989	856	938
Heat (MWh)	1,603	1,682	1,628	1,434	1,673
Cooling (MWh)	268	449	464	506	493
Total energy usage (MWh)	2,676	2,960	3,081	2,795	3,104
Waste					
Incinerated with energy recovery (tonnes)	2,850	2,588	2,650	2,400	2,550
Recycled waste (tonnes)	2,001	651	615	1,259	1,333
Hazardus and pharma waste (tonnes)	1,519	1,160	1,641	2,424	976
Total waste (tonnes)	6,370	4,399	4,906	6,083	4,859
Recycled/(recycled+energy recovery) (%)	41	20	19	34	34

Data cover Orexo group.

	2017		2018		2019		2020		2021	
Flight travel	Sweden	US	Sweden	US	Sweden	US	Sweden	US	Sweden	US
CO_2 emissions (tonnes)	219	234	380	114	68	100	80	34	35	33

Data cover Orexo AB 2017–2018 and Orexo group from 2019.

Sustainable supply chain

Supplier evaluation	Tier A supplier	Tier B supplier
Number of suppliers in scope	7	23
Evaluated 2021 %	86	27
Re-evaluation started 2021 %	50	0

Data cover Orexo group.

UN Global Compact

Human rights	
Principle 1 **38–39, 45–46**	Businesses should support and respect the protection of internationally proclaimed human rights and.
Principle 2 **38–39, 45–46**	Make sure that they are not complicit in human rights abuses.
Labour	
Principle 3 **38–39, 45–46**	Businesses should uphold the freedom of association and the effective recognition of the right to collective bargaining.
Principle 4 **38–39, 45–46**	The elimination of all forms of forced and compulsory labour.
Principle 5 **38–39, 45–46**	The effective abolition of child labour.
Principle 6 **38–39, 43–46**	The elimination of discrimination in respect of employment and occupation.
Environment	
Principle 7 **38–39, 47–48**	Businesses should support a precautionary approach to environmental challenges.
Principle 8 **38–39, 47–48**	Undertake initiatives to promote greater environmental responsibility.
Principle 9 **38–39, 47–48**	Encourage the development and diffusion of environmentally friendly technologies.
Anti-Corruption	
Principle 10 **38–39**	Businesses should work against corruption in all its forms, including extortion and bribery.

Auditor's opinion

**To the general meeting of
the shareholders of Orexo AB,
corporate identity number 556500-0600**

Engagement and responsibility
It is the board of directors who is responsible for the statutory sustainability statement for the year 2021 on pages 34–50 and that it has been prepared in accordance with the Annual Accounts Act.

The scope of the audit
Our examination has been conducted in accordance with FAR's auditing standard RevR 12 The auditor's opinion regarding the statutory sustainability statement. This means that our examination of the corporate governance statement is different and substantially less in scope than an audit conducted in accordance with International Standards on Auditing and generally accepted auditing standards in Sweden. We believe that the examination has provided us with sufficient basis for our opinions.

Opinions
A statutory sustainability statement has been prepared.

Stockholm, March 30 2022
Ernst & Young AB.

Anna Svanberg
Authorized Public Accountant.

The share

Orexo's share is listed on Nasdaq Stockholm and available as American Depository Receipts (ADR) on OTCQX Market in the US. At year-end, Orexo had a total of 7,272 shareholders and the non-Swedish shareholding amounted to 43 percent.

The Orexo share is listed on Nasdaq Stockholm Mid Cap under the symbol ORX and can be traded on the US market, via an ADR available on OTCQX Market under the symbol ORXOY. During the year the share price decreased by 31 percent and the last price paid in 2021 was SEK 34.50 (50.00). This corresponds to a market capitalization of SEK 1,198 million (1,736). The highest closing price during the year for the share was SEK 55.90 quoted on January 20. The lowest quotation was SEK 29.70 on November 9.

Liquidity

In total 25.8 million (42.5) shares were traded in 2021, corresponding to a value of approximately SEK 1,091 million (2,500).

The daily average trading volume was 102,114 shares (167,984), corresponding to a value of SEK 4.3 million (9.9).

Ownership

At year-end, Orexo had 7,272 shareholders (8,814), of which 632 were registered as legal entities and 6,640 as private individuals. Of the share capital, 57 percent (53) is held by shareholders registered in Sweden and 43 percent (47) by non-Swedish shareholders. The largest proportion of shareholders registered outside Sweden can be found in Denmark, whose holding amounts to 34 percent (35).

Key Facts

Orexo Share

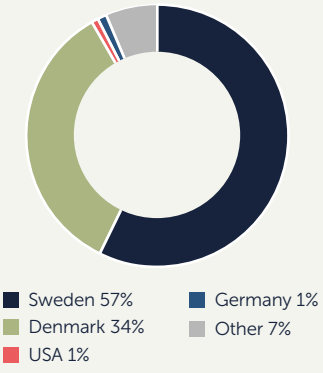
Listing	Nasdaq Stockholm, Sweden
Number of Shares	34,710,639
Market Capitalization, December 31, 2021	SEK 1,198 million
ISIN Code	SE0000736415
Ticker Code	ORX

Orexo ADR

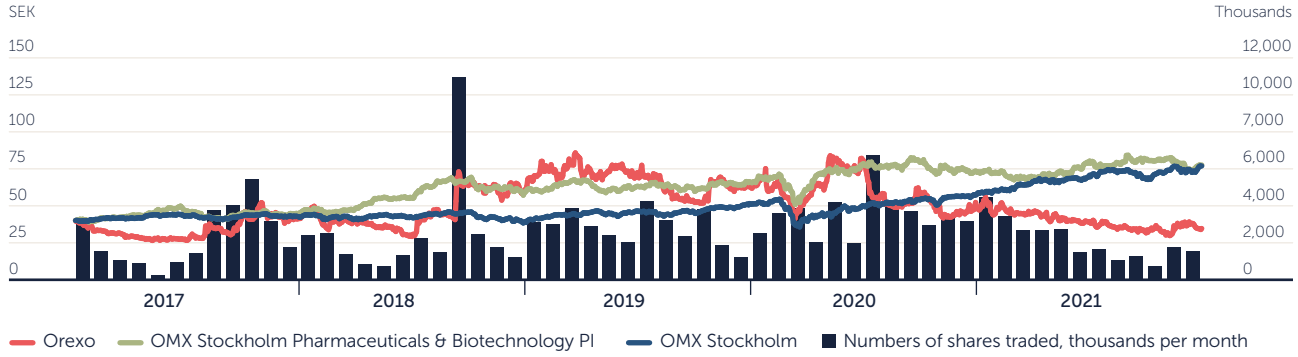
Trading Platform	OTC, US
Deposit Bank	Citibank N.A.
ISIN Code	US68616W1027
Ticker Code	ORXOY
Ratio	1:1

Ownership categories, December 31 2021

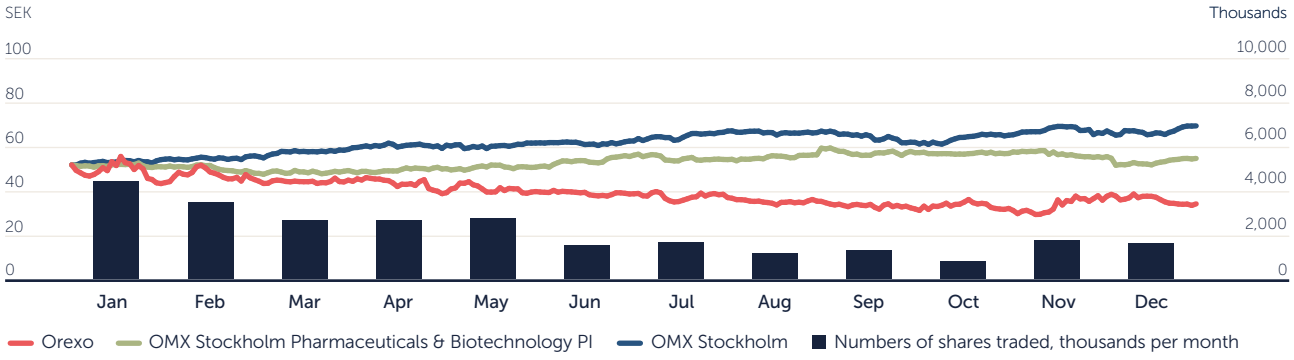
Ownership distribution per country, December 31 2021



Five-year performance



Performance in 2021



Shareholders, December 31 2021

Owners	No. of Common Shares	Share of Capital (%)
Novo Holdings A/S	9,643,184	27,80
Avanza Pension	2,752,367	7,90
ATP (Arbejdsmarkedets Tillægspension)	2,040,633	5,90
Anders Walldov, directly and indirectly	1,600,000	4,60
Life Insurance Skandia	980,411	2,80
Swedbank Insurance	896,894	2,60
Sixth Swedish National Pension Fund	768,850	2,20
Fourth Swedish National Pension Fund	646,328	1,90
Lancelot Asset Management AB	525,000	1,50
Handelsbanken Funds	384,163	1,10
Orexo AB	382,732	1,10
Stefan Hansson	290,965	0,80
Futur Pension	234,492	0,70
SEB Funds	212,545	0,60
Thomas Lundqvist	204,567	0,60
Total top 15	**21,563,131**	**62,10**
Others	**13,147,508**	**37,90**
Total	**34,710,639**	**100,00**

Source page 52–53: Monitor by Modular Finance AB, Euroclear Sweden AB and Nasdaq Stockholm

Owner Structure, December 31 2021

	No. of Shareholders	No. of Common Shares	Share of Capital %
1–100	2,887	112,902	0
101–500	2,124	592,849	2
501–1,000	792	652,244	2
1 001–5,000	1,042	24,426,75	7
5,001–10,000	206	15,679,62	5
10,001–20,000	116	16,737,62	5
20,001–	105	27,668,245	80
Total	**7,272**	**34,710,639**	**100**

Analysts monitoring Orexo

- Carnegie, Erik Hultgård
- Erik Penser Bank, Klas Palin
- Redeye, Gergana Almqvist
- RX Securities, Dr Samir Devani

Board of directors' report

The board of directors and the president of Orexo AB (publ), corporate registration number 556500-0600, hereby submit the Annual Report and consolidated financial statements for the fiscal year January 1 – December 31, 2021. Orexo's registered office is in Uppsala, Sweden.

Operations

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 commercializes it's lead product. ZUBSOLV® which was approved by the US Food and Drug Administration (FDA) on July 3, 2013, and launched on the US market on September 16, 2013. Digital therapy deprexis® was launched on July 1, 2020 and vorvida® on July 20, 2020 on the US market. In Q4 2021 an awareness and educational campaign for MODIA™ was initiated focusing on our existing ZUBSOLV® customers.

Orexo has to date developed the following proprietary commercial products:

- ZUBSOLV®, for treatment of opioid dependence, is approved for use in the US, in the EU and in Australia. In the US the product is commercialized by Orexo whereas Accord Healthcare has an exclusive licensing agreement for the commercialization of ZUBSOLV® in 29 European countries with the first launches expected to start in Q1 2022.
- Abstral®, for the treatment of breakthrough pain in cancer patients, is approved for use in e.g. the EU, the US, Japan, South Korea, Middle East, Israel and Australia. The product was sold in the US by Sentynl Therapeutics until October 31, 2019. The European contract with Kyowa Kirin expired as of December 31, 2019. Abstral® patents for EU and the US expired in October 2019. For most other markets the patents are valid until September 2024.
- Edluar®, a sublingual tablet containing zolpidem to treat insomnia, is approved for use in the US, Canada and the EU and are sold in these markets by Mylan.
- Diabact®, a tablet for diagnosis of the gastric ulcer bacterium helicobacter pylori, was divested together with the subsidiary Kibion in 2015.

The company focuses on developing and commercializing new, improved pharmaceuticals by combining well known substances with innovative and proprietary formulation technologies. This results in new, patentable products that improve patient care and convenience within the growing space of addiction. In addition the company develops evidence-based digital therapies as a standalone or complementary treatment.

Orexo's business model provides the opportunity to develop products with a lower level of development risk, and in a shorter time, compared to the development of new chemical substances.

Orexo's revenues derive from launched products and royalties and milestone payments from licensing agreements.

Organization

The Parent company Orexo AB is responsible for the Group head quarter functions, R&D, Corporate Development, Global Regulatory, Supply Chain and Group Business Support.

The US subsidiary, Orexo Inc., is responsible for the US commercialization of pharma products and digital therapies for which it possesses a full commercial infrastructure. Orexo today has commercial operations promoting ZUBSOLV® to physicians in most larger cities in the US. During 2021 sales force activity was impacted by the Covid-19 pandemic, restricting face to face access by our field force to waivered healthcare providers. The key focus for the company has been to maintain the market access in light of the intensified competition from new generic entrants, while continuing to optimize the profit contribution from the US operations.

For DTx commercial partnership agreement was signed with Sober Grid in Q2 2021. Sober Grid is the largest global social media network for people in addiction recovery, giving a large group of users access to vorvida® and deprexis®. In Q3 2021 commercial agreement for vorvida® and deprexis® was signed with Benefis Health System, a leading regional health network.

The development organization focused during the year on progressing the pipeline of internal development projects. As a result, in the Q4 2021 Interim Report, Orexo announced positive study results for the pivotal trial for the lead pharmaceutical pipeline asset OX124, a high-dose overdose rescue medication. Upon approval by the FDA, the plan is to initiate the US launch late in 2023. Futhermore in the same quarter Orexo shared information about a new drug delivery platform amorphOX™, which has been developed along with our nasal overdose medications, OX124 and OX125. The platform has several significant advantages to a broad range of products, such as rapid dissolve time and excellent stability. It is a very dynamic platform which will form the backbone of Orexo's pharmaceutical developments in the coming years.

In Q1 2021 a new patent for OX124, with protection until 2039, was issued by the US Patent and Trademark Office (USPTO). In Q2 2021 two new patents for ZUBSOLV®, with protection until 2032, was issued by the US Patent and Trademark Office (USPTO).

Orexo has broad-based competence throughout the value chain, with a focus on pharmaceutical formulation, clinical development, registration, pharmaceutical manufacturing and commercialization.

Orexo works with highly competent external partners for the manufacture of products for commercial use, clinical trials and manufacturing.

Orexo also collaborates with contract research organizations for certain aspects of drug development, such as clinical studies. Orexo deploys a project led organization, in which skills are combined based on the specific demands of individual projects.

Orexo has established a Supplier Code of Conduct that will guide in the procurement of goods and services and align requirements and expectations between Orexo and suppliers. All new potential suppliers are assessed in accordance with the Supplier Code of Conduct. The assessment includes key suppliers sustainability efforts and performance.

At year end, Orexo had a total of 121 (138) employees.

Key events

2021 has seen progress on many fronts, with US Pharma improved EBIT margin, Digital Therapeutics (DTx) testing new reimbursement routes and new commercialization concepts as well as initiating educational campaign for MODIA™ focusing on our existing ZUBSOLV® customers.

Legal disputes

On July 14, 2020, Orexo's US subsidiary received subpoenas for the purpose of enabling US authorities to obtain certain information in relation to sales and marketing of ZUBSOLV® and other buprenorphine products. Orexo has no knowledge of the background to the requests and is collaborating with the US authorities to ensure they receive the necessary information and to understand the scope of the investigations.

On August 10, 2020, the company announced it has received a "paragraph IV" patent certification notice from Sun Pharmaceutical Industries Limited ("Sun"). The Notice Letter advises Orexo of Sun's filing of an Abbreviated New Drug Application ("ANDA") with the US Food and Drug Administration (FDA) seeking approval of generic versions of ZUBSOLV® before the expiration of Orexo's patents listed in the Orange Book.

As a response to above notice Orexo on September 13, 2020, filed a patent infringement action in the US District Court for the District of New Jersey, against Sun. The filing statutorily precludes FDA from approving Sun's ANDA for 30 months, or until a district court decision finds the patents to be invalid or not infringed, whichever occurs first.

Orexo currently has nine patents listed in the Orange Book (US Patent Nos. 8,470,361; 8,658,198; 8,940,330; 9,259,421; 9,439,900; 10,874,661;10,946,010; 11,020,387 and 11,020,388) with expiration dates ranging from December 2027 to September 2032. All nine listed patents have been asserted in patent infringement actions against Sun in the US District Court for the District of New Jersey.

ZUBSOLV® US market access update

The Covid-19 pandemic continued to cause challenges to the business as access to meeting face to face with waivered physicians, healthcare providers and other customers remained well below pre-pandemic levels. The planning for ZUBSOLV® commercial program continued to be impacted due to Covid-19 in the U.S. with many states and municipalities continuing to institute restrictions and lockdowns at various times causing significant reduction in customer interactions. Sales force access to offices has improved but access to physicians themselves has not improved even though restrictions began to ease mid-year. Despite the limitations, ZUBSOLV® had mild year over year declines in the reimbursed open formulary businesses of the market. The previously exclusive reimbursement contracts and cash segments of the market saw continued declines. There's also been continued improvement in ZUBSOLV® market access, with the third largest Medicaid volume state, Kentucky, adding Zubsolv mid-year.

Financial Performance

Condensed consolidated statement of operations

SEK million	2021	2020
Net revenues	565.0	663.6
Cost of goods sold	–78.9	–65.6
Gross profit	486.1	598.0
Selling expenses	–280.4	–286.6
Administrative expenses	–151.5	–102.8
Research and development costs	–272.3	–224.9
Other operating income and expenses	4.0	–3.6
Operating earnings	–214.1	–19.9
Net financial items	–8.4	–18.4
Earnings after financial items	–222.5	–38.3
Income tax	–1.0	–46.1
Net earnings for the period	–223.5	–84.4

Revenues

Net revenues

Net revenues were distributed as follows:

Net revenues

SEK million	2021	2020
ZUBSOLV® US product sales	522.7	623.3
US Pharma – total	**522.7**	**623.3**
Digital Therapeutics (DTx) product sales	1.1	0.0
Digital Therapeutics (DTx) – total	**1.1**	**0.0**
Abstral® – royalty	32.1	29.7
Edluar® – royalty	9.1	10.4
ZUBSOLV® – ex US	0.0	0.1
HQ & Pipeline – total	**41.2**	**40.2**
Total	**565.0**	**663.6**

Commercial products

Total net revenues for the year amounted to SEK 565.0 million (663.6). Lower ZUBSOLV® US revenue in 2021 explain the decrease.

ZUBSOLV® US revenue ended at SEK 522.7 million (623.3), 16 percent below the previous year's level. The US buprenorphine/naloxone market grew by 7.5% slowed down temporarily by Covid-19.

Within the commercial payer segment, ZUBSOLV® was nearly universally reimbursed in 2021. Total Commercial volume declined due to United Healthcare's addition of generics to a formerly exclusive ZUBSOLV® formulary. However, ZUBSOLV® saw growth in the national formularies of 2 major national PBMs, CVS Caremark and Express Scripts.

Within the public category, Ohio, Wisconsin, Colorado, and Louisiana Medicaid were the core ZUBSOLV® growth drivers, with Louisiana leveraging the improved formulary position gained in 2021. Overall, ZUBSOLV®'s public volume declined due to the addition of generics to the formerly exclusive Humana Medicare, as well as loss of access in New York Medicaid's CDPHP and IHA. However, ZUBSOLV®'s volume in Open Medicaid grew.

In 2021, the Open segment of the market where ZUBSOLV® retains the greatest reimbursement position, grew at a greater rate than the non-reimbursed segment.

DTx sales efforts have focused on testing new reimbursement routes and new commercialization concepts. The recognized net revenues amounted to SEK 1.1 million and deferred income to SEK 0.2 million.

Total Abstral® royalties during the year amounted to SEK 32.1 million (29.7). Royalties for sales in Europe were received until December 31, 2019 when the European contract with Kyowa Kirin expired. Patents for Abstral® expired in October in all markets except in Japan and Australia where they are valid until September 2024.

Royalty revenues from Edluar® during the year amounted to SEK 9.1 million (10.4).

Expenses and earnings

Cost of goods sold

Cost of goods sold amounted to SEK 78.9 million (65.6), explained by US Pharma of SEK 67.5 million (61.0). Royalties and technical infrastructure costs for DTx amounted to SEK 11.0 million (4.6).

Selling expenses

Selling expenses amounted to SEK 280.4 million (286.6), the decrease is due to lower selling expenses in US Pharma.

Administrative expenses

Administrative expenses amounted to SEK 151.5 million (102.8). The higher expense level in 2021 is mainly explained by higher legal costs related to protection of IP rights and subpoena.

Research and development costs

Research and development costs amounted to SEK 272.3 million (224.9) explained by higher costs for the clinical trial of MODIA™ and for OX124.

Other income and expenses

Other income and expenses amounted to SEK 4.0 million (–3.6) mainly explained by exchange-rate gains derived from revaluations of parent company balance sheet items in foreign currency, predominantly in USD.

Depreciation

Depreciation and amortization amounted to SEK 53.0 million (38.9). The increase is mainly related to amortization of DTx milestones and depreciation of DTx enterprice platform. This also includes amortization of previously capitalized R&D expenses related to the ZUBSOLV® induction label.

Net financial items

Net financial items amounted to SEK –8.4 million (–18.4) explained by higher positive unrealized exchange rate impact of SEK 25.0 million derived from the parent company's foreign currency bank accounts mainly in USD partly offset by higher costs of SEK 14.3 million for the corporate bond loan and by lower earned interest on bank accounts in the US of SEK 0.8 million.

Income tax

Income tax for the year amounted to SEK –1.0 million (–46.1). The decrease is explained by absence of negative impact of SEK –49.0 m from decreased parent company tax asset in 2020 and by negative adjustment to deferred tax assets related to temporary differences of SEK –1.2 m (2.9).

Orexo performs regular assessments of its deferred tax asset and makes adjustments according to the recognition requirements of IAS 12.

Net earnings

Net earnings amounted to SEK –223.5 million (–84.4).

Segment reporting

Orexo Group has its operations in Sweden and the US. With effect from Q1 2020, operations are monitored and presented in the segments US Pharma, Digital Therapeutics (DTx) and HQ & Pipeline. See Note 6.

US Pharma

US Pharma net revenues amounted to SEK 522.7 million (623.3).

The decrease in US Pharma revenues was driven by lower demand due to competition in previously exclusive plans and declining Commercial segment while Covid-19 held society in a tight grip. Lower adjustments of accrued product returns were partly offset by improved pricing. Also unfavourable exchange rates had a negative impact. In local currency US Pharma net revenues amounted to USD 60.9 million (67.6) .

The EBIT contribution from US Pharma amounted to SEK 278.2 million (331.2), equal to an EBIT margin of 53.2 percent (53.1). The decrease is explained by lower sales and gross profit partly offset by lower operating costs.

Digital Therapeutics (DTx)

Sales efforts during the year focused testing new reimbursement routes and new commercialization concepts. The recognized net revenues were SEK 1.1 million and deferred income SEK 0.2 million.

EBIT amounted to SEK –249.7 million (–175.4), mainly explained by costs related to building up the business and the continued launch of vorvida® and deprexis®.

HQ & Pipeline

Partner revenues amounted to SEK 41.2 million (40.2) mainly explained by lower Edluar® royalty amounted to SEK 9.1 million (10.4). Abstral® royalty amounted to SEK 32.1 million (29.7).

EBIT amounted to SEK –242.6 million (–175.8), mainly explained by higher costs for the clinical trial of MODIA ™, for OX124 and by higher legal IP costs.

Financial position

On December 31, 2021, cash and cash equivalents amounted to SEK 504.1 million (505.3) and interest-bearing liabilities to SEK 492.3 million (224.5).

The interest-bearing liabilities are all associated with corporate bonds. During the year Orexo exercised its option for early redemption of the bonds 2017/2021 in full and issued senior unsecured callable floating rate bonds in the amount of SEK 500 million, under a framework of SEK 1,000 m with final maturity in February 2025 (the "New Bonds"). The New Bonds carry a floating rate interest of 3-month Stibor + 375 bps per annum.

Negative cash flow from operating activities for the year amounted to SEK –229.0 million (16.8) and was driven by negative operating earnings.

Shareholders' equity on December 31, 2021 was SEK 349.6 million (558.5) and the equity/assets ratio was 27.4 percent (45.3).

The cash position enables Orexo to continue investments in DTX and OX124.

Investments

Gross investments in tangible and intangible fixed assets amounted to SEK 52.9 million (189.8). Lower investment is mainly explained by a payment of non-refundable milestone for deprexis® and MODIA™, investments in the DTx enterprise platform and in equipment for the development organization in 2020.

Parent Company

Parent company's operations consist of Business Development, R&D, Global Lifecycle Management, Global regulatory, Supply Chain and Group Business Support. Net revenues amounted to SEK 365.9 million (446.4), of which group internal sales amounted to SEK 324.7 million (406.2). Earnings after financial items were SEK –219.8 million (–23.5), mainly explained by investments in DTx and development projects. As of December 31, 2021, cash and cash equivalents in the Parent Company amounted to SEK 444.5 million (361.3).

Outlook 2022

- Due to the continuing pandemic the buprenorphine/naloxone market will show a growth pace in line with 2021, and reach a level of 5–8 percent.

- ZUBSOLV® net sales will decline slightly in H1 2022 vs H2 2021. In H2 ZUBSOLV® net sales will increase comparing to H1.
- OPEX in line with 2021, with R&D expenses increasing and selling expenses declining.
- US Pharma EBIT margin will exceed 50 percent.

With the Covid-19 pandemic continuing, the financial outlook is associated with increased uncertainties. All numbers are based on exchange rates in December 2021.

Risks

Significant risks and uncertainties

Significant risks are essentially the same for the Parent Company and the Group. The risks may be classified as financial and operational. The financial risks are described in Note 3 on pages 75–76. A summary description of the operational risks attributable to research and development, production, sales and other risks is presented below.

For further information regarding financial risk see Note 3.

Market risks

The main market risks for Orexo are price pressure, reimbursement restrictions by payers and the launch of new and competing products.

For ZUBSOLV® to be successful in the US, it is of the utmost importance that ZUBSOLV® has access to patients and reimbursement to the same extent as competitors.

The US payer structure and reimbursement system is very large and complex and therefore Orexo has established its own team of experienced people focusing only on improving market and reimbursement access for ZUBSOLV®.

The payers are constantly reviewing their formularies and this can lead to significant changes in market access. Orexo's products are sold in a highly competitive market, with competition from both other products and other treatment methods, and the launch of new products by competitors is an inherent market risk. In all markets for Orexo's products there is intensive development of new and improved treatments, which may prove to have a better clinical effect than those of today. Orexo is constantly working to proactively analyze these risks and develop action plans for alternative market scenarios. This is being done together with local external expertise.

The commercialization rights in relation to several of the Group's other pharmaceuticals and digital therapies are held by the Group's various commercialization partners. The Group is therefore dependent on maintaining relevant distribution and commercialization arrangements in order to commercialize its products. There is a risk of such commercialization arrangements are terminated and that the Group is unable to replace such partnership in a timely manner, or at all, which could lead to lost business opportunities, delayed deliveries or increased costs.

Furthermore, the Group relies on third party partnerships to market and distribute its products, conduct clinical trials and develop and manufacture certain products utilizing the Issue's innovative drug-delivery platforms. Should such third parties fail to fulfil its contractual obligations vis-á-vis the Group, whether of financial or operational nature, fail to meet deadlines or expected levels of quality or accuracy, the Group's marketing activities and clinical trials may be extended, delayed or terminated. Any failure by such partners would negatively affect the Group's ability to develop, commercialize and license its products, which would have a negative effect on the Issuer's business and results of operations. The company considers that the probability of the above risks occurring is medium. If the risks would materialize, the Issuer considers the potential negative impact to be low.

R&D does not achieve the expected results

Development of a new product is by nature a complicated and risky process that requires considerable financial resources. Orexo's strategy is to develop improved products at a lower cost, in a shorter period of time and at a lower risk by combining previously known substances with proprietary technologies. The process is controlled by a multidisciplinary organization that handles all critical issues during the development process on the way to an approved product. As Orexo is a relatively small organization, it is necessary to focus on a small number of prioritized projects with high market potential.

The development of these prioritized projects towards an approved product may fail or be delayed due to several factors, such as:

- unfavorable results in clinical trials
- failure to gain the authority approval required for sales of the pharmaceutical product
- a change in the requirements of the regulatory authorities.

During 2021 the development organization focused on progressing the pipeline of internal development projects. As a result, in the Q4 2021 Interim Report, Orexo announced positive study results for the pivotal trial for the lead pharmaceutical pipeline asset OX124, a high-dose overdose rescue medication. Futhermore in the same quarter Orexo shared information about a new drug delivery platform amorphOX™, which has been developed along with our nasal overdose medications, OX124 and OX125. In Q1 2021 a new patent for OX124, with protection until 2039, was issued by the US Patent and Trademark Office (USPTO).

In Q2 2021 two new patents for ZUBSOLV®, with protection until 2032, was issued by the US Patent and Trademark Office (USPTO).

Difficulties in obtaining and protecting patents

Being able to obtain and maintain patents and other intellectual property rights protecting Orexo's technologies and products is an important part of Orexo's ability to create long-term value for its shareholders. Obtaining patents related to pharmaceuticals is a complex process that involves both scientific and legal expertise. Even if a patent has been granted, it may later be challenged legally, declared invalid or bypassed, which may limit Orexo's ability to market its new products.

On August 10, 2020, the company announced it has received a "paragraph IV" patent certification notice from Sun Pharmaceutical Industries Limited ("Sun"). The Notice Letter advises Orexo of Sun's filing of an Abbreviated New Drug Application ("ANDA") with the US Food and Drug Administration (FDA) seeking approval of generic versions of ZUBSOLV® before the expiration of Orexo's patents listed in the Orange Book.

As a response to above notice Orexo on September 13, 2020, filed a patent infringement action in the US District Court for the District of New Jersey, against Sun. The filing statutorily precludes FDA from approving Sun's ANDA for 30 months, or until a district court decision finds the patents to be invalid or not infringed, whichever occurs first.

Orexo currently has nine patents listed in the Orange Book (US Patent Nos. 8,470,361; 8,658,198; 8,940,330; 9,259,421; 9,439,900; 10,874,661;10,946,010; 11,020,387 and 11,020,388) with expiration dates ranging from December 2027 to September 2032. All nine listed patents have been asserted in patent infringement actions against Sun in the US District Court for the District of New Jersey

Production process

Production and packing of Orexo's products is today done entirely by external partners.

ZUBSOLV® is manufactured and packed by third party contractors located in the US and the manufacturing and packing facilities are carefully assessed against Orexo's Supplier Code of Conduct.

High demands are placed on methods and processes and these must meet "Good Manufacturing Practice" standards (GMP). Orexo constantly evaluates the fulfilment of GMP both internally and by all strategic subsuppliers. Orexo and its subsuppliers may be inspected by different authorities that have the power to grant approval. Orexo's production comprises highly potent controlled substances. There are strict rules and laws for these regarding manufacturing, storage, handling, freight, import and export, and waste management. Access to pharmaceutical ingredients may be uncertain and entail long delivery times. Orexo must therefore ensure that it can gain access to these substances at an early stage.

To ensure safe supply of products that are vital to patients a significant inventory of ZUBSOLV® must be maintained. Carrying a high inventory level creates a risk of write-offs of expired products. Orexo is constantly working to minimize this risk by managing the inventory according to demand and by working to improve the product's lifetime.

Effect of political and regulatory decisions
The pharmaceutical market is greatly affected by political decisions that may affect, for example, reimbursement levels for pharmaceutical expenses and limits for the prescription of products. Especially the market for controlled substances is under tight surveillance and control by authorities who can change the market conditions with new policies and legislation.

Dependence on key persons
Orexo is dependent on a number of key persons within various different areas. The ability to recruit and retain qualified staff is of very great importance for ensuring that there is adequate expertise in the company.

Risks related to Covid-19
Current risk the company sees is that it could cause some delays within the development chain which can result in unexpected delays in the pharmaceutical projects. Currently the company is working with several parties in different geographies to avoid any delivery delays. Within other operational areas, such as the supply chain and sales, Orexo sees limited impact on its business. From a financial perspective Orexo currently expects Covid-19 to have non or limited impact, both related to funding and performance.

Employees
Orexo offers a dynamic and innovative place to work. The company fosters an environment where employees respect each other's views, competences and decisions. At Orexo, employees are given substantial responsibility and every person's contribution is important. At end of period Orexo had 121 employees.

Sustainable governance and guidelines
The company has prepared a Sustainability Report in accordance with the Swedish Annual Accounts Act and according to the reporting guidelines of the United Nations Global Compact. See pages 34–50.

Remuneration
Guidelines for executive remuneration[1]
The executive management of Orexo AB (publ) ("Orexo" or the "company") falls within the provisions of these guidelines. Executive management refers to board members, the CEO and other members of the executive management, which comprised six persons by the end of 2021. The guidelines are forward-looking, i.e. they are applicable to remuneration agreed, and amendments to remuneration already agreed, after adoption of the guidelines by the annual general meeting 2022. These guidelines do not apply to any remuneration decided or approved by the general meeting.

Remuneration under employments subject to other rules than Swedish may be duly adjusted to comply with mandatory rules or established local practice, taking into account, to the extent possible, the overall purpose of these guidelines.

The guidelines' promotion of the company's business strategy, long-term interests and sustainability
The company's business strategy is the following.

Orexo has developed from being an R&D stage company to becoming a profitable fully integrated specialty pharmaceutical company with its own commercial business in the US. From a strong operational and financial platform, Orexo is aiming to become a leader in the field of substance use disorder. To achieve this, the commercial business will be broadened through business development, M&A and launch of proprietary pharmaceuticals and digital therapies.

Orexo's objectives and strategies onwards is to broaden the US commercial platform to leverage scale and expand sales, further accelerate Orexo US performance and EBIT construction as well as to launch at least one new product from the pipeline within three years.

A prerequisite for the successful implementation of the company's business strategy and safeguarding of its long-term interests, including its sustainability, is that the company is able to recruit and retain qualified personnel. To this end, it is necessary that the company offers competitive remuneration. These guidelines enable the company to offer the executive management a competitive total remuneration. Long-term share-related incentive plans have been implemented in the company. Such plans have been resolved by the general meeting and are therefore excluded from these guidelines. The long-term share-related incentive plans for certain senior executives and key employees within the Orexo group and for Group Management Team and US Leadership Team employees, respectively, proposed by the board of directors and submitted to the annual general meeting 2022 for approval are excluded for the same reason. The proposed plans include similar performance criteria as 2021 plans for senior executives and key employees. The current plans include certain executives and key employees within the Orexo group. The performance criteria used to assess the outcome of the plans are distinctly linked to the business strategy and thereby to the company's long-term value creation, including its sustainability. These performance criteria currently comprise the share price development, the surpassing of a certain index or the meeting of certain financing and operating objectives, and thereby organic growth and product development. Further, the plans are conditional upon certain holding periods.

Variable cash remuneration covered by these guidelines shall aim at promoting the company's business strategy and long-term interests, including its sustainability.

Types of remuneration, etc.
Orexo shall offer terms of employment that are in line with market rates so that the company can recruit and retain skilled personnel. Remuneration to the executive management shall comprise a fixed salary, variable remuneration, long-term incentive programs, pensions and other customary benefits. Remuneration is based on the individual's commitment and performance in relation to previously established goals, both individual goals and goals for the entire company. Individual performance is continuously evaluated.

Fixed salary is generally reviewed on an annual basis and shall be based on the qualitative performance of the individual. The fixed salary of the executive management shall be in line with market conditions.

The executive management may be offered cash bonuses. The satisfaction of criteria for awarding variable cash remuneration shall be measured over a period of one year. Variable remuneration shall take into account the individual's level of responsibility and degree of influence. The size of variable remuneration is based on the percentage of predetermined and measurable criteria which can be financial or non-financial. They may also be individualized, quantitative or qualitative objectives. The criteria shall be designed so as to contribute to the company's business strategy and long-term interests, including its sustainability, by for example being clearly linked to the business strategy or promoting the executive's long-term development. To which extent the criteria for awarding variable cash remuneration has been satisfied shall be evaluated/determined when the measurement period has ended. The remuneration committee is responsible for the evaluation of the variable cash remuneration to the CEO and the other executives. For financial objectives, the evaluation shall be based on the latest financial information made public by the company. The variable remuneration shall amount to a maximum of 40 percent of the annual fixed cash salary for the CEO, up to 30 percent of the annual fixed cash salary for other members of the executive management in Sweden and up to 60 percent of the annual fixed cash salary for members of the executive management employed in the US subsidiary. The majority of the variable remuneration shall be based on the sales development and the financial results at group and subsidiary level. The percentage rate in relation to US employees reflects the subsidiary's significance for the group's earnings as well as an American labor market that is requiring an increased share of variable remuneration in order to attract and retain key employees. Furthermore, the board of directors shall have the option of allocating further variable non-recurring remuneration to the management when the

[1] The guidelines were adopted by the Annual General Meeting on April 13, 2021 and are forward-looking.

board deems it to be appropriate. Such allocation of non-recurring remuneration may, after consolidation with other variable remuneration, amount to a maximum of 70 percent of the annual fixed cash salary.

The CEO and the other members of the executive management are covered by defined contribution pension plans, including health insurance (Sw. sjukförsäkring). Variable cash remuneration shall not qualify for pension benefits except to the extent required by mandatory collective agreement provisions applicable to the executive. The pension premiums paid by the company to the CEO and other members of the executive management may amount to not more than 20 percent of the annual fixed cash salary.

The employment agreement with the CEO may be terminated with six months' notice. Employment agreements with the other members of the executive management may be terminated with a notice of between zero and six months. The CEO is entitled to severance pay equivalent to six months' salary if employment is terminated by the company. The other members of the executive management are entitled to severance pay equivalent to between 3 and 12 months' salary if employment is terminated by the company. Upon notice from the executive, there is no right to severance pay.

In addition, remuneration may be paid for non-compete undertakings. Such remuneration shall compensate for loss of income and shall only be paid in so far as the previously employed executive is not entitled to severance pay. The remuneration shall be based on the fixed cash salary at the time of termination of employment and be paid during the time the non-compete undertaking applies, however not for more than 12 months following termination of employment.

Executives may be awarded customary other benefits, such as company car and travel between the place of residence and the workplace. Such other benefits may amount to not more than 20 percent of the fixed annual cash salary.

The board is entitled, if it assesses that this is warranted in an individual case, to assign company work to a board member over and above the board assignment, in which case the board member may be granted reasonable remuneration.

For employments governed by rules other than Swedish, pension benefits and other benefits may be duly adjusted for compliance with mandatory rules or established local practice, taking into account, to the extent possible, the overall purpose of these guidelines. Executives who are expatriates to or from Sweden may receive additional remuneration and other benefits to the extent reasonable in light of the special circumstances associated with the expat arrangement, taking into account, to the extent possible, the overall purpose of these guidelines. Such benefits may not in total exceed 30 percent of the fixed annual cash salary.

Salary and employment conditions for employees

In the preparation of the board of directors' proposal for these remuneration guidelines, salary and employment conditions for employees of the company have been taken into account by including information on the employees' total income, the components of the remuneration and increase and growth rate over time, in the remuneration committee's and the board of directors' basis of decision when evaluating whether the guidelines and the limitations set out herein are reasonable.

The decision-making process to determine, review and implement the guidelines

The board of directors has established a remuneration committee. The committee's tasks include preparing the board of directors' decision to propose guidelines for executive remuneration. The board of directors shall prepare a proposal for new guidelines at least every fourth year and submit it to the general meeting. The guidelines shall be in force until new guidelines are adopted by the general meeting.

The remuneration committee shall also monitor and evaluate programs for variable remuneration for the executive management, the application of the guidelines for executive remuneration as well as the current remuneration structures and compensation levels in the company. The members of the remuneration committee are independent of the company and its executive management. The CEO and other members of the executive management do not participate in the board of directors' processing of and resolutions regarding remuneration-related matters in so far as they are affected by such matters.

Derogation from the guidelines

The board of directors may temporarily resolve to derogate from the guidelines, in whole or in part, if in a specific case there is special cause for the derogation and a derogation is necessary to serve the company's long-term interests, including its sustainability, or to ensure the company's financial viability. As set out above, the remuneration committee's tasks include preparing the board of directors' resolutions in remuneration-related matters. This includes any resolutions to derogate from the guidelines.

Largest shareholders

At year-end 2021 Orexo had one shareholder with holdings of more than 10 percent of the total number of shares; Novo Holding A/S 27.8 percent with 9,643,184 shares.

Number of shares

Company shares total 34,710,639 (including buyback of shares) an there are 34,710,639 votes in the company.

Proposed appropriation of profit

The following funds are at the disposal of the Annual General Meeting:

	SEK thousands
Share premium reserve	1,187,617
Loss carried forward	–966,843
Profit/loss for the year	–219,762
Total	**1,012**

The Board proposes that the funds at their disposal SEK 1,012 thousands be carried forward.

Corporate Governance

Information on Orexo's application of the Swedish Code of Corporate Governance and more can be found in the corporate governance report on page 101.

Financial information in brief – Group

Statement of operations information

SEK million	2021	2020	2019	2018	2017
Net revenues	565.0	663.6	844.8	783.1	643.7
Cost of goods sold	–78.9	–65.6	–105.6	–171.8	–164.4
Gross Profit	**486.1**	**598.0**	**739.2**	**611.4**	**479.3**
Selling expenses	–280.4	–286.6	–191.9	–191.4	–190.5
Administrative expenses	–151.5	–102.8	–139.6	–166.7	–96.1
Research and development costs	–272.3	–224.9	–181.3	–166.8	–134.2
Other operative income and expenses	4.0	–3.6	4.8	9.3	–1.1
Operating earnings	**–214.1**	**–19.9**	**231.2**	**95.8**	**57.4**
Net financial items	–8.4	–18.4	–3.3	–3.6	–27.7
Earning after financial items	**–222.5**	**–38.3**	**227.9**	**92.2**	**29.7**
Income tax	–1.0	–46.1	–8.8	45.7	–6.5
Net earning for the year	**–223.5**	**–84.4**	**219.1**	**137.9**	**23.2**

Balance sheet information

SEK million	2021	2020	2019	2018	2017
Intangible fixed assets	248.9	252.8	113.9	103.9	121.0
Tangible fixed assets	65.9	47.3	22.0	20.0	20.1
Right-of-use assets	59.2	67.8	57.0	0.0	0.0
Deferred tax	33.4	32.7	85.5	92.8	28.3
Other financial assets	0.8	0.7	1.4	10.4	7.1
Inventories	92.3	108.4	131.8	173.6	250.2
Accounts receivable	214.0	165.2	233.8	264.5	218.4
Other current assets	55.2	52.6	38.8	31.6	30.9
Cash and bank balance	504.1	505.3	816.8	589.8	327.9
Total assets	**1,273.7**	**1,232.9**	**1,501.1**	**1,286.7**	**1,003.9**
Shareholders' equity	349.6	558.5	706.4	476.1	329.1
Interest-bearing liabilities	492.3	291.0	344.3	320.6	319.1
Non-interest bearing liabilities and provisions	431.7	383.4	450.3	489.9	355.7
Total shareholders' equity and liabilities	**1,273.7**	**1,232.9**	**1,501.1**	**1,286.7**	**1,003.9**

Cash flow information

SEK million	2021	2020	2019	2018	2017
Cash flow from operating activities before changes in working capital	–245.5	–35.2	252.5	127.9	110.3
Cash flow changes in working capital	16.5	52.0	34.5	114.1	36.3
Cash flow from operating activities	–229.0	16.8	287.0	242.0	146.6
Acquisition of tangible, intangible and financial assets	–52.9	–189.7	–32.0	–6.2	–1.6
Disposal of financial assets	–	0.6	9.5	–	–
Cash flow after investing activities	–281.9	–172.3	264.6	235.8	145.0
Amortization of loans	–239.5	–84.0	–55.8	–	–404.7
Borrowings	490.1	–	–	–	319.2
New share issues	–	–	2.0	0.1	0.1
Buyback of shares	–	–27.3	–	–0.1	–
Cash flow for the year	–31.2	–283.7	210.8	235.8	59.6
Cash and cash equivalents at year-end	504.1	505.3	816.8	589.8	327.9

Other key figures

	2021	2020	2019	2018	2017
EBIT margin, %	–37.9	–3.0	27.4	12.2	8.9
Return on shareholder equity, %	–49.2	–13.3	37.1	34.3	7.3
Net debt, SEK million[1]	–11.7	–280.8	–527.2	–269.2	–8.8
Debt/equity ratio, %	140.8	40.2	41.0	67.3	97.0
Equity/assets ratio, %	27.4	45.3	47.1	37.0	32.8
Number of shares, before dilution	34,319,649	34,398,815	34,621,646	34,560,456	34,540,271
Number of shares, after dilution	34,319,649	34,398,815	35,348,484	35,095,980	34,650,835
Earnings per share, before dilution, SEK	–6.51	–2.45	6.33	3.99	0.67
Earnings per share, after dilution, SEK	–6.51	–2.45	6.20	3.93	0.67
Number of employees at the end of the period	121	138	127	129	90
Shareholders' equity, SEK million	349.6	558.5	706.4	476.1	329.1
Capital employed, SEK million	841.9	783.0	996.0	796.7	648.2
Working capital, SEK million	–18.8	–50.5	–56.7	–13.7	149.6

For alternative key figures see definitions and reconciliations of key figures on page 99.
[1] Net debt calculated exclusive of leases.

Financial reports and notes

Consolidated statement of operations

SEK million	Notes	2021	2020
Net revenues	5	565.0	663.6
Cost of goods sold	7	–78.9	–65.6
Gross profit		**486.1**	**598.0**
Selling expenses	7, 9, 10, 31	–280.4	–286.6
Administrative expenses	7, 9, 10, 29, 31	–151.5	–102.8
Research and development costs	7, 9, 10, 31	–272.3	–224.9
Other operating income	8, 11	10.9	17.6
Other operating expenses	7, 11	–6.9	–21.2
Operating earnings		**–214.1**	**–19.9**
Financial income	12	38.3	60.7
Financial expense	12	–46.7	–79.1
Earnings after financial items		**–222.5**	**–38.3**
Tax	13	–1.0	–46.1
Net earnings for the year		**–223.5**	**–84.4**
Earnings for the year attributable to:			
Parent company shareholders		–223.5	–84.4
Earnings per share during the year attributable to parent company shareholders (expressed in SEK)			
– before dilution	14	–6,51	–2.45
– after dilution	14	–6,51	–2.45

Consolidated statement of comprehensive income

SEK million	Notes	2021	2020
Net earnings for the year		**–223.5**	**–84.4**
Other comprehensive income			
Items that may subsequently be reversed to the statement of operations:			
Translation differences	17	13.0	–16.5
Other comprehensive earnings for the year, net after tax		**13.0**	**–16.5**
Comprehensive earnings for the year		**–210.5**	**–100.9**
Comprehensive earnings attributable to:			
Parent company shareholders		–210.5	–100.9
Non–controlling interests		–	–

Consolidated balance sheet

SEK million	Notes	2021 Dec 31	2020 Dec 31
ASSETS			
Fixed assets			
Tangible fixed assets	9, 15	65.9	47.3
Intangible assets	9, 16	248.9	252.8
Right-of-use assets	31	59.2	67.8
Deferred tax assets	30	33.4	32.7
Other financial assets	18	0.8	0.7
Total fixed assets		**408.2**	**401.3**
Current assets			
Inventories	19	92.3	108.4
Accounts receivable	20	214.0	165.2
Other receivables	21	24.1	25.7
Prepayment and accrued income	22	31.1	26.9
Cash and cash equivalents	18, 23	504.1	505.3
Total current assets		**865.5**	**831.6**
TOTAL ASSETS		**1,273.7**	**1,232.9**
SHAREHOLDERS' EQUITY AND LIABILITIES			
Shareholders' equity			
Share capital		14.2	14.2
Other contributed capital	24	1 816.0	1,814.4
Reserves	17	–0.4	–13.4
Profit carried forward including net earnings for the year		–1,480.2	–1,256.7
Total shareholder's equity		**349.6**	**558.5**
Long–term liabilities and provisions			
Provisions	24, 25	13.5	25.7
Interest bearing liabilities	18, 26	492.3	–
Lease liabilities, long-term		38.0	47.4
Total long–term liabilities		**543.9**	**73.1**
Current liabilities			
Accounts payable	18	49.2	47.0
Provisions	25	160.1	197.3
Other liabilities	27	16.9	6.2
Accrued expenses	27	133.7	107.2
Lease liabilities, current		20.2	19.1
Interest bearing liabilities, current	18, 26	–	224.5
Total current liabilities		**380.2**	**601.3**
Total liabilities		**924.1**	**674.4**
TOTAL SHAREHOLDERS' EQUITY AND LIABILITIES		**1,273.7**	**1,232.9**

Changes in consolidated shareholders' equity

Attributable to parent company shareholders[1] SEK million	Notes	Share capital	Other contributed capital	Reserves[2]	Profit carried forward including Net earnings for the year	Total shareholders' equity
Opening balance at January 1, 2020		**14.2**	**1,861.4**	**3.1**	**–1,172.3**	**706.4**
Comprehensive income						
Net earnings for the year					–84.4	–84.4
Other comprehensive income						
Translation differences				–16.5		–16.5
Total comprehensive income		**0.0**	**0.0**	**–16.5**	**–84.4**	**–100.9**
Transactions with shareholders						
Share-based payments	24		–19.7			–19.7
Buyback of shares			–27.3			–27.3
Total transactions with shareholders		**0.0**	**–47.0**	**0.0**	**0.0**	**–47.0**
Closing balance at December 31, 2020		**14.2**	**1,814.4**	**–13.4**	**–1,256.7**	**558.5**
Opening balance at January 1, 2021		**14.2**	**1,814.4**	**–13.4**	**–1,256.7**	**558.5**
Comprehensive income						
Net earnings for the year					–223.5	–223.5
Other comprehensive income						
Translation differences				13.0		13.0
Total comprehensive income		**0.0**	**0.0**	**13.0**	**–223.5**	**–210.5**
Transactions with shareholders						
Share-based payments	24		1.5			1.5
Total transactions with shareholders		**0.0**	**1.5**	**0.0**	**0.0**	**1.5**
Closing balance at December 31, 2021		**14.2**	**1,816.0**	**–0.4**	**–1,480.2**	**349.6**

[1] There are no non–controlling interests
[2] Note 17

The total number of shares as of December 31, 2021, was 34,710,639, of which 382,732 were owned by the company. The number of outstanding shares thus amounts to 34,327,907 as of December 31, 2021.

Consolidated cash flow statement

SEK million	Notes	2021	2020
Operating earnings		–214.1	–19.9
Adjustment for non-cash items	32	–16.8	–7.1
Interest received		0.0	3.0
Interest paid		–22.9	–11.8
Tax paid		8.2	0.6
Cash flow from operating activities before changes in working capital		**–245.5**	**–35.2**
Changes in working capital			
Change in inventories		27.8	10.1
Change in receivables		–21.8	25.2
Change in current liabilities		10.6	16.7
Cash flow from operating activities		**–229.0**	**16.8**
Investing activities			
Investments in tangible fixed assets	15	–24.7	–29.4
Investments in intangible assets	16	–28.1	–160.3
Disposal of financial assets		–	0.6
Cash flow from investing activities		**–52.9**	**–189.1**
Financing activities			
Buyback of shares		–	–27.3
Issuance of loans		490.1	–
Repayment of loans	26,31	–239.5	–84.0
Cash flow from financing activities		**250.6**	**–111.3**
Cash flow for the year		**–31.2**	**–283.7**
Cash and cash equivalents at the beginning of the period		505.3	816.8
Exchange-rate differences in cash and cash equivalents		30.0	–27.8
Change in liquidity		–1.2	–311.5
Cash and cash equivalents at the end of the period	23	**504.1**	**505.3**

Parent company statement of operations

SEK million	Notes	2021	2020
Net revenues	5	365.9	446.4
Cost of goods sold	7	–71.2	–79.7
Gross profit		**294.7**	**366.7**
Selling expenses	7, 9, 10, 31	–227.3	–190.7
Administrative expenses	7, 9, 10, 29, 31	–92.3	–53.1
Research and development costs	7, 9, 10, 31	–226.0	–180.1
Other operating income	8, 11	43.6	70.2
Other operating expenses	7, 11	–6.9	–20.2
Operating earnings		**–214.2**	**–7.2**
Other interest income and similar income	12	38.3	59.9
Other interest expenses and similar expenses	12	–43.8	–76.2
Net financial items		**–5.6**	**–16.3**
Earnings before tax		**–219.8**	**–23.5**
Tax on earnings for the year	13	–	–49.0
Net earnings for the year		**–219.8**	**–72.5**

Parent company statement of comprehensive income

SEK million	Notes	2021	2020
Net earnings for the year		–219.8	–72.5
Other comprehensive income for the period, net after tax		–	–
Total comprehensive income for the period		**–219.8**	**–72.5**

Parent company balance sheet

SEK million	Notes	2021 Dec 31	2020 Dec 31
ASSETS			
Fixed assets			
Patents and intellectual property rights and proprietary intangible asset	9, 16	214.2	234.4
Equipment, renovation of the property of others	9, 15	65.9	47.2
Shares and participations in group companies	28	162.5	160.4
Total fixed assets		**442.6**	**442.0**
Current assets			
Inventories	19	67.8	90.9
Accounts receivable	20	5.6	21.5
Other receivables	21	7.6	8.0
Receivables from group companies		82.6	65.1
Prepaid expenses and accrued income	22	19.7	16.7
Cash and bank	23	444.5	361.3
Total current assets		**627.7**	**563.5**
TOTAL ASSETS		**1,070.2**	**1,005.5**
SHAREHOLDERS' EQUITY AND LIABILITIES			
Shareholders' equity			
Restricted shareholders' equity			
Share capital		14.2	14.2
Statutory reserve		290.8	290.8
Total restricted shareholders' equity		**305.0**	**305.0**
Non-restricted shareholders' equity			
Share premium reserve	24	1,187.6	1,186.1
Accumulated deficit		–966.8	–894.3
Net earnings for the year		–219.8	–72.5
Total non-restricted shareholders' equity		**1.0**	**219.3**
Total shareholders' equity		**306.0**	**524.2**
Long-term liabilities			
Other provisions	24, 25	12.8	24.5
Interest bearing liabilities	26	492.3	–
Total long-term liabilities		**505.1**	**24.5**
Current liabilities			
Accounts payable		17.1	17.3
Interest bearing liabilities	26	–	224.5
Other liabilities	27	9.1	6.2
Liabilities to group companies		207.9	187.2
Accrued expenses and deferred income	27	25.0	21.6
Total current liabilities		**259.1**	**456.8**
TOTAL SHAREHOLDERS' EQUITY AND LIABILITIES		**1,070.2**	**1,005.5**

Changes in parent company shareholders' equity

SEK million	Notes	Share capital	Statutory reserve	Share premium reserve	Accumulated deficit including Net earnings for the year	Total shareholders' equity
Opening shareholders' equity at January 1, 2020		**14.2**	**290.8**	**1,206.1**	**–867.0**	**644.0**
Net earnings for the year					–72.5	–72.5
Other comprehensive income						
Total comprehensive income		**0.0**	**0.0**	**0.0**	**–72.5**	**–72.5**
Share based payments	24			–20.0		–20.0
New share issues					–27.3	–27.3
Closing shareholders' equity at December 31, 2020		**14.2**	**290.8**	**1,186.1**	**–966.8**	**524.2**
Opening shareholders' equity at January 1, 2021		**14.2**	**290.8**	**1,186.1**	**–966.8**	**524.2**
Net earnings for the year					–219.8	–219.8
Other comprehensive income						
Total comprehensive income		**0.0**	**0.0**	**0.0**	**–219.8**	**–219.8**
Share based payments	24			1.6		1.6
Closing shareholders' equity at December 31, 2021		**14.2**	**290.8**	**1,187.7**	**–1,186.6**	**306.0**

The total number of shares as of December 31, 2021, was 34,710,639, of which 382,732 were owned by the company. The number of outstanding shares thus amounts to 34,327,907 as of December 31, 2021.

Parent company cash flow statement

SEK million	Notes	2021	2020
Operating activities			
Operating earnings		–214.2	–7.2
Adjustment for non-cash items	32	22.5	23.0
Interest received		0.0	2.2
Interest paid		–22.9	–11.8
Tax paid		—	—
Cash flow from operating activities before change in working capital		**–214.6**	**6.3**
Change in working capital			
Change in inventories		23.1	22.5
Change in accounts receivable and other current receivables		–2.2	95.6
Change in current liabilities		26.8	35.7
Cash flow from operating activities		**–167.0**	**160.1**
Investing activities			
Investments in tangible fixed assets	15	–24.8	–29.3
Investments in intangible assets	16	–10.2	–139.4
Cash flow from investing activities		**–35.0**	**–168.7**
Financing activities			
Buyback of shares		—	–27.3
Issuance of loans	26	490.1	—
Repayment of loans	26	–224.8	–66.6
Cash flow from financing activities		**265.4**	**–93.9**
Cash flow for the year		**63.4**	**–102.5**
Cash and cash equivalents at beginning of period		361.3	469.0
Exchange-rate differences in cash and cash equivalents		19.8	–5.2
Change in liquidity		83.2	–107.7
Cash and cash equivalents at end of period	23	**444.5**	**361.3**

Notes

NOTE 1 GENERAL INFORMATION

Orexo AB (publ) 556500-0600, the parent company, and its subsidiaries (together the Group) are together an integrated pharma company with commercial operations in the United States and R&D in Sweden. The company develops improved drugs and digital therapies that meet an important need in the growing the field of mental illness and addictive disorders. The products are commercialized by Orexo in the United States or through partners worldwide.The main market today is the US market for buprenorphine/naloxone products where Orexo sells its leading product ZUBSOLV® for the treatment of opioid dependence.

The parent company is the limited liability company Orexo AB (publ), with its registered office in Uppsala, Sweden. The address of thecompany's head office is Virdings allé 32 A, Uppsala, Sweden.

The parent company's share is listed on Nasdaq Stockholm.

The Board of Directors approved these consolidated financial statements for publication on March 25, 2022.

The statement of operations and balance sheet will be presented to the Annual General Meeting on April 21, 2022, for adoption.

NOTE 2 SUMMARY OF IMPORTANT ACCOUNTING POLICIES

The most significant accounting policies applied during the preparation of these consolidated financial statements are specified below. Unless otherwise stated, these policies have been applied consistently for all years presented.

2.1 Basis for preparation of the financial statements

The consolidated financial statements for Orexo were prepared in accordance with the Swedish Annual Accounts Act, RFR 1 Supplementary Accounting Rules for Groups, as well as International Financial Reporting Standards (IFRS) and interpretations as adopted by the EU. It has been prepared in accordance with the cost method unless otherwise stated below.

The parent company applies the same accounting policies as the Group. Any deviations that occur between the policies of the parent company and the Group are due to restrictions in the ability to apply IFRS to the parent company pursuant to the Swedish Annual Accounts Act (ÅRL), RFR 2 and the Pension Obligations Vesting Act and, in some instances, for tax purposes.

Refer also to 2.21.

2.1.1 Amendments to accounting policies and disclosures

The new or changed standards or interpretations that IASB has published are not expected to have an impact on the Group's or the parent company's financial reports.

(a) New and amended standards applied by the Group

No new standards, amendments or interpretations of existing standards have been applied by the Group during the financial year.

(b) New standards and interpretations of existing standards that have not yet been applied by the Group

No new standards or interpretations of existing standards that have not yet been applied by the Group during the financial year.

2.2 Consolidated financial information

Subsidiaries

Subsidiaries are all companies where the Group has a controlling interest. The Group controls a company when it is exposed to or is entitled to a variable return from its holding in the company and is able to impact the return through its interest in the company.

Subsidiaries are included in the consolidated financial statements as of the date on which the controlling interest is transferred to the Group. They are excluded from the consolidated financial statements as of the date on which the controlling interest ceases to apply.

The purchase method is used to recognize the Group's business combinations.

Intra-Group transactions, balance sheet items and non-realized gains and losses resulting from intra-Group transactions are eliminated. Where necessary, the accounting policies for subsidiaries have been adjusted to guarantee consistent application of the Group's policies.

2.3 Segment reporting

Operating segments are recognized in a manner that corresponds to the structure of internal reports submitted to the chief operating decision maker. The chief operating decision maker is responsible for the allocation of resources and assessment of the operating segments' results. For the Group, this function has been identified as Executive Management.

2.4 Translation of foreign currency

(a) Functional currency and reporting currency

Items included in the financial reports of the different units in the Group are valued in the currency used in the economic environment in which each company mainly operates (functional currency). In the consolidated financial statements SEK is used, which is the parent company's functional currency and reporting currency.

(b) Transactions and balance sheet items

Transactions in foreign currencies are translated to the functional currency using the exchange rates prevailing on the transaction date. Exchange-rate gains and losses arising from the payment of such transactions and in the translation of monetary assets and liabilities in foreign currency at the closing date are recognized in the statement of operations among Other operating income and Other operating expenses.

The parent company's bank balances in foreign currency are translated to the functional currency according to the exchange rates applicable on the transaction date. Exchange-rate gains and losses arising from the translation are recognized in the statement of operations financial income and expenses.

(c) Group companies

The earnings and financial position of all Group companies (none of which use a high inflation currency as their functional currency) that use a functional currency other than the reporting currency are restated at the Group's reporting currency as follows:

- assets and liabilities for each of the balance sheets are restated at the exchange rate applicable on the closing date,
- income and expenses for each of the statements of operations are translated at an average currency exchange rate, and
- all exchange-rate differences are recognized in other comprehensive income.

Note 2 cont.

Exchange-rate differences arising as a consequence of the translation of net investment in foreign operations for such investments are recognized as other comprehensive income. An accumulated gain or loss in shareholders' equity is recognized in the statement of operations when a foreign operation is divested either wholly or in part.

Goodwill and adjustments of fair value arising in the event of acquisition of a foreign operation are treated as assets and liabilities for this operation and translated at the exchange rate on the closing date.

2.5 Tangible fixed assets

Tangible fixed assets are recognized as cost, less depreciation and impairment, if any. Subsequent expenditures are added to the carrying amount of the asset or recognized as a separate asset, depending on which is appropriate, only when it is probable that the future economic benefits related to the asset will accrue to the Group and the cost of the asset can be measured reliably. Expenses incurred for repairs and maintenance are recognized as costs.

Tangible fixed assets are depreciated over the estimated useful life of the asset. When the depreciation amount for assets is determined, the asset's residual value is taken into account where appropriate.

Straight-line depreciation methods are used for all types of tangible fixed assets. The following depreciation periods are applied:

Improvements leasehold	20 years
Machinery and equipment	5 years
Computers	3–5 years

In the event that an asset's carrying amount exceeds its estimated recoverable value, the asset is immediately impaired to its recoverable value under "Other operating income" and "Other operating expenses".

The residual value and useful life of assets are tested on every closing date and adjusted where necessary.

Gains and losses from sales are determined by means of a comparison between the sales proceeds and carrying amount and are recognized as "Other operating income" and "Other operating expenses" in the statement of operations.

2.6 Intangible assets

Intangible assets are recognized in the balance sheet when it is probable that the future economic benefits related to the asset will accrue to the Group and the asset's value can be measured reliably. Development expenses are capitalized and recognized in the balance sheet as intangible assets if the criteria for recognition in the balance sheet as stipulated in IAS 38 Intangible Assets are satisfied.

Group intangible fixed assets consist of:

(a) Acquired research and development

Acquired R&D consists of acquired individual projects and the surplus values arising in conjunction with business combinations. Ongoing R&D projects acquired through business combinations are recognized at cost as "Acquired R&D". Expenses for continuing research in acquired projects are booked as they arise until the project reaches the stage that the activation criterias under IAS 38 are met. Following initial recognition, the assets are recognized in line with the cost method, meaning that Acquired R&D is recognized at cost after deductions for any accumulated amortization and impairment. Amortization according to plan commences when the R&D project in question results in a product that can be used.

(b) Patents and rights

Patents and rights are recognized at cost. Patents and rights have a limited useful life and are recognized at cost less accumulated amortization. Amortization is applied straight-line in an effort to distribute the cost of patents and rights across their estimated useful life. The following amortization periods are applied:

Patents and rights	3–10 years
IT systems	5 years

(c) Proprietary intangible asset

The proprietary intangible asset consists of clinical studies and registration expenses for these that are considered to contribute to future economic advantages for the Group. These studies are linked to products that have already been approved and commercialized. Other clinical studies are carried as an expense.

The assets have a limited useful life and are recognized at cost less accumulated amortization and impairment, if any. Amortization is applied straight-line in an effort to distribute the cost of proprietary intangible assets across their estimated useful life, which for held assets is 10 years.

2.7 Impairment of non-financial assets

Assets with an indefinite useful life are not depreciated/amortized in consolidation but are instead reviewed annually, or in the event of any indication of a decline in value, to identify any impairment requirement. Assets that are depreciated/amortized are assessed in terms of the value of decline whenever events or conditions indicate that the carrying amount is perhaps no longer recoverable. An impairment loss is recognized in the amount by which the asset's carrying amount exceeds its recoverable amount. The recoverable amount is the higher of the asset's fair value less selling expenses and value in use. In the case of assets other than financial assets that were previously impaired, a test is conducted on the closing date to determine whether a reversal is warranted.

2.8 Inventories

Inventories are recognized at the lower of cost and net sales value. Cost is determined on the basis of the first in, first out (FIFO) principle. The cost for finished products and work in progress consists of raw materials, direct salaries, other direct costs and attributable indirect manufacturing costs (based on normal manufacturing capacity). The net sales value is the estimated sales price in current operations, less deductions for applicable variable selling expenses. Tests for obsolete stock is performed on quarterly basis based on sales forecast and shelf life of material in inventory.

2.9 Financial instruments

Financial instruments are recognized in the balance sheet when the Group becomes a party in accordance with the contractual terms of the instrument. A receivable is recognized when the company has performed and there is a contractual obligation for the counterparty to pay. A liability is recognized when the counterparty has performed and there is a contractual obligation to pay. The business model for which the financial asset or liability was acquired or entered into and the nature of the contractual cash flows is crucial for the classification. Group financial assets and liabilities are classified in the categories shown below:

- Financial assets at amortized cost
- Financial liabilities at amortized cost

The Group does not actively trade in financial instruments that are not related to the Group's operations. Because of this, the financial assets and liabilities recognized in the balance sheet are primarily cash and cash equivalents, accounts receivable, accounts payable and interest-bearing liabilities. During the financial year and the comparative year, the Group did not have any financial instruments that are valued at fair value, either through statement of operations or other comprehensive income.

Financial assets classified at amortized cost are initially measured at fair value with the addition of transaction costs. Receivables against customers are initially recognized at the invoiced value. After initial recognition, the assets are valued according to the effective interest method. Assets classified at amortized cost are held according to the business model to collect contractual cash flows that are only payments of principal amounts and interest on the outstanding capital amount. The assets are covered by a loss reserve for expected loan losses.

Financial liabilities recognized at amortized cost are initially measured at fair value including transaction costs. After the first accounting date, they are valued at accrued acquisition value according to the effective interest method.

2.10 Offset of financial instruments

Financial assets and liabilities are offset and recognized at a net amount in the balance sheet only when there is a legal right to offset the recognized amounts and an intention to settle with a net amount or simultaneously realize the asset and settle the liability.

2.11 Cash and cash equivalents
Cash and cash equivalents include cash, bank balances and other current investments that mature within three months of the date of acquisition and which are exposed only to a minor risk of value fluctuation.

2.12 Accounts receivable
Accounts receivable are reported at amortized cost. A provision for expected credit losses is recorded based on the Group's forward-looking expected credit losses (ECL). An analysis of expected credit losses is performed, taking into account historical, current and forward-looking factors. The effect of recognition of the provision amount is reported in the statement of operations.

2.13 Provisions
Provisions are recognized in the balance sheet when the Group has a legal or informal undertaking as a result of an event that has occurred and when it is probable that an outflow of resources will be required to settle the undertaking.

The provision is recognized in the amount expected to be required to settle the undertaking.

2.14 Interest-bearing liabilities
Interest-bearing liabilities are reported at amortized cost. Borrowings are subsequently recognized at amortized cost and any difference between the amount received (net after transaction costs) and the repayment amount is recognized in the statement of operations allocated over the borrowing period by applying the effective interest method.

Borrowings are classified as a current liability unless the Group has an unconditional right to defer payment of the liability by at least 12 months.

2.15 Shareholders' equity
Transaction costs that may be directly attributed to the issuance of new shares or options are recognized net after tax in shareholders' equity as a deduction from the issue proceeds.

The following are recognized as "Other contributed capital":

- The difference between the share's quotient value and the redemption price of exercised warrants.
- The difference between the share's quotient value and the calculated value of newly issued shares and warrants (option premium).
- Employee stock options, value of employees' services.

2.16 Current and deferred income tax
The tax expense for the period comprises current tax calculated on the basis of the taxable earnings for the period according to current tax rates. The current tax expense is adjusted by changes in deferred tax assets and liabilities attributable to temporary differences and non-utilized losses.

The current tax expense is estimated on the basis of the tax regulations on the closing date that are decided, or have essentially been decided, in the countries in which the parent company and its subsidiaries are active and generate taxable income.

Deferred tax is recognized on all temporary differences that arise between carrying amounts of assets and liabilities and their value for tax purposes in the consolidated financial statements.

Deferred income tax is calculated using tax rates (and legislation) that have been decided or announced by the closing date and are expected to apply when the deferred tax asset in question is realized or the deferred tax liability is settled.

Deferred tax assets are recognized to the extent that it is likely that future taxable income will be available, against which temporary differences can be used.

Current and deferred tax is recognized in the statement of operations, except when the tax refers to items that are recognized directly against shareholders' equity or in other comprehensive income. In these cases, tax is also recognized in shareholders' equity or in other comprehensive income.

2.17 Employee benefits
(a) Pension obligations
A defined-contribution pension plan is a pension plan according to which the Group pays fixed fees to a publicly or privately administrated pension insurance scheme and for which the Group has no further payment obligations once the fees are paid.

The Group uses only defined-contribution pension plans. Prepaid fees are recognized as an asset to the extent that cash repayments or a reduction in future payments may be credited to the Group.

(b) Share-based payments
The Group has a number of share-based compensation plans in the form of share rights and employee stock options. During the vesting period the incentive program is reported as a cost and a long-term provision. Outstanding share programs and employee stock option programs are reported in accordance with IFRS 2 Share-based Payment.

Employee stock options give the right to subscribe for new shares in Orexo. Share rights gives one share per share right. Share rights and employee stock options are earned provided that the holder is still either an employee or a board member in Orexo on the vesting date,

Share rights and employee stock options whose earnings are dependent on performance conditions which are not market conditions are valued with the Black & Scholes model, and options and share rights whose earnings are dependent on performance conditions that are market conditions are valued through Monte Carlo simulations. The share price and the risk-free interest rate used are those valid at the valuation date. In assessing the volatility which is taken into account in the valuation, it is based on the historical volatility in the share during an interval between 2–7 years.

Based on the assessment that there is an in-substance obligation for the company to settle share-based payments instruments in cash, the accounting treatment for cash-based instruments is applied. This means that a provision is recorded based on the fair value of the instrument as per above, and which is revalued at each reporting date. More detailed description of the long-term incentive programs can be found in Note 24.

Employee stock options program
The value of the employee stock options program is recognized as a personnel cost, with a corresponding increase in long-term liabilities. The total amount that is expensed is based on the fair value of the allotted options:

- including all market-related conditions,
- excluding any effect of service conditions and non-market-related vesting conditions (for example, the employee remains employed at the company for a stipulated period of time), and excluding the effect of conditions that are not vesting conditions,
- including internal operational targets approved by the Board.

Non-market-related vesting conditions are taken into account in the assumption of the number of options that are expected to be vested. The total cost is recognized over the entire vesting period, which is the period during which all of the stipulated vesting conditions are to be fulfilled. At the end of each reporting period, the company reviews its assessment of how many shares can be expected to be vested based on the non market-related vesting conditions. Any divergences from the original assessments prompted by the review are recognized in the statement of operations and a corresponding adjustment is made in long-term liabilities.

Social security expenses on the benefits that are expected to arise in conjunction with value increases are recognized over the vesting period with due consideration of value changes.

Share awards
The fair value of the share awards are entered as an expense over the vesting period, with a corresponding increase in long-term liabilities. Assessment of how many shares are expected to be vested is based on non-market-related vesting conditions. Estimates are reconsidered at the end of each reporting period and any deviations are recognized in the statement of operations and corresponding adjustments are made in long-term liabilities.

Social security expenses on the benefits that are expected to arise in conjunction with value increases are recognized over the vesting period with due consideration of value change.

(c) Severance payments
Severance payments are made when the Group serves notice to an employee prior to the normal pension date or when an employee voluntarily accepts redundancy in exchange for such remuneration.

Note 2 cont.

The Group recognizes severance payments when it is clearly obliged to give notice to an employee according to a detailed formal plan with no possibility of it being revoked, or to provide remuneration in conjunction with termination of employment as a result of an offer made to encourage voluntary redundancy.

(d) Accounting policies for bonus plans

The Group has a bonus system that covers members of the Executive Management team and key persons. The bonus system is based on achievement of company goals and is paid out in proportion to annual salary. During the fiscal year, the estimated bonuses vested for the year are calculated and expensed.

2.18 Revenue recognition

Revenues comprise the fair value of goods and services sold, excluding value-added tax, rebates, returned goods and after eliminated intra-Group sales.

Revenues are recognized as follows:

(a) Sale of goods

Revenues from the sale of goods are recognized on the date when control is transferred to the customer, which usually is when the goods are delivered to the retailers which are the Group's customers. The transaction price is usually not known at the time of delivery, as the final price depends on the discount that will be paid to the public or private insurers which pays the patients' drug costs. Because the final transaction price is not known, the Group estimates a discount deduction from a statistical model that is based on prescription data. Retailers have the right to return unsold goods, and therefore the Group estimates a deduction for expected future returns. Revenues from the sale of goods is only reported to the extent that it is very likely that a substantial reversal of accumulated revenue which is reported does not occur when the uncertainty associated with the estimated price deduction ceases.

(b) Royalty revenues

Royalties are normally received on a rolling basis when distributors recognize sales. Recognition is in the same period during which sales were made. When royalties are paid in advance, the revenue is recognized in the periods that sales are recognized. In cases where royalty income for the period is not known, these are estimated based on the company's forecast. Income from royalties is reported only to the extent that it is very likely that an essential reversal of reported accumulated revenues does not occur when the uncertainty associated with the estimated sales ceases.

(c) License revenues

Revenue from milestone payments is reported at that time when the commitment to transfer intellectual property rights to the counterparty has been fulfilled, and the uncertainty about it that the milestone will be achieved has ceased. Orexo's license agreement usually includes one or more of the following types milestone payments:

- One-time compensation when entering into an agreement. Usually refers to the right to register, market and sell Orexos patent protected products within a specified geographical area but can also constitute compensation for technology or knowledge transfer that must take place to the partner.
- Compensation for research collaboration. These are obtained continuously and is reported over the time it relates and the work is performed. Milestones fall out when research goals or sales targets have reached according to definitions in each agreement, for example when granting of patent, termination of clinical trial or approval of registrations. Such remuneration is reported when all the conditions for remuneration according to the agreement is met, and the uncertainty thus has ceased.
- License revenues for Digital Therapeutics (DTx) are recognized over the time during which the license is granted, as the license grant has been determined to be a "right to access" performance obligation. In cases where there is a right to return products, an estimated returns rate is applied which reduces the net revenues. Revenues from licenses are only reported to the extent that it is very likely that a substantial reversal of revenue reported will not occur.

(d) Interest income

Interest income is recognized over the time to maturity using the effective interest method.

2.19 Leasing

Orexo AB applies IFRS 16. According to the standard most leased assets must be recognized in the balance sheet and the lessee shall report leasing costs as interest payments and depreciation of the asset. The parent company applies the exception rule in RFR 2.

2.20 Cost of goods sold

Cost of goods sold consists of the cost of goods for the products that the Group sells. This includes costs for raw materials, direct and indirect cost of goods.

2.21 Basis for preparation of the financial statements for the parent company

Orexo AB, the parent company, has prepared its annual accounts in accordance with the Swedish Annual Accounts Act and the Swedish Financial Accounting Standards Council's recommendations RFR 2. RFR 2 stipulates that the parent company must apply International Financial Reporting Standards (IFRS) as adopted by the EU, to the extent that this is possible within the framework of the Swedish Annual Accounts Act and the Pension Obligations Vesting Act and taking into account the relationship between accounting and taxation. The recommendation specifies the exceptions and additions to be made in relation to IFRS.

Consequently, the parent company applies the policies presented in the consolidated financial statements, with the exceptions outlined below. The policies are applied consistently to all years presented, unless otherwise stated.

Presentation forms

The statement of operations and balance sheet comply with the forms set down in the Swedish Annual Accounts Act.

(a) Shares and participations in subsidiaries

Shares and participations in subsidiaries are recognized at cost with deductions for any impairment.

When there are indications that shares and participations in subsidiaries have declined in value, an estimate is made of the recoverable amount. If this is lower than the carrying amount, impairment is applied. Impairment losses are recognized in the items "Results from participations in Group companies".

(b) Group and shareholders' contributions

Shareholders' contributions granted are recognized as an increase in the value of shares and participations. An assessment is then made as to whether there is a need for impairment of the value of the shares and participations in question.

In the recognition of Group contributions, the Group can either apply the main rule or the alternative rule. The rule chosen shall be applied consistently to all Group contributions.

Under the main rule, Group contributions received from subsidiaries are recognized as revenue in the parent company's statement of operations and Group contributions granted by the parent company are recognized as an increase in participations in affiliated companies.

Under the alternative rule, both contributions received and contributions granted are recognized as appropriations. The Group did not have any Group contributions during the period.

c) Deferred income tax

Amounts allocated to untaxed reserves represent taxable temporary differences. Due to the relationship between accounting and taxation, however, in a legal entity deferred tax liabilities on untaxed reserves are recognized as part of untaxed reserves.

d) Leasing

All leasing agreements, irrespective of whether they are financial or operational, are recognized as operating expenses over the lease period.

NOTE 3 FINANCIAL AND OPERATIONAL RISK MANAGEMENT

The Group's operations are exposed to a number of risks. These risks can be categorized into operational risks and financial risks. The operational risks are described in the Board of Directors report on pages 57–58. The financial risks are described below.

Financial risks and policies

To efficiently manage financial risks, Orexo has drawn up a series of guidelines and a detailed financial policy in respect of the manner in which such risks are to be managed and mitigated. Orexo's financial policy also establishes the distribution of responsibility and reporting instructions for Executive Management. The main purpose of Orexo's financing operation is to limit negative deviations in the results, shareholders' equity and cash flow as the result of fluctuations in interest rates or exchange rates and underlying market conditions.

The President of the Group is responsible for producing, implementing and following up the Group's financial policy, which is subsequently approved by the Board of Directors.

The Group's CFO is responsible for the day-to-day financial administration and reports regularly to the Group President.

3.1. Currency risks

Orexo's financial statements are prepared in SEK. The Group sells its products in countries other than Sweden and receives revenues in currencies other than SEK, primarily in dollars and euros. Revenues and expenses in foreign currency give rise to transaction exposure. The Group has assets (accounts receivable and liquid funds) and liabilities (accounts payable) in foreign currencies, as well as investments in the form of net wealth in foreign subsidiaries. This gives rise to translation exposure.

A substantial share of Orexo's currency exposure is attributable to the sale and manufacture of ZUBSOLV® in the US and royalty income for the Group's products in currencies other than SEK. The license agreements written with counterparties are frequently denominated in some other currency than SEK, primarily USD and EUR.

The Group has the option of hedging transaction exposure. The financial policy permits exchange-rate hedging instruments to be used to eliminate or minimize the currency risks arising in the Group. Currency hedging must always be linked to a confirmed underlying exposure. The permitted hedging instruments are currency futures, acquired currency options (call and put options), currency accounts and loans in foreign currency. No hedging instruments have been used by the Group during the year or in the prior year.

A substantial share of Orexo's operating expenses is in currencies other than SEK, primarily USD, which leads to a certain amount of currency risks. During the 2021 fiscal year, sales in USD accounted for 98 (92) percent of net revenues and sales in EUR accounting for 2 (8) percent. During the same period, 73 (70) percent of total operating expenses were in foreign currency with 67 (63) percent in USD, 1 (3) percent in EUR and 2 (3) percent in GBP.

In currencies in which the Group has flows in the same currency, the flows are to be matched to the greatest extent possible.

A change in the value of USD against SEK of 10 percent and with balance sheet exposure at the closing date entails a change in other operating income and expenses of approximately SEK 7,5 million.

The corresponding change in GBP entails a change of approximately SEK 0,2 million and in EUR of approximately SEK 0,1 million, neither has material impact.

The effect of the change in the value of USD on earnings is primarily due to the fact that a large part of the Group's internal receivables and liabilities are attributable to Orexo Inc in the USA. Translation exposure arises when the Group's equity is influenced by exchange-rate fluctuations when assets and liabilities for foreign subsidiaries are translated to SEK. This exposure is not hedged at present. A 10 percent movement in USD entails an impact on equity of approximately SEK 14,6 million.

3.2 Interest-rate risk

The primary objective of Orexo's interest-rate risk management is to reduce the negative effects of interest-rate movements on earnings. To reduce the impact of interest-rate movements on earnings, Orexo mainly uses short-term investments and aims for the time to maturity of financial liabilities to correspond as far as possible to the time to maturity of financial assets. At year-end, all of Orexo's cash and cash equivalents were invested in short-term assets.

Orexo's policy is that all financial investments apart from bank balances must be made in financial instruments with high liquidity and low credit risk.

The Group had interest-bearing liabilities totaling SEK 492.3 million on December 31, 2021 and these are attributable to a corporate bond loan. This loan has a variable interest rate, STIBOR +3.75 percent (STIBOR is calculated as zero at the lowest).

The impact on earnings of a change in interest rates of 0.5 percent would entail an increase/decrease of SEK 1,0 million.

3.3 Credit risk and counterparty risk

Credit and counterparty risk is the risk that the counterparty will not fulfill its undertakings to repay a liability or pay interest on such a liability and the risk associated with balances with credit institutions.

For the Group, there are mainly two categories of payment flows in which credit risks could arise: in the subsidiary Orexo US Inc's sales to distributors and in the payment flows from Orexo's license agreements with other parties.

With regard to Orexo US Inc's distributors, credit risks are reviewed on an ongoing basis based on the customer's financial position and other factors.

An extensive evaluation of the counterparty is always undertaken prior to the signing of a license agreement.

Accounts receivable are continuously monitored, with checks performed on due customer invoices. Of total accounts receivable at December 31, 2021, the four largest customers accounted for 96 percent. No other single customer accounted for more than 2 percent of total accounts receivable. Note 20 presents the amounts due.

The Group's financial transactions shall only be carried out with banks or financial instruments with an official rating not below A1/P1 according to credit rating from Moody's.

3.4 Liquidity risk

Liquidity risk is defined as the risk that Orexo will be unable to fulfill its undertakings to repay or refinance its debts on time or at a reasonable cost. Liquidity risk is managed by means of sufficient cash and cash equivalents to ensure continuing operations.

Cash flow forecasts are prepared each month. Executive Management continuously monitors forecasts to ensure that the Group has sufficient cash funds to meet the requirements of continuing business operations.

The table below shows the Group's contractual non-discounted cash flows from financial liabilities, distributed on the basis of the period remaining to maturity on the closing date.

At December 31, 2021	Less than 1 year	Between 1 and 2 years	Between 2 and 5 years
Accounts payable	49.2	—	—
Accrued costs	133.7	—	—
Interest bearing liabilities	18.8	37.5	502.2
Leasing	20.8	45.6	—

At December 31, 2020	Less than 1 year	Between 1 and 2 years	Between 2 and 5 years
Accounts payable	47.0	—	—
Accrued costs	107.2	—	—
Interest bearing liabilities	226.3	—	—
Leasing	19.7	56.1	—

3.5 Commercial market risk and inventory risk

Orexo's most important market risks are price pressure, limited reimbursements and the launch of new competing products.

To be successful in the US it is of the utmost importance that ZUBSOLV® obtains reimbursements on a par with those of competitors. Due to the complex American market, with many different payers and a complicated reimbursement system, Orexo has established a professional team focusing only on improving market access and reimbursement for ZUBSOLV®. The payers are constantly reviewing their formu-

Note 3 cont.

laries and this can lead to significant changes in market access. By the end of 2021 ZUBSOLV® had access to 98 percent of the commercial category and 42 percent of the public category in the US.

Orexo's products are sold in a market characterized by tough competition from other products and methods of treatment and there is always a risk that competitors launch new products. In all of Orexo's markets there is intense development of new and improved treatments that can prove to have a better clinical effect than those that already exist.

Orexo is constantly and proactively working to analyze these risks and develops action plans for different market scenarios. This work is done in collaboration with local external specialists.

In order to secure delivery of the products which are critical for patients, Orexo must hold considerable inventories of ZUBSOLV®. High inventory levels entail a risk of impairment of products that have expired. Orexo is constantly working to minimize this risk by adapting inventories to demand, and through the work on improving the product's shelf life.

Being able to obtain and maintain patents and other intellectual property rights protecting Orexo's technologies and products is an important part of Orexo's strategy of creating long-term value for its business. Obtaining patents related to pharmaceuticals is a complex process that involves both scientific and legal expertise. Even if a patent has been granted, it may later be challenged legally, declared invalid or bypassed, which may limit Orexo's ability to market new products. For an update on ongoing litigation cases see the section 'Corporate Governance Report 2021'.

3.6 Capital structure

The Group's objective for its capital structure is to safeguard the Group's ability to continue its operations so it can generate a return for the shareholders and benefits for other stakeholders, as well as maintain an optimum capital structure to keep capital costs down.

The Group's capital is assessed on the basis of its equity/assets ratio. The equity/assets ratio at December 31, 2021 and 2020 is presented in the table below:

	2021	2020
Shareholders' equity	349.6	558.5
Total assets	1,273.7	1,232.9
Equity/assets ratio	**27%**	**45%**

NOTE 4 CRITICAL ACCOUNTING ESTIMATES AND JUDGEMENTS

Estimates and judgments are continuously evaluated and are based on historical experience and other factors, including expectations of future events deemed reasonable under prevailing circumstances.

4.1 Critical estimates and assessments for accounting purposes

The Group makes assessments and assumptions about the future. The resulting accounting estimates will, by definition, seldom correspond to the actual results. Estimates and assumptions that entail a significant risk of material adjustment to the recognized amounts of assets and liabilities during the next fiscal year are outlined below.

(a) Impairment testing of intangible assets

Amortization of intangible assets related to Digital Therapeutics was begun in October 2020 for vorvida® and in November 2020 for deprexis® after the products first sales in the US. Assets consist of milestone payments for licenses and similar rights as well as intangible assets related to enterprise platform for which impairment will be carried out over a period of 10 years. The most significant assumption utilized was projected future revenue growth, as the value of the assets is dependent on the company successfully commercializing the products. The period for which cash flows are projected is longer than five years, due to the early phase of commercialization the Digital Therapeutics products are currently in.

No indication of impairment need has been identified during the year.

Amortization of proprietary intangible assets was begun in August 2015 after the FDA approved ZUBSOLV® for initiation of buprenorphine for maintenance treatment of patients with opioid dependence. Impairment will be carried out over a period of 10 years. Testing to ensure that the carrying amount does not exceed the recoverable amount is thereby only carried out in the event of a negative event that can create an urgent need for impairment. This impairment testing comprises a risk analysis that includes experience-based estimates of the amount of future incoming and outgoing payments. The probability of the occurrence of income-generating events and the probability that the projects will result in products that reach the market are estimated based on available industry statistics. These probabilities vary depending on the phase of development that the R&D projects are in. Future incoming and outgoing payments are adjusted to the level of probability and subsequently discounted by applying an interest rate that reflects the cost of capital and risk.

No indication of impairment need has been identified during the year.

(b) Royalty revenues

Royalties may be impacted by external factors, including sales limitations or price regulations initiated by authorities in the countries in which sales are conducted. This is out of the control of the company and information of this nature does not normally reach the company until it has occured. When reporting the royalty income, an estimate of the sale of the period is required.

(c) Revenues from sale of goods

Revenues from ZUBSOLV® are recognized when they are delivered to wholesalers. Revenues for ZUBSOLV® are calculated as gross income invoiced to wholesalers, with a deduction for actual and estimated discounts to public and private insurance providers ("the payers"), provisions for potential returns, costs for patient support programs and fees to wholesalers and distributors. Since not all of the volume invoiced to wholesalers has reached patients at the closing date, several of the deductions from gross income are partly based on estimates.

(d) Inventory valuation

In order to ensure safe supply of ZUBSOLV® in the American market, Orexo has established inventory level of raw materials, semi-finished products and finished products. The valuation of the inventory and the assessment of the risk of potential write-down is based on continually updated market forecasts and assumptions regarding the shelf-life of various chemical compounds. The shelf-life of semi-finished products and finished products is based on documented stability studies.

(e) Deferred tax assets

Orexo has significant loss carry-forwards as historically the company has made losses. Carry-forwards losses are activated only to the extent that it is probable that the deductions can be offset against surplus on future taxation. The loss carry-forwards for tax purposes in the Group amounted to SEK 1,364 million (1,188) at December 31, 2021. No deferred tax assets for tax-loss carry-forwards have been capitalized.

4.2 Critical judgments in the application of the company's accounting policies

(a) Assessment as to whether a license agreement entails the divestment or a transfer of rights

Certain license agreements entail that global rights are transferred to a business partner. Since Orexo retains the intellectual property rights, which may also be retrieved under certain circumstances, these agreements are not recognized as though the licensing agreement implies a divestment. For Orexo, this means that these assets remain in the balance sheet item "Acquired research and development"

Note 4 cont.

(b) Revenue recognition

Executive Management assesses the probability of whether future financial value will accrue to the Group on the basis of a number of factors, such as the customer's payment history and credit worthiness. If the Group deems a receivable to be doubtful, a provision is made until it is possible to determine whether or not the Group will receive payment.

A milestone payment is an item of revenue related to achieved goals specified in the agreement with the partner in question. Such goals may include the start of clinical trials or the granting of product registration approval by an authority. Revenues from intermediate milestone payments are recognized once the goal has been achieved and the Group has fulfilled its undertakings.

(c) Research and development

Costs attributable to research are expensed as they arise. Assessments of which costs can be capitalized or not are done continuously. Costs attributable to development projects are recognized as intangible assets in the balance sheet when these costs are expected to generate financial benefits in the future. Other development costs are expensed as they arise. Development costs that are expensed are not recognized as an asset in subsequent periods.

NOTE 5 REVENUE FROM CONTRACTS WITH CUSTOMERS

	2021					
Group	ZUBSOLV®	Abstral®	Edluar®	vorvida®	deprexis®	Total
Segment						
US Pharma	522.7	–	–	–	–	**522.7**
Digital Therapeutics	–	–	–	1.0	0.1	**1.1**
HQ & Pipeline	–	32.1	9.1	–	–	**41.2**
Total revenue from contracts with customers	**522.7**	**32.1**	**9.1**	**1.0**	**0.1**	**565.0**
Geographical markets						
US	522.7	–	2.9	1.0	0.1	**526.8**
EU	–	31.0	3.1	–	–	**34.1**
Rest of the world	–	1.1	3.0	–	–	**4.2**
Total revenue from contracts with customers	**522.7**	**32.1**	**9.1**	**1.0**	**0.1**	**565.0**

	2020					
Group	ZUBSOLV®	Abstral®	Edluar®	vorvida®	deprexis®	Total
Segment						
US Pharma	623.3	–	–	–	–	**623.3**
Digital Therapeutics	–	–	–	0.0	0.0	**0.0**
HQ & Pipeline	0.1	29.7	10.4	–	–	**40.2**
Total revenue from contracts with customers	**623.4**	**29.7**	**10.4**	**0.0**	**0.0**	**663.6**
Geographical markets						
US	623.3	–	3.1	0.0	0.0	**626.4**
EU	0.1	28.9	2.7	–	–	**31.7**
Rest of the world	–	0.8	4.7	–	–	**5.5**
Total revenue from contracts with customers	**623.4**	**29.7**	**10.4**	**0.0**	**0.0**	**663.6**

	2021					
Parent company	ZUBSOLV®	Abstral®	Edluar®	vorvida®	deprexis®	Total
Segment						
US Pharma (intragroup)	324.0	–	–	–	–	**324.0**
Digital Therapeutics (intragroup)	–	–	–	0.7	0.1	**0.7**
HQ & Pipeline	–	32.1	9.1	–	–	**41.2**
Total revenue from contracts with customers	**324.0**	**32.1**	**9.1**	**0.7**	**0.1**	**365.9**
Geographical markets						
US	324.0	–	2.9	0.7	0.1	**327.6**
EU	–	31.0	3.1	–	–	**34.1**
Rest of the world	–	1.1	3.0	–	–	**4.2**
Total revenue from contracts with customers	**324.0**	**32.1**	**9.1**	**0.7**	**0.1**	**365.9**

Note 5 cont.

	2020					
Parent company	**ZUBSOLV®**	**Abstral®**	**Edluar®**	**VORVIDA®**	**DEPREXIS®**	**Total**
Segment						
US Pharma (intragroup)	406.2	–	–	–	–	**406.2**
Digital Therapeutics (intragroup)	–	–	–	–	–	**0.0**
HQ & Pipeline	0.1	29.7	10.4	–	–	**40.2**
Total revenue from contracts with customers	**406.3**	**29.7**	**10.4**	**0.0**	**0.0**	**446.4**
Geographical markets						
US	406.2	–	3.1	–	–	**409.3**
EU	0.1	28.9	2.7	–	–	**31.7**
Rest of the world	–	0.8	4.7	–	–	**5.5**
Total revenue from contracts with customers	**406.3**	**29.7**	**10.4**	**0.0**	**0.0**	**446.4**

Sales, products

Revenues for the sale of goods are reported in its entirety at the time when the control of the goods is transferred to the counterparty, which is usually when the goods are delivered to the wholesalers who are the Group's customers. The transaction price is usually not known at the time of delivery, as the final price is dependent on the discount that will be paid to the public or private insurers who pay patients' drug costs. Since the final transaction price is not known, the Group estimates a discount deduction based on a statistical model that is based, among other things, on prescription data. The cumulative discount deduction is reported in the item provisions, and amounted to SEK 139.4 million (170.3) at the balance sheet date. Retailers have the right to return unsold goods, and the Group therefore estimates a deduction for expected future returns. The accumulated return deduction is reported under the item provisions, and amounted to SEK 20.7 million (27.0) at the balance sheet date. During the period, the Group reversed provisions for discounts and returns from previous periods to an amount of SEK 6.7 million (9.0). Estimates of discounts and returns are associated with significant uncertainty, see Note 4.

Royalties

Revenues from royalties are recognized at the time when the commitment to transfer intellectual property rights to the counterparty has been fulfilled, and the sales that form the basis of royalties have occurred. In practice, this means that revenues from royalties for such products where the transfer of the intellectual property rights has already taken place are reported when the sale of the goods that form the basis of royalties takes place. The Group usually does not receive information on actual sales in connection with the financial statements, and therefore estimates earned royalties during the end of the period. The estimate of earned royalties is associated with significant uncertainty, see Note 4.

Licenses

License revenues for Digital Therapeutics (DTx) are recognized over the time during which the license is granted, as the license grant has been determined to be a "right to access" performance obligation. In cases where there is a right to return products, an estimated returns rate is applied which reduces the net revenues. Revenues from licenses are only reported to the extent that it is very likely that a substantial reversal of revenue reported will not occur.

Milestones

Revenues from milestone payments are reported at the time when the obligation to transfer intellectual property rights to the counterparty has been fulfilled, and the uncertainty about the milestone being achieved has ceased. In practice, this means that revenue from milestone payments for such products where the transfer of the intellectual property assets has already taken place are reported when the milestones are achieved.

Other

The Group's sales are mainly based on payment terms on 0–45 days, and no elements of significant financing components exist. The Group reports receivables against counterparties at the time of sale, and at the balance sheet date there were no contractual assets or contractual liabilities. No significant unfulfilled or partially fulfilling performance commitments existed on the balance sheet date.

NOT 6 DISTRIBUTION OF REVENUE AND EBIT PER SEGMENT

US Pharma segment comprises the distribution and sale of ZUBSOLV® for treatment of opioid use disorder in the US. Digital Therapeutics segment comprise the distribution and sale of digital therapies which complement existing treatments and provide patients with access to highly sophisticated and individualized support when they need it most in the US. HQ & Pipeline consists of the Group head quarter functions. R&D. Business Development. Global Regulatory and Supply Chain.

SEK m	2021	2020
US Pharma		
Net revenues	522.7	623.3
Operating earnings (EBIT)	278.2	331.2
Depreciation and amortization	–15.4	–15.4
Digital Therapeutics		
Net revenues	1.1	0.0
Operating earnings (EBIT)	–249.7	–175.4
Depreciation and amortization	–18.6	–3.2
HQ & Pipeline		
Net revenues	41.2	40.2
Operating earnings (EBIT)	–242.6	–175.8
Depreciation and amortization	–19.1	–20.3
Group		
Net revenues	565.0	663.6
Operating earnings (EBIT)	–214.1	–19.9
Depreciation and amortization	–53.0	–38.9
Net financial items	–8.4	–18.4
Earnings before tax	–222.5	–38.3

Revenues from customer in Sweden amounted to SEK 9.0 million during 2021
Fixed assets in Sweden amounted to SEK 56.1 million at December 31. 2021
Intangible assets in Sweden amounted to SEK 248.9 million at December 31. 2021

NOTE 7 COSTS BY TYPE OF COST

	Group		Parent company	
	2021	2020	2021	2020
Raw materials and consumables	78.9	65.6	71.2	79.7
Other external expense	402.2	354.7	433.1	322.7
Personnel costs	249.0	220.6	76.0	78.3
Depreciation/amortization and impairment	53.0	38.9	36.6	23.0
Total	**783.1**	**679.9**	**616.8**	**503.7**

NOTE 8 OTHER OPERATING INCOME

	Group		Parent company	
	2021	2020	2021	2020
Exchange gains	10.8	17.8	10.8	17.8
Other income	0.1	–0.2	32.9	52.4
Total	**10.9**	**17.6**	**43.6**	**70.2**

Other income mainly refers to a transfer pricing related regulation. i.e. the profit of the US subsidiary is regulated to a percentage of sales. Excess profit goes to the parent company.

NOTE 9 DEPRECIATION/AMORTIZATION AND IMPAIRMENT

Depreciation, amortization and impairment are divided up by function as follows:

	Group		Parent company	
	2021	2020	2021	2020
Tangible fixed assets				
Sales	–	–	–	–
Administration	1.9	1.8	1.9	1.8
Research and development	4.3	2.2	4.3	2.2
Total tangible fixed assets	**6.2**	**4.1**	**6.2**	**4.1**
Intangible assets				
Selling	–	0.5	–	–
Administration	0.3	0.4	0.3	0.4
Research and development	34.4	18.6	30.1	18.6
Total intangible assets	**34.6**	**19.5**	**30.4**	**18.9**
Right-of use assets				
Selling	0.3	2.0	–	–
Administration	1.6	2.6	–	–
Research and development	10.5	10.8	–	–
Total right-of use assets	**12.3**	**15.3**	**0.0**	**0.0**
Total depreciation/amortization and impairment	**53.0**	**38.9**	**36.6**	**23.0**

NOTE 10 REMUNERATION TO EMPLOYEES

Average number of employees

Group	2021 Average number of employees	Of whom men	2020 Average number of employees	Of whom men
Sweden	57	31	55	25
USA	78	28	80	32
Total for Group	**135**	**59**	**135**	**57**

Parent company	2021 Average number of employees	Of whom men	2020 Average number of employees	Of whom men
Sweden	57	31	55	25
Total for parent company	**57**	**31**	**55**	**25**

	Group		Parent company	
Costs and remuneration to all employees and board, SEK thousands	2021	2020	2021	2020
Salaries, remuneration and social security fees				
Salaries and other remuneration to the Board, President and Executive Management	43,691	45,703	24,612	23,064
Salaries and other remuneration to other employees	142,947	125,329	35,981	28,080
Pension cost for the Board, President and Executive Management[1]	2,161	2,112	1,710	1,694
Pension cost for other employees[1]	11,934	11,329	7,202	6,880
Social security fees for the Board, President and Executive Management[2]	3,995	3,010	4,435	3,405
Social security fees for other employees[2]	17,385	13,724	10,721	7,347
Other personnel costs	24,088	33,343	2,096	7,753
Total	**246,200**	**234,551**	**86,756**	**78,223**

[1] Pertains in its entirety to defined-contribution pension plan.
[2] Pertains to estimated costs for social security fees for employee stock option program.

Note 10 cont.

Costs and remuneration to the board, president and senior executives 2021, SEK thousands

SEK thousands	Basic salary/ Board fees	Variable remuneration	Other benefits	Pension costs	Share-based payment	Other remuneration	Total remuneration
Board of directors							
James Noble, Chairman	1,500	–	–	–	–	–	–
Henrik Kjaer Hansen, Board member[1)]	0	–	–	–	–	–	–
Fred Wilkinson, Board member	400	–	–	–	–	–	–
Staffan Lindstrand, Board member	350	–	–	–	–	–	–
Mary Pat Christie, Board member	400	–	–	–	–	–	–
Charlotte Hansson, Board member	600	–	–	–	–	–	–
David Colpman, Board member	450	–	–	–	–	–	–
Kirsten Detrick, Board member	400	–	–	–	–	–	–
Subtotal	**4,100**	**0**	**0**	**0**	**0**	**0**	**0**
President and senior executives							
Nikolaj Sørensen, President and CEO	3,617	1,354	110	748	4,022	–	9,851
Other senior executives (6)	19,828	7,288	980	1,413	2,384	–	31,894
Total	**27,545**	**8,642**	**1,090**	**2,161**	**6,407**	**0**	**45,845**

[1] Refrained from Board fee

Costs and remuneration to the board, president and senior executives 2020, SEK thousands

SEK thousands	Basic salary/ Board fees	Variable remuneration	Other benefits	Pension costs	Share-based payment	Other remuneration	Total remuneration
Board of directors							
James Noble, Chairman[1)]	699	–	–	–	–	–	699
Henrik Kjaer Hansen, Board member[2)]	0	–	–	–	–	–	0
Fred Wilkinson, Board member	300	–	–	–	–	–	300
Staffan Lindstrand, Board member	350	–	–	–	–	–	350
Mary Pat Christie, Board member	300	–	–	–	–	–	300
Charlotte Hansson, Board member[1)]	333	–	–	–	–	–	333
David Colpman, Board member	350	–	–	–	–	–	350
Kirsten Detrick, Board member	300	–	–	–	–	–	300
Subtotal	**2,630**	**0**	**0**	**0**	**0**	**0**	**2,630**
President and senior executives							
Nikolaj Sørensen, President and CEO	3,428	1,354	89	692	3,133	–	8,697
Other senior executives (6)	20,287	7,696	812	1,420	3,774	2,533	36,523
Total	**26,345**	**9,050**	**901**	**2,112**	**6,908**	**2,533**	**47,850**

[1] New members since the Annual General meeting in April 2020
[2] Refrained from Board fee

Board members and senior executives

	2021		2020	
	Number on the closing date	Of whom men	Number on the closing date	Of whom men
Group (incl. subsidiaries)				
Board members	8	63%	8	63%
President and other senior executives	7	86%	8	88%
Parent company				
Board members	8	63%	8	63%
President and other senior executives	4	75%	5	80%

Remuneration to CEO and senior executives consists of fixed salary, varibale remuneration, share-based remuneration, pension and other benefits (mainly company car). All employees are covered by defined-contribution plans including health insurance. Variable remuneration refers to variable bonuses based on the fixed portion of basic salary. The employment agreement with the CEO may be terminated with a six-month notice period. Employment agreements for other senior executives can be terminated with between zero and six months' notice. For a further description, see the board of directors report on page 54. Refer to Note 24 for a description of the share-based remuneration

Other senior executives, as of December 31, 2021 refers to Robert A. DeLuca, Michael Sumner, Johannes Doll (EVP and Chief Commercial Officer until September 30, 2021), Joseph DeFeo, Dennis Urbaniak, Robert Rönn and Cecilia Coupland.

The number of shares and options held by the President and senior executives is shown in the information regarding the Board on page 108 and Management on page 110.

NOTE 11 EXCHANGE-RATE DIFFERENCES

The statement of operations includes exchange-rate differences on operating receivables and operating liabilities as follows:

	Group		Parent company	
	2021	2020	2021	2020
Other operating income	10.8	17.8	10.8	17.8
Other operating expenses	–6.9	–20.2	–6.9	–20.2
Total	**3.9**	**–2.4**	**3.9**	**–2.4**

For exchange rate effect in net financial items see Note 12.

NOTE 12 FINANCIAL INCOME AND EXPENSES

	Group		Parent company	
	2021	2020	2021	2020
Financial income				
Other interest income	0.0	1.6	0.0	0.8
Buyback bond	–	1.4	–	1.4
Exchange rate effect	38.2	57.7	38.2	57.7
Total financial income	**38.3**	**60.7**	**38.3**	**59.9**
Financial expenses				
Interest expense from corporate bonds	–18.1	–11.8	–18.1	–11.8
Other interest expense	–2.8	–2.9	–0.0	0.0
Borrowing costs, corporate bonds	–7.3	–1.5	–7.3	–1.5
Exchange rate effect	–18.4	–62.9	–18.4	–62.9
Total financial expenses	**–46.7**	**–79.1**	**–43.8**	**–76.2**
Net Financial items	**–8.4**	**–18.4**	**–5.6**	**–16.3**

NOTE 13 TAX

	Group		Parent company	
	2021	2020	2021	2020
Current tax	–4.5	–5.2	–	–
Deferred tax	3.5	–40.9	–	–49.0
Total	**–1.0**	**–46.1**	**0.0**	**–49.0**
Difference between the Group's tax expense and tax expense based on current tax rate				
Recognized pre-tax earnings	–222.5	–38.3	–219.8	–23.4
Tax under current tax rate	45.8	8.2	45.3	5.0
Tax effect of foreign tax rates	–6,5	–0.3	–	–
Tax effect of non-deductible costs	–0.1	–0.1	–0.1	–0.1
Tax relating to previous years	5,0	–	–	–
Unrecognized carry-forward losses	–45.2	–	–45.2	–
Recognized carry-forward losses	–	–53.9	–	–53.9
Tax on earnings for the year according to the statement of operations	**–1.0**	**–46.1**	**0.0**	**–49.0**

NOTE 14 EARNINGS PER SHARE

Earnings per share before dilution are calculated by dividing the earnings attributable to the parent company by a weighted average number of common shares outstanding during the period, as shown in the presentation below.

	Group	
Group	**2021**	**2020**
Earnings used for the calculation of earnings per share before dilution, MSEK	–223.5	–84.4
Average number of shares before dilution	34,319,649	34,398,815
Earnings per share before dilution (SEK per share)	–6.51	–2.45
Average number of shares after dilution	34,319,649	34,398,815
Earnings per share after dilution (SEK per share)	–6.51	–2.45
Options/share rights outstanding	1,629,022	1,630,875

For calculating the earnings per share after dilution, the weighted average number of common shares outstanding is adjusted for the dilution effects of all potential common shares. The potential common shares in the parent company are represented by employee stock options and share rights.

Group	**2021**	**2020**
Average number of shares before dilution	34,319,649	34,398,815
Potential shares from options and share rights	0	0
Average number of shares after dilution	34,319,649	34,398,815

NOTE 15 TANGIBLE FIXED ASSETS

Group	**Equipment and machinery**	**Computers**	**Improvement expenses other's property**	**Total**
Fiscal year 2020				
Opening balance	39.2	2.9	36.2	78.2
Additions	29.4	—	—	29.4
Disposals	—	—	—	—
Outgoing accumulated acqusitions	**68.6**	**2.9**	**36.2**	**107.7**
Ingoing depreciation	–31.1	–3.0	–22.2	–56.3
Acumulated depreciation disposal	—	—	—	—
Depreciation	–2.3	—	–1.8	–4.1
Accumulated depreciation	**–33.4**	**–3.0**	**–24.0**	**–60.4**
At December 31, 2020				
Cost	68.6	2.9	36.2	107.7
Accumulated depreciation and impairment	–33.4	–3.0	–24.0	–60.4
Carrying amount	**35.2**	**–0.1**	**12.2**	**47.3**
Fiscal year 2021				
Opening balance	68.6	2.9	36.2	107.7
Additions	24.8	—	—	24.8
Disposals	—	—	—	—
Outgoing accumulated acqusitions	**93.4**	**2.9**	**36.2**	**132.5**
Ingoing depreciation	–33.4	–3.0	–24.0	–60.4
Acumulated depreciation disposal	—	—	—	—
Depreciation	–4.4	—	–1.8	–6.2
Accumulated depreciation	**–37.7**	**–3.0**	**–25.8**	**–66.6**
At December 31, 2021				
Cost	93.4	2.9	36.2	132.5
Accumulated depreciation and impairment	–37.7	–3.0	–25.8	–66.6
Carrying amount	**55.7**	**–0.1**	**10.4**	**65.9**

Note 15 cont.

Parent company	Equipment and machinery	Computers	Improvement expenses other's property	Total
Fiscal year 2020				
Opening balance	35.7	1.1	36.2	72.9
Additions	29.3	—	—	29.3
Disposals	—	—	—	—
Outgoing accumulated acquisitions	**65.0**	**1.1**	**36.2**	**102.3**
Ingoing depreciation	–27.7	–1.1	–22.1	–51.0
Accumulated depreciation disposal	—	—	—	—
Depreciation	–2.3	—	–1.8	–4.1
Accumulated depreciation	**–30.0**	**–1.1**	**–23.9**	**–55.1**
At December 31, 2020				
Cost	65.0	1.1	36.2	102.3
Accumulated depreciation and impairment	–30.0	–1.1	–23.9	–55.1
Carrying amount	**35.0**	**0.0**	**12.3**	**47.2**
Fiscal year 2021				
Opening balance	65.0	1.1	36.2	102.3
Additions	24.8	—	—	24.8
Disposals	—	—	—	—
Outgoing accumulated acquisitions	**89.8**	**1.1**	**36.2**	**127.0**
Ingoing depreciation	–30.0	–1.1	–23.9	–55.1
Accumulated depreciation disposal	—	—	—	—
Depreciation	–4.4	—	–1.8	–6.2
Accumulated depreciation	**–34.3**	**–1.1**	**–25.7**	**–61.3**
At December 31, 2021				
Cost	89.8	1.1	36.2	127.1
Accumulated depreciation and impairment	–34.3	–1.1	–25.7	–61.3
Carrying amount	**55.5**	**0.0**	**10.5**	**65.9**

NOTE 16 INTANGIBLE FIXED ASSETS

Group	Acquired R&D	Patents and rights	Proprietary intellectual property right	Other	Total
Fiscal year 2020					
Opening balance	435.1	53.7	153.6	14.0	656.4
Additions	—	140.4	—	19.9	160.3
Exchange rate differences	—	–2.0	—	—	–2.0
Outgoing accumulated acquisitions	**435.1**	**192.1**	**153.6**	**33.9**	**814.7**
Accumulated amortization and impairment	–435.1	–27.4	–67.8	–12.2	–542.5
Amortization	—	–3.2	–15.4	–0.9	–19.5
Accumulated amortization and impairment	**–435.1**	**–30.6**	**–83.2**	**–13.1**	**–562.0**
At December 31, 2020					
Cost	435.1	192.1	153.6	33.9	814.8
Accumulated amortization and impairment	–435.1	–30.6	–83.2	–13.1	–562.0
Carrying amount	**0.0**	**161.5**	**70.4**	**20.8**	**252.8**
Fiscal year 2021					
Opening balance	435.1	192.1	153.6	33.9	814.7
Additions	—	10.2	—	18.0	28.1
Exchange rate differences	—	—	—	2.6	2.6
Outgoing accumulated acquisitions	**435.1**	**202.3**	**153.6**	**54.4**	**845.4**
Accumulated amortization and impairment	–435.1	–30.6	–83.2	–13.1	–562.0
Amortization	—	–14.4	–19.6	–0.7	–34.6
Accumulated amortization and impairment	**435.1**	**–45.0**	**–102.8**	**–13.7**	**–596.6**
At December 31, 2021					
Cost	435.1	202.3	153.6	54.4	845.4
Accumulated amortization and impairment	–435.1	–45.0	–102.8	–13.7	–596.6
Carrying amount	**0.0**	**157.3**	**50.8**	**40.7**	**248.9**

Note 16 cont.

Parent company	Acquired R&D	Patents and rights	Proprietary intellectual property right	Other	Total
Fiscal year 2020					
Opening balance	435.1	53.7	153.6	14.0	656.4
Additions	—	138.4	—	1.0	139.4
Outgoing accumulated acqusitions	**435.1**	**192.1**	**153.6**	**15.0**	**795.8**
Accumulated amortization and impairment	–435.1	–27.4	–67.8	–12.2	–542.5
Amortization	—	–2.7	–15.4	–0.9	–18.9
Accumulated amortization and impairment	**–435.1**	**–30.1**	**–83.2**	**–13.1**	**–561.5**
At December 31, 2020					
Cost	435.1	192.1	153.6	15.0	795.8
Accumulated amortization and impairment	–435.1	–30.1	–83.2	–13.1	–561.5
Carrying amount	**0.0**	**162.0**	**70.4**	**1.9**	**234.4**
Fiscal year 2021					
Opening balance	435.1	192.1	153.6	15.0	795.8
Additions	—	10.2	—	—	10.2
Outgoing accumulated acqusitions	**435.1**	**202.3**	**153.6**	**15.0**	**806.0**
Accumulated amortization and impairment	–435.1	–30.1	–83.2	–13.1	–561.5
Amortization	—	–14.4	–15.4	–0.7	–30.4
Accumulated amortization and impairment	**–435.1**	**–44.5**	**–98.5**	**–13.8**	**–591.9**
At December 31, 2021					
Cost	435.1	202.3	153.6	15.0	806.0
Accumulated amortization and impairment	–435.1	–44.5	–98.5	–13.8	–591.9
Carrying amount	**0.0**	**157.8**	**55.1**	**1.2**	**214.2**

Proprietary intangible asset at December 31, 2021

A proprietary intangible asset amounting to SEK 50.8 million (70.4) is attributable to expenses for clinical studies and a registration expense for these studies. Executive Management assesses that these will give the Group future economic benefits in the form of expanded use of ZUBSOLV®. The expanded label (initiation of treatment of opioid dependence) was approved by the FDA, the US Food and Drug Administration, in August 2015 and in conjunction with this amortization was begun and will occur over a time period of 10 years. During the year there was no impairment of proprietary intangible assets.

Research and development costs

Research and development costs during the period amounted to SEK 272.3 million (224.9).

Parent company intangible assets comprise patents, rights, a proprietary intellectual property right and IT systems. Investments consists mainly of non-refundable milestones of SEK 10.2 million for DTx.

NOTE 17 RESERVES

	Translation reserve	Total
Opening balance at January 1, 2020	**3.1**	**3.1**
Translation differences	–16.5	–16.5
Closing balance at December 31, 2020	**–13.4**	**–13.4**
Opening balance at January 1, 2021	**–13.4**	**–13.4**
Translation differences	13.0	13.0
Closing balance at December 31, 2021	**–0.4**	**–0.4**

Impairment testing

During the year the group has performed impairment tests of its intangible assets related to Digital Therapeutics. As of December 31, 2021 the group has intangible assets for Digital Therapeutics of SEK 192.6 million, consisting of milestone payments for licenses and similar rights as well as intangible assets related to enterprise platform. The impairment tests were performed based on discounted cash flows for the years 2022 to 2030 for vorvida® and deprexis®, both launched in 2020, and 2022 to 2031 for MODIA™ which is not yet launched. The most significant assumption utilized was projected future revenue growth, as the value of the assets is dependent on the company successfully commercializing the products and earning positive cash flows. The period for which cash flows were projected was longer than five years, due to the early phase of commercialization the Digital Therapeutics products are currently in. A risk-adjusted discount rate (WACC) of 30.0% was applied to the tests to compensate for the high uncertainty related to these cash flows. The tests performed did not indicate any impairment.

The products are currently earning limited revenue, and the recoverable value is entirely dependent on substantial future sales growth to earn positive cash flows. A reasonably possible change in key assumtions would hence cause the carrying amount to exceed the recoverable amount, as such growth may not materialize or be lower than anticipated. In addition, the recoverable amount of assets related to vorvida® exceeds the carrying amount by 4 MSEK, and an increase in WACC, everything else held equal, of 1.4%, would result in the assets having a recoverable amount equal to their carrying amount.

NOTE 18 INFORMATION ON FINANCIAL INSTRUMENTS IN THE GROUP

Classification and categorization of assets and liabilities in the group 2021

December 31, 2021	Financial assets measured at amortized cost	Total financial assets	Non-financial assets	Total
Assets				
Tangible fixed assets	–	**0.0**	65.9	**65.9**
Intangible fixed assets	–	**0.0**	248.9	**248.9**
Right-of-use asset	–	**0.0**	59.2	**59.2**
Deferred tax asset	–	**0.0**	33.4	**33.4**
Inventories	–	**0.0**	92.3	**92.3**
Financial assets	0.8	**0.8**	–	**0.8**
Accounts receivable	214.0	**214.0**	–	**214.0**
Other current receivables	–	**0.0**	24.1	**24.1**
Prepaid expenses and accrued income	–	**0.0**	31.1	**31.1**
Cash and cash equivalents	504.1	**504.1**	–	**504.1**
Total assets	**718.9**	**718.9**	**554.9**	**1 273.7**

December 31, 2021	Financial liabilities measured at amortized cost	Total financial liabilities	Non-financial liabilities	Total
Shareholders' equity and liabilities				
Shareholders' equity	–	**0.0**	349.6	**349.6**
Long-term liabilities, provision	–	**0.0**	13.5	**13.5**
Leasing, long-term	38.0	**38.0**	–	**38.0**
Borrowings	492.3	**492.3**	–	**492.3**
Accounts payable	49.2	**49.2**		**49.2**
Provisions	–	**0.0**	160.1	**160.1**
Other current liabilities	112.5	**112.5**	13.2	**125.6**
Leasing, short-term	20.2	**20.2**	–	**20.2**
Prepaid expenses	13.0	**13.0**	12.0	**25.0**
Total shareholders' equity and liabilities	**725.1**	**725.1**	**548.4**	**1 273.7**

Classification and categorization of assets and liabilities in the Group 2020

December 31, 2020	Financial assets measured at amortized cost	Total financial assets	Non-financial assets	Total
Assets				
Tangible fixed assets	–	**0.0**	47.3	**47.3**
Intangible fixed assets	–	**0.0**	252.8	**252.8**
Right-of-use asset	–	**0.0**	67.8	**67.8**
Deferred tax asset	–	**0.0**	32.7	**32.7**
Inventories	–	**0.0**	108.4	**108.4**
Financial assets	0.7	**0.7**	–	**0.7**
Accounts receivable	165.2	**165.2**	–	**165.2**
Other current receivables	–	**0.0**	25.7	**25.7**
Prepaid expenses and accrued income	–	**0.0**	26.9	**26.9**
Cash and cash equivalents	505.3	**505.3**	–	**505.3**
Total assets	**671.2**	**671.2**	**561.6**	**1,232.9**

December 31, 2020	Financial liabilities measured at amortized cost	Total financial liabilities	Non-financial liabilities	Total
Shareholders' equity and liabilities				
Shareholders' equity	–	**0.0**	558.5	**558.5**
Long-term liabilities, provision	–	**0.0**	25.7	**25.7**
Leasing, long-term	47.4	**47.4**	–	**47.4**
Borrowings	224.5	**224.5**	–	**224.5**
Accounts payable	47.0	**47.0**	–	**47.0**
Provisions	–	**0.0**	197.3	**197.3**
Other current liabilities	86.2	**86.2**	5.7	**91.9**
Leasing, short-term	19.1	**19.1**	–	**19.1**
Prepaid expenses	7.3	**7.3**	14.2	**21.5**
Total shareholders' equity and liabilities	**431.5**	**431.5**	**801.4**	**1,232.9**

For all items above the carrying amount is an approximation of the fair value, and therefore these items are not divided up into levels in the measurement hierarchy. The reported value of the bond loan amounted to SEK 492.3 million, the fair value according to level 2 amounted to a substantially equal amount.

Other borrowings have variable interest rates so book values in all material deemed to approximate fair values. Description of Company's borrowings can be found in Note 26.

NOTE 19 INVENTORIES

	Group		Parent company	
	2021	2020	2021	2020
Raw materials	47.5	68.1	47.5	68.1
Work in progress	17.0	22.8	17.0	22.8
Finished products	27.8	17.6	3.3	0.0
Total	**92.3**	**108.4**	**67.8**	**90.9**

The cost of goods from inventory expensed in the Group amounted to SEK 79.0 million (63.5) and in the parent company to SEK 57.0 million (82.8). Write-downs amounted to SEK 0.0 million (2.1).

NOTE 20 ACCOUNTS RECEIVABLE

Impairment losses on accounts receivable amounted to SEK 0.0 million (0.2) in the Group. The carrying amount corresponds to fair value since all receivables are current and are due within one year.

In the Parent company Impairment losses on accounts receivable amounted to SEK 0.0 million (0.0). The carrying amount corresponds to fair value.

Carrying amounts in SEK per currency for the Group's accounts receivable are as follows:

	Group		Parent company	
	2021	2020	2021	2020
SEK	0.0	0.0	0.0	0.0
USD	211.2	161.3	2.7	17.7
EUR	2.8	3.8	2.8	3.8
Total	**214.0**	**165.1**	**5.6**	**21.5**

Credit concentration

The Group has a limited number of customers, which means that a certain risk of credit centration exists.

Of the Group's total accounts receivable, SEK 205.3 million (152.7) is held by the Group's four largest customers. Each of the following:

	Group	
	2021	2020
Customer 1	88.8	62.3
Customer 2	79.4	41.4
Customer 3	34.6	31.5
Customer 4	2.5	17.5
Total	**205.3**	**152.7**

Accounts receivable due

At December 31, 2021, accounts receivable amounting to SEK 57.8 million (1.5) fell due for payment without any impairment requirement being considered necessary.

These apply to a few independent customers who have previously settled their overdue invoices.

An age analysis of these accounts receivable is presented below:

	Group		Parent company	
	2021	2020	2021	2020
Less than 30 days	47.1	0.0	0.0	0.0
31 days and older	10.7	1.5	–	0.0
Total	**57.8**	**1.5**	**0.0**	**0.0**

NOTE 21 OTHER RECEIVABLES

	Group		Parent company	
	2021	2020	2021	2020
VAT receivable	4.1	3.8	4.1	3.8
Tax receivable	19.2	20.4	2.7	2.7
Other	0.8	1.5	0.8	1.5
Total	**24.1**	**25.7**	**7.6**	**8.0**

NOTE 22 PREPAID EXPENSES AND ACCRUED INCOME

	Group		Parent company	
	2021	2020	2021	2020
Prepaid rents	–	–	4.1	4.1
FDA annual fee	12.5	10.3	–	–
Other interim receivables	18.6	16.6	15.6	12.6
Total	**31.1**	**26.9**	**19.7**	**16.7**

NOTE 23 CASH AND CASH EQUIVALENTS

	Group		Parent company	
	2021	2020	2021	2020
Cash and bank balances	504.1	505.3	444.5	361.3
Total	**504.1**	**505.3**	**444.5**	**361.3**

The Group has no unused credit facilities at December 31, 2021.

Reported amounts in SEK million per currency for the Group's cash and cash equivalents is presented below:

	Group		Parent company	
	2021	2020	2021	2020
SEK	210.2	100.8	208.6	94.8
USD	291.8	394.4	233.8	256.4
EUR	1.4	10.0	1.4	10.0
GBP	0.7	0.0	0.7	0.0
Total	**504.1**	**505.3**	**444.5**	**361.3**

Orexo has made the assessment there is no need for a reserve for expected credit losses as the group is not exposed to significant credit risk for cash and cash equivalents. This is driven by the fact that cash and cash equivalents are held entirely in banks, Nordea and Danske Bank, whom have minimal credit risk.

NOTE 24 SHARE-BASED PAYMENTS

Orexo has introduced share-based payments in the form of share awards and employee stock options designed to motivate and reward through ownership, thereby promoting the company's long-term interests. Share awards and employee stock options are vested provided that the holder remains employed or is a Board member in Orexo on this date, see below for detailed descriptions of the performance criterias for the specific programs.

As of December 31, 2021 there were a total of 1,629,022 options and share awards outstanding. These consist of 1,009,929 options that qualify for subscription of shares in Orexo. The number of share awards is 619,093 and each share award provides entitlement to one share in Orexo.

Options and share options whose earnings are dependent on non-market conditions of performance are valued with the Black & Scholes model, and options and share options whose earnings are dependent on performance conditions that are market terms are valued through Monte Carlo simulations.

The share price and the risk-free rate used are the valid ones at the valuation date. The volatility taken into account in the valuation is based on the historical volatility of the stock over a period of 2–7 years.

Cost per fiscal year	Total cost
2020	–10.9
2021	–2.8

Employee stock options/share awards allotted	Number	Exercise price, weighted average
At Dec 31, 2019	**1,505,307**	**64**
Allotted during the period	646,812	78
Redeemed during the period	–489,174	54
Forfeited during the period	–32,070	79
At Dec 31, 2020	**1,630,875**	**74**
Allotted during the period	961,974	45
Redeemed during the period	–319,134	29
Forfeited during the period	–644,693	78
At Dec 31, 2021	**1,629,022**	**57**

Employee stock options/ share awards per year	Number outstanding at Dec 31, 2021	Number vested at Dec 31, 2021	Exercise price, range	Value per allotted option, range	Volatility, option, weighted average	Value per share, range	Value per option weighted average	Maturity date
LTIP 2019	178,600	0	0.0	40.4–73.1	38%	73.1	60.0	2022-06-15
2020 LTIP Stay on	20,802	0	55.9	22.0–57.0	57%	57.0	39.5	2023-08-31–2024-08-03
LTIP 2020 Options	365,661	0	78.6	27.7	56%	76.2	27.7	2023-06-29
LTIP 2020 PSU	156,685	0	0.0	76.2	56%	76.2	76.2	2023-06-29
2021 LTIP Stay on	6,074	0	37.2	14.7–38.6	55%	38.6	26.7	2024-08-31–2025-08-02
LTIP 2021 Options	630,830	0	45.3	13.1	56%	39.9	13.1	2024-06-15
LTIP 2021 PSU	270,370	0	0.0	39.9	56%	39.9	39.9	2024-06-15
Total employee stock options/share awards	**1,629,022**							

Employee stock options/ share awards per year	Number outstanding at Dec 31, 2020	Number vested at Dec 31, 2020	Exercise price, range	Value per allotted option, range	Volatility, option, weighted average	Value per share, range	Value per option weighted average	Maturity date
2011 (LTIP2011)	97,763	97,763	29.0	6.2–7.4	35%	28.2	28.2	2021-02-16
2013 (LTIP2011)	268,945	268,945	51.2–131.6	15.5–43.8	35%	24.2–130.6	53.6	2021-02-16
2014 (LTIP2011)	74,475	74,475	112.9–165.1	14.7–21.9	35%	106.6–166.8	151.3	2021-02-16
2018 (LTIP2018)	343,100	0	0.0	7.1–30.2	38%	30.2	30.2	2021-06-30
2019 (LTIP2019)	212,950	0	0.0	40.4–73.1	38%	73.1	73.1	2022-06-15
2020 (LTIP2020 PSU)	182,005	0	0.0	50.0–76.2	56%	75.4	75.4	2023-06-29
2020 (LTIP2020 options)	424,819	0	0.0	10.7–26.6	56%	75.4	75.4	2023-06-29
2020 (Stay on PSU)	13,409	0	0.0	57.0	57%	56.4	56.4	2023-08-03
2020 (Stay on options)	13,409	0	0.0	22.0	57%	56.4	56.4	2023-08-31
Total employee stock options/share awards	**1,630,875**							

During 2021 the company allotted 961,974 employee stock options, of which the CEO and other senior executives were allotted 267,898, corresponding to 28 percent. The financial and operational targets set by the Board for 2021 reached a score of 64 percent and hence 24 percent of the allocated share awards pertaining to performance target 2 will forfeit. In total 644,693 options were forfeited during 2021. As of December 31, 2021 the liability for LTIP amounted to SEK 13.5 million, see note 25. Changes in and holdings of employee stock options/share awards at the closing date for the CEO and Board members.

Owned by	Number outstanding at Jan 1, 2021	Change	Number outstanding at Dec 31, 2021
President and CEO Nikolaj Sørensen	354,483	–161,523	192,960
Board member James Noble	0	–	0
Board member Henrik Kjaer Hansen	0	–	0
Board member Fred Wilkinson	0	–	0
Board member Mary Pat Christie	0	–	0
Board member Staffan Lindstrand	0	–	0
Board member Charlotte Hansson	0	–	0
Board member Kirsten Detrick	0	–	0
Board member David Colpman	0	–	0

Note 24 cont.

Performance criteria LTIP 2019
LTIP 2019 is a share-based program where 20% of the shares are vested based on employment, 40% based on the share price development and the remaining vested based on the company's operational performance and time.

Performance criterion 1
This target is fulfilled if the holder is employed at the end of the vesting period.

Performance criterion 2
This target pertains to the fulfilment of the financial and operational targets for the financial year 2019 as established by the board of directors and relates to Orexo's key KPIs such as revenue, profitability and achieved milestones, etc. Performance achievement of individual targets is weighted into an overall average performance achievement. The outcome will be measured linearly, meaning that none of the Share Awards will vest unless a minimum threshold of 100 percent of the overall average performance of the financial and operational targets is achieved for LTIP 2019. All Share Awards will vest and entitle to one share each if 100 percent of the overall average performance is acheived. When calculating the overall performance achievement, individual targets may account for a maximum of 120 percent achievement, but the overall average performance is capped at 100 percent. If performance achievement falls below 80 percent for an individual target, then this individual target accounts for zero in the calculation of the overall average achieved.

Performance criterion 3
This target pertains to the development of the Orexo share price over the period from the date of the 2019 Annual General Meeting up to and including April 11, 2022. The share price will be measured as the volume weighted average share price 60 trading days prior to the measurement dates. The measurement dates are date defined as the date of the 2019 Annual General Meeting and April 11, 2022. If the Orexo share's share price exceeds Nasdaq Stockholm Midcap GI Index during the measurement period 100% will vest. If not, all share rights under Performance Objective 3 is forfeitted.

Performance criteria LTIP 2020
LTIP 2020 is a program program based on share awards and employee stock options where 33% of the shares are vested based on employment and 67% is vested based on the company's operational performance. Of each Participant's granted Employee Stock Options, 100 percent will pertain to Performance Target 1, meaning that no Employee Stock Options will vest unless the performance target is met. The allotment of Shares that each participant later may receive depends on achievement of the Performance Targets.

Performance criterion 1
This target is fulfilled if the holder is employed at the end of the vesting period.

Performance criterion 2
This target pertains to the fulfilment of the financial and operational targets for the financial year 2020 as established by the board of directors and relates to Orexo's key KPIs such as revenue, profitability and achieved milestones, etc. Performance achievement of individual targets is weighted into an overall average performance achievement. The outcome will be measured linearly, meaning that none of the Share Awards will vest unless a mimum threshold of 100 percent of the overall average performance of the financial and operational targets is achieved for LTIP 2020. All Share Awards will vest and entitle to one share each if 100 percent of the overall average performance is achieved. When calculating the overall performance achievement, individual targets may account for a maximum of 120 percent achievement, but the overall average performance is capped at 100 percent. If performance achievement falls below 80 percent for an individual target, this individual target accounts for zero in the calculation of the overall average achieved.

Performance criteria LTIP 2021
LTIP 2021 is a program based on share awards and employee stock options where 33% of the shares are vested based on employment and 67% is vested based on the company's operational performance and time. Of each Participant's granted Employee Stock Options, 100 percent will pertain to Performance Target 1, meaning that no Employee Stock Options will vest unless the performance target is met. The allotment of Shares that each participant later may receive depends on achievement of the Performance Targets.

Performance criterion 1
This target is fulfilled if the holder is employed at the end of the vesting period.

Performance criterion 2
This target pertains to the fulfilment of the financial and operational targets for the financial year 2021 as established by the board of directors and relates to the Company's key KPIs as for example revenue, profitability and achieved milestones, etc. Performance achievement of individual targets is weighted into an overall average performance achievement. The outcome will be measured lineally; meaning that from zero to 100 percent of the Share Awards will Vest depending on the overall average rate of performance of the financial and operational targets. All Share Awards will Vest and entitle to one Share each if 100 percent of the overall average performance is achieved. When calculating the overall performance achievement, individual targets may account for a maximum of 120 percent achievement, but the overall average performance is capped at 100 percent. If performance achievement falls below 80 percent for an individual target, this individual target accounts for zero in the calculation of the overall average achieved.

NOTE 25 PROVISIONS

Long-term provisions	Group 2021	Group 2020	Parent company 2021	Parent company 2020
On January 1	**25.7**	**10.7**	**24.5**	**8.2**
Additional provisions	–4.7	18.0	–4.3	19.0
Utilized during the year	–7.5	–2.9	–7.4	–2.7
Reversed unused amounts	–	–	–	–
Per December 31	**13.5**	**25.7**	**12.8**	**24.5**

Long-term provisions primarily refer to estimated costs for incentive programs settled in cash, as well as estimated costs for social security fees in respect of employee incentive programs.

Short-term provisions, rebates and chargebacks	Group 2021	Group 2020	Parent company 2021	Parent company 2020
On January 1	**197.3**	**269.3**	**0.0**	**0.0**
Additional provisions	599.0	606.3	–	–
Utilized during the year	–644.0	–616.4	–	–
Reversed unused amounts	–12.9	–29.2	–	–
Exchange rate difference	20.6	–32.6	–	–
Per December 31	**160.1**	**197.3**	**0.0**	**0.0**

Short-term provisions primarily refer to estimated costs for accrued rebates and returns.

NOTE 26 BORROWINGS

	Group	Parent company
January 1, 2020	**291.4**	**291.4**
Repurchase bond	–66.6	–66.6
Interest expenses	11.8	11.8
Interest paid	–11.8	–11.8
Recognition of loan issuance cost	1.5	1.5
December 31, 2020	**226.3**	**226.3**
January 1, 2021	**226.3**	**226.3**
Repurchase bond	–224.8	–224.8
Issuance of bonds	490.1	490.1
Interest expenses	18.1	18.1
Interest paid	–17.2	–17.2
Recognition of loan issuance cost	2.4	2.4
December 31, 2021	**495.0**	**495.0**

The long-term portion consists of a bond loan amounting to a total of SEK 500.0 million. It matures on February 11, 2025. The loan has a variable interest rate of STIBOR 3 months +3.75 percent (STIBOR is calculated as zero at the lowest) and has a total framework amount of SEK 1,000 million. The loan agreement contains limitations regarding any change in the company's ownership structure, so-called change-of-control, and quarterly reporting of maintenance test and, when applicable, incurrence test.

	Group	Parent company
2020-12-31		
Interest-bearing liabilities	224.5	224.5
Accrued interest costs	1.8	1.8
	226.3	**226.3**
2021-12-31		
Interest-bearing liabilities	492.3	492.3
Accrued interest costs	2.7	2.7
	495.0	**495.0**

NOTE 27 ACCRUED EXPENSES AND OTHER LIABILITIES

Other liabilities	Group 2021	Group 2020	Parent company 2021	Parent company 2020
Employee withholding tax	1.7	2.1	1.7	2.1
Social security fees	1.5	1.5	1.5	1.5
Special salary tax	2.2	2.1	2.2	2.1
Other current liabilities	11.4	0.5	3.7	0.5
Sum Other liabilities	**16.9**	**6.2**	**9.1**	**6.2**

Accrued expenses	Group 2021	Group 2020	Parent company 2021	Parent company 2020
Accrued salaries	24.3	19.0	2.5	2.7
Accrued vacation pay	6.0	6.7	6.0	6.7
Accrued social security fees	2.5	3.2	2.5	3.2
Accrued expenses interest rates	2.7	1.8	2.7	1.8
Trade allowance	44.0	41.7	–	–
Wholesaler fee reserve	21.9	8.3	–	–
Other accrued expenses	32.4	26.6	11.3	7.2
Sum accrued expenses	**133.7**	**107.2**	**25.0**	**21.6**
Sum other liabilities and accrued expenses	**150.6**	**113.4**	**34.1**	**27.8**

NOTE 28 SHARES IN SUBSIDIARIES AND JOINT VENTURES

Direct and indirect holdings Dec 31, 2021	Corp. Reg. No.	Reg. office	Number of shares	Shareholding	Cost/Contribution	Accumulated impairment	Carrying amount
Biolipox AB	556588-3658	Stockholm	12,883,944	100%	106.0	—	106.0
Orexo US Inc	90-0643931	USA	100	100%	56.4	—	56.4
Orexo Pharmaceuticals Inc	87-3270695	USA	100	100%	0.0	—	0.0
Total							**162.4**

All holdings are owned directly, except Orexo Pharmaceuticals, which is owned by Orexo US Inc.
Shareholders Equity amounted to SEK 146.2 million and net revenue amounted to SEK 13,4 thousand in Biolipox AB[1]
Shareholders Equity amounted to SEK 119.3 million and net revenue amounted to SEK 19.2 million in Orexo US Inc[1]
Shareholders Equity amounted to SEK 0.0 million and net revenue amounted to SEK 0.0 million in Orexo Pharmaceuticals Inc

Change in carrying amount of direct holdings

2020	Opening carrying amount	Acquisition	Contribution	Sales	Impairment	Closing carrying amount
Pharmacall AB	0.1	—	—	—	—	0.1
Biolipox	106.0	—	—	—	—	106.0
Orexo US inc	49.5	—	4.8	—	—	54.3
Total	**155.6**	**0.0**	**4.8**	**0.0**	**0.0**	**160.4**

2021	Opening carrying amount	Acquisition	Contribution	Sales	Impairment	Closing carrying amount
Pharmacall AB	0.1	—	—	–0.1	—	—
Biolipox AB	54.3	—	2.2	—	—	56.4
Orexo US Inc	106.0	—	—	—	—	106.0
Orexo Pharma-ceuticals Inc	—	0.0	—	—	—	0.0
Total	**160.4**	**0.0**	**2.2**	**–0.1**	**0.0**	**162.4**

[1] Shareholders Equity and net revenue refers to established numbers as of December 31, 2020.

NOTE 29 AUDITORS' FEES

	Group		Parent company	
	2021	2020	2021	2020
Audit assignment				
Ernst & Young	1.8	1.7	1.8	1.7
Non-auditing assignments				
Ernst & Young	0.3	0.4	0.3	0.4
Tax advice				
Ernst & Young	—	0.4	—	0.4
Other services				
Ernst & Young	—	—	—	—
Total	**2.1**	**2.5**	**2.1**	**2.5**

Audit assignment refers to the auditing of the annual report and accounting records as well as the administration of the Board and the President, other tasks required by the company's auditors, and advisory services and other assistance required as a result of observations arising from such audits or such other tasks. Everything else comes under other assignments.

NOTE 30 DEFERRED TAX

The tax-loss carry-forward in the Group amounts to SEK 1,364 million (1,188) as of December 31, 2021 and refers to the Swedish companies. No deferred tax assets for tax-loss carry-forwards have been capitalized as per December 31, 2021. There is no time limit for when the remaining tax-loss carry-forwards can be utilized.

	Group		Parent company	
	2021	2020	2021	2020
Deferred tax assets				
Capitalized tax loss carryforwards	—	—	—	—
Temporary differences in current provision	11.6	24.7	—	—
Other temporary differences	21.8	8.0	—	—
Total	**33.4**	**32.7**	—	**—**

Temporary differences for short-term provisions are related to non-deductible short-term provisions for sales rebates, returns, distribution and other relevant deductions in Orexo Inc, as well as intercompany gains on inventory. No deferred tax relating to Swedish companies in the Group has been activated during the period.

Deferred tax assets have, in view of the taxable income attributable to the Swedish companies in recent years, been reported only insofar as management estimates that there are factors convincingly suggesting that sufficient taxable surpluses will be generated in the future.

NOTE 31 LEASING

The Group has leases for mainly premises, cars and other equipment used in the business.

The term of the lease extends between 3–6 years.

The Group also has certain leases for machines with rental terms of 12 months or less and leases for equipment with low value. The Group applies the exceptions to short-term leasing agreements and leasing of low-value assets for these leases. The costs for these agreements are shown below.

During the year, the Group did not have any revenue from releasing rights of use, nor any profits or losses from sale and leaseback transactions.

The Groups leasing contracts regarding facilities in Sweden is subject to variable leasing fees in the form of indexation, which is not included in the valuation of leasing liabilities until the increase is known. The Group has no other costs relating to variable leasing fees that are not included in the valuation of leasing liabilities.

Leasing of low value assets in 2021 amounted to SEK 0.3 million.

Carrying amounts of right-of-use assets recognised and the movements during the period:

Group	Offices	Motor vehicles	Other	Total
1 January 2020	47.3	8.8	1.0	57.0
Disposals	—	–0.7	—	–0.7
Additions	26.9	1.5	0.8	29.2
Depreciation expense	–13.9	–1.0	–0.3	–15.3
Translation difference	–1.7	–0.7	0.0	–2.4
31 December 2020	**58.6**	**7.8**	**1.4**	**67.8**
1 January 2021	58.6	7.8	1.4	67.8
Disposals	—	–1.2	—	–1.2
Additions	1.3	1.5	—	2.9
Depreciation expense	–14.7	–3.1	–0.5	–18.4
Translation difference	4.1	3.8	0.2	8.1
31 December 2021	**49.3**	**8.8**	**1.1**	**59.2**

Set out below are the carrying amounts of lease liabilities (included under interest-bearing loans and borrowings) a.8nd the movements during the period:

Group	Offices	Motor vehicles	Other	Total
1 January 2020	45.4	8.4	0.9	54.6
Disposals	—	–0.7	—	–0.7
Additions	26.9	1.5	0.8	29.2
Interest expense	2.5	0.3	0.0	2.8
Payments	–15.4	–1.3	–0.2	–17.0
Translation difference	–1.6	–0.9	0.0	–2.5
31 December 2020	**57.8**	**7.2**	**1.5**	**66.5**
1 January 2021	57.8	7.2	1.5	66.5
Disposals	—	–1.2	—	–1.2
Additions	1.3	1.5	—	2.9
Interest expense	2.6	0.3	0.1	2.9
Payments	–14.2	–0.4	–0.2	–14.8
Translation difference	1.5	0.5	0.1	2.1
31 December 2021	**48.9**	**7.9**	**1.5**	**58.3**

	Group	
	2021	2020
Depreciation of right of use assets	–18.4	–15.3
Interest expense on lease liabilities	–2.9	–2.8
Expenses for short-term leases	–0.3	–0.3
Variable lease payments	—	—
Total lease amounts in statement of operations	**–21.5**	**–18.4**
Total cash outflow for leases	14.8	17.3

Set out below is the nominal value of future leasing fees for non-cancellable leasing contracts:

	Group		Parent company	
	2021	2020	2021	2020
Within one year	20.8	19.7	13.7	13.3
After one year but not more than five years	45.6	56.1	28.9	41.0
More than five years	—	0.6	—	—
Summa	**66.4**	**76.4**	**42.6**	**54.3**

The group has no lease extension options which have been determined as virtually certain to be utilized, and hence has not included any such extensions in the calculation of lease liabilities.

NOTE 32 DISCLOSURES ON THE CASH FLOW STATEMENT

	Group		Parent company	
	2021	2020	2021	2020
Adjustments for items not included in cash flow comprise the following:				
Depreciation and impairment	53.0	38.9	34.5	23.0
Change in provisions	–67.4	–28.5	–11.7	16.3
Share based payments	1.5	–19.7	1.6	–18.7
Exchange rate income and expense	–3.9	2.4	–3.9	2.4
Other non-cash items	—	—	2.1	—
Total	**–16.8**	**–7.1**	**22.5**	**23.0**

NOTE 33 RELATED PARTY TRANSACTIONS

Purchases and sales between Group companies

The following transactions took place between the companies in the Group:

	2021	2020
Forward invoicing of costs		
Orexo US Inc	–22.9	–11.4
Sale of goods and services		
Orexo US Inc	324.7	406.2
Marketing support		
Orexo US Inc	–194.1	–137.4
Total	**107.7**	**257.4**

The Group has no losses or doubtful credits on receivables from related parties.

Remuneration and other commitments regarding pensions and similar benefits to Board members and the President and CEO, see Note 10.

There have been no other related party transactions.

NOTE 34 SUBSEQUENT EVENTS

In collaboration with Sober Grid, vorvida® and deprexis® will be made available at Walgreen's Find Care® during Q1, 2022.

As of March 22, 2022, ZUBSOLV® will be available to all patients with Medicaid insurance in NY state.

Fredrik Järrsten was appointed as new CFO and as a member of the management team, starting at latest in early September, 2022.

NOTE 35 APPROPRIATION OF PROFIT

Proposed appropriation of profit

The following funds are at the disposal of the Annual General Meeting:

SEK thousands	
Share premium reserve	1,187,617
Loss carried forward	–966,843
Profit/loss for the year	–219,762
Total	**1,012**

The Board proposes that the funds at their disposal SEK 1,012 thousand be carried forward.

NOTE 36 PLEDGED ASSETS AND CONTINGENT LIABILITIES

No collateral or contingent liabilities exists as of December 31, 2021, or as of December 31, 2020.

Assurance of the board of directors and president

The Board of Directors and President hereby give their assurance that the consolidated financial statements have been prepared in accordance with the International Financial Reporting Standards (IFRS), as adopted by the EU, and present a true and fair view of the Group's financial position and earnings. The Annual Report has been prepared in accordance with generally accepted accounting principles and presents a true and fair view of the parent company's financial position and earnings.

The Board of Directors' Report for the Group and the parent company presents a true and fair review of the Group's and the parent company's operations, financial positions and earnings and describes the significant risks and uncertainties facing the parent company and the companies included in the Group.

Uppsala, Sweden, March 25, 2022

Orexo AB (publ)

James Noble
Chairman of the Board

Fred Wilkinson
Board member

Staffan Lindstrand
Board member

Charlotte Hansson
Board member

Henrik Kjaer Hansen
Board member

David Colpman
Board member

Kirsten Detrick
Board member

Mary Pat Christie
Board member

Nikolaj Sørensen
President and CEO

Our audit report was submitted on March 30, 2022

Ernst & Young Aktiebolag

Anna Svanberg
Authorized Public Accountant

Auditor's report

To the general meeting of the shareholders of Orexo AB,
Corporate identity number 556500-0600.

Report on the annual accounts and consolidated accounts

Opinions

We have audited the annual accounts and consolidated accounts of Orexo AB for the year 2021. The annual accounts and consolidated accounts of the company are included on pages 54–94 in this document.

In our opinion, the annual accounts have been prepared in accordance with the Annual Accounts Act and present fairly, in all material respects, the financial position of the parent company as of 31 December 2021 and its financial performance and cash flow for the year then ended in accordance with the Annual Accounts Act. The consolidated accounts have been prepared in accordance with the Annual Accounts Act and present fairly, in all material respects, the financial position of the group as of 31 December 2021 and their financial performance and cash flow for the year then ended in accordance with International Financial Reporting Standards (IFRS), as adopted by the EU, and the Annual Accounts Act. The statutory administration report is consistent with the other parts of the annual accounts and consolidated accounts.

We therefore recommend that the general meeting of shareholders adopts the income statement and balance sheet for the parent company and the group.

Our opinions in this report on the annual accounts and consolidated accounts are consistent with the content of the additional report that has been submitted to the parent company's audit committee in accordance with the Audit Regulation (537/2014) Article 11.

Basis for Opinions

We conducted our audit in accordance with International Standards on Auditing (ISA) and generally accepted auditing standards in Sweden. Our responsibilities under those standards are further described in the Auditor's Responsibilities section. We are independent of the parent company and the group in accordance with professional ethics for accountants in Sweden and have otherwise fulfilled our ethical responsibilities in accordance with these requirements. This includes that, based on the best of our knowledge and belief, no prohibited services referred to in the Audit Regulation (537/2014) Article 5.1 have been provided to the audited company or, where applicable, its parent company or its controlled companies within the EU.

We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our opinions.

Key Audit Matters

Key audit matters of the audit are those matters that, in our professional judgment, were of most significance in our audit of the annual accounts and consolidated accounts of the current period. These matters were addressed in the context of our audit of, and in forming our opinion thereon, the annual accounts and consolidated accounts as a whole, but we do not provide a separate opinion on these matters. For each matter below, our description of how our audit addressed the matter is provided in that context.

We have fulfilled the responsibilities described in the Auditor's responsibilities for the audit of the financial statements section of our report, including in relation to these matters. Accordingly, our audit included the performance of procedures designed to respond to our assessment of the risks of material misstatement of the financial statements. The results of our audit procedures, including the procedures performed to address the matters below, provide the basis for our audit opinion on the accompanying financial statements.

Revenue from contracts with customers

Description	How our audit addressed this key audit matter
Revenue from contracts with customers for 2021 was MSEK 565.0 in the consolidated income statement and MSEK 365.9 MSEK in the parent company income statement. As is stated in Note 5, revenue from the sale of goods is calculated net of deductions including actual and estimated rebates to public and private insurers and provisions for potential returns. These gross-to-net adjustments are based partly on management's estimates. The extent of deductions of revenue from rebates, returns etc. and the accounting for royalties connected to licensing agreements are affected by estimates and judgments made by management. A description of the judgments on which revenue recognition is based is provided in the section "Important estimations and judgments for accounting purposes" in Note 4. In summary, revenue recognition for the group contains significant elements of judgment, and for this reason revenue recognition has been determined to be a key audit matter.	In our audit we have reviewed the company's processes over revenue recognition, and reviewed significant agreements to assess whether the accounting for these is compliant with relevant standards. We have also performed sample testing of accruals. We have also reviewed the calculation models on which the deductions from gross sales are based, as well as the reasonableness of key assumptions on which the calculations are based, such as the distribution between different payer categories and expected future returns. Finally, we have reviewed disclosures provided in the annual report.

Intangible assets

Description	How our audit addressed this key audit matter
Intangible assets are recorded at MSEK 248.9 in the consolidated balance sheet and MSEK 214.2 in the parent company balance sheet as of December 31, 2021. The Company tests, when there is an indication of impairment, but at least annually for intangible assets not yet in use, that carrying amounts do not exceed estimated recoverable amounts for these assets. Recoverable amounts are determined through generally adopted models utilizing discounted cash flows based on management's assessments of future cash flows and other significant assumptions such as discount rate and growth that can have a major impact on the estimated recoverable amount. The impairment test of intangible assets performed by management has therefore been considered to be a key audit matter. A description of the impairment test is provided in Note 16 and in the section "Important estimates and assessments for accounting purposes" in Note 4.	In our audit we have reviewed management's models, assessments and assumptions that are utilized for calculating the recoverable amount of the intangible assets. We have reviewed and compared management's forecasts from prior periods against outcomes, and reviewed the plausibility of the forecasts and assumptions underlying this year's impairment test. With the support of our valuation specialists, we have reviewed the company's models and method for conducting impairment tests. We have conducted our own sensitivity analyses of key assumptions and possible impact factors. Finally, we have reviewed disclosures provided in the annual report.

Other Information than the annual accounts and consolidated accounts

This document also contains other information than the annual accounts and consolidated accounts and is found on pages 1–53 and 99–115. The report on management remuneration is also considered to be other information. The Board of Directors and the Managing Director are responsible for this other information.

Our opinion on the annual accounts and consolidated accounts does not cover this other information and we do not express any form of assurance conclusion regarding this other information.

In connection with our audit of the annual accounts and consolidated accounts, our responsibility is to read the information identified above and consider whether the information is materially inconsistent with the annual accounts and consolidated accounts. In this procedure we also take into account our knowledge otherwise obtained in the audit and assess whether the information otherwise appears to be materially misstated.

If we, based on the work performed concerning this information, conclude that there is a material misstatement of this other information, we are required to report that fact. We have nothing to report in this regard.

Responsibilities of the Board of Directors and the Managing Director

The Board of Directors and the Managing Director are responsible for the preparation of the annual accounts and consolidated accounts and that they give a fair presentation in accordance with the Annual Accounts Act and, concerning the consolidated accounts, in accordance with IFRS as adopted by the EU. The Board of Directors and the Managing Director are also responsible for such internal control as they determine is necessary to enable the preparation of annual accounts and consolidated accounts that are free from material misstatement, whether due to fraud or error.

In preparing the annual accounts and consolidated accounts, The Board of Directors and the Managing Director are responsible for the assessment of the company's and the group's ability to continue as a going concern. They disclose, as applicable, matters related to going concern and using the going concern basis of accounting. The going concern basis of accounting is however not applied if the Board of Directors and the Managing Director intends to liquidate the company, to cease operations, or has no realistic alternative but to do so.

The Audit Committee shall, without prejudice to the Board of Director's responsibilities and tasks in general, among other things oversee the company's financial reporting process.

Auditor's responsibility

Our objectives are to obtain reasonable assurance about whether the annual accounts and consolidated accounts as a whole are free from material misstatement, whether due to fraud or error, and to issue an auditor's report that includes our opinions. Reasonable assurance is a high level of assurance, but is not a guarantee that an audit conducted in accordance with ISAs and generally accepted auditing standards in Sweden will always detect a material misstatement when it exists. Misstatements can arise from fraud or error and are considered material if, individually or in the aggregate, they could reasonably be expected to influence the economic decisions of users taken on the basis of these annual accounts and consolidated accounts.

As part of an audit in accordance with ISAs, we exercise professional judgment and maintain professional skepticism throughout the audit. We also:

- Identify and assess the risks of material misstatement of the annual accounts and consolidated accounts, whether due to fraud or error, design and perform audit procedures responsive to those risks, and obtain audit evidence that is sufficient and appropriate to provide a basis for our opinions. The risk of not detecting a material misstatement resulting from fraud is higher than for one resulting from error, as fraud may involve collusion, forgery, intentional omissions, misrepresentations, or the override of internal control.
- Obtain an understanding of the company's internal control relevant to our audit in order to design audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the company's internal control.
- Evaluate the appropriateness of accounting policies used and the reasonableness of accounting estimates and related disclosures made by the Board of Directors and the Managing Director.
- Conclude on the appropriateness of the Board of Directors' and the Managing Director's use of the going concern basis of accounting in preparing the annual accounts and consolidated accounts. We also draw a conclusion, based on the audit evidence obtained, as to whether any material uncertainty exists related to events or conditions that may cast significant doubt on the company's and the group's ability to continue as a going concern. If we conclude that a material uncertainty exists, we are required to draw attention in our auditor's report to the related disclosures in the annual accounts and consolidated accounts or, if such disclosures are inadequate, to modify our opinion about the annual accounts and consolidated accounts. Our conclusions are based on the audit evidence obtained up to the date of our auditor's report. However, future

events or conditions may cause a company and a group to cease to continue as a going concern.
- Evaluate the overall presentation, structure and content of the annual accounts and consolidated accounts, including the disclosures, and whether the annual accounts and consolidated accounts represent the underlying transactions and events in a manner that achieves fair presentation.
- Obtain sufficient and appropriate audit evidence regarding the financial information of the entities or business activities within the group to express an opinion on the consolidated accounts. We are responsible for the direction, supervision and performance of the group audit. We remain solely responsible for our opinions.

We must inform the Board of Directors of, among other matters, the planned scope and timing of the audit. We must also inform of significant audit findings during our audit, including any significant deficiencies in internal control that we identified.

We must also provide the Board of Directors with a statement that we have complied with relevant ethical requirements regarding independence, and to communicate with them all relationships and other matters that may reasonably be thought to bear on our independence, and where applicable, actions taken to eliminate threats or related safeguards applied.

From the matters communicated with the Board of Directors, we determine those matters that were of most significance in the audit of the annual accounts and consolidated accounts, including the most important assessed risks for material misstatement, and are therefore the key audit matters. We describe these matters in the auditor's report unless law or regulation precludes disclosure about the matter

Report on the audit of the administration and the proposed appropriations of the company's profit or loss

Opinions

In addition to our audit of the annual accounts and consolidated accounts, we have also audited the administration of the Board of Directors and the Managing Director of Orexo AB for the year 2021 and the proposed appropriations of the company's profit or loss.

We recommend to the general meeting of shareholders that the profit be appropriated (loss be dealt with) in accordance with the proposal in the statutory administration report and that the members of the Board of Directors and the Managing Director be discharged from liability for the financial year.

Basis for opinions

We conducted the audit in accordance with generally accepted auditing standards in Sweden. Our responsibilities under those standards are further described in the Auditor's Responsibilities section. We are independent of the parent company and the group in accordance with professional ethics for accountants in Sweden and have otherwise fulfilled our ethical responsibilities in accordance with these requirements.

We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our opinions.

Responsibilities of the Board of Directors and the Managing Director

The Board of Directors is responsible for the proposal for appropriations of the company's profit or loss. At the proposal of a dividend, this includes an assessment of whether the dividend is justifiable considering the requirements which the company's and the group's type of operations, size and risks place on the size of the parent company's and the group's equity, consolidation requirements, liquidity and position in general.

The Board of Directors is responsible for the company's organization and the administration of the company's affairs. This includes among other things continuous assessment of the company's and the group's financial situation and ensuring that the company's organization is designed so that the accounting, management of assets and the company's financial affairs otherwise are controlled in a reassuring manner. The Managing Director shall manage the ongoing administration according to the Board of Directors' guidelines and instructions and among other matters take measures that are necessary to fulfill the company's accounting in accordance with law and handle the management of assets in a reassuring manner.

Auditor's responsibility

Our objective concerning the audit of the administration, and thereby our opinion about discharge from liability, is to obtain audit evidence to assess with a reasonable degree of assurance whether any member of the Board of Directors or the Managing Director in any material respect:
- has undertaken any action or been guilty of any omission which can give rise to liability to the company, or
- in any other way has acted in contravention of the Companies Act, the Annual Accounts Act or the Articles of Association.

Our objective concerning the audit of the proposed appropriations of the company's profit or loss, and thereby our opinion about this, is to assess with reasonable degree of assurance whether the proposal is in accordance with the Companies Act.

Reasonable assurance is a high level of assurance, but is not a guarantee that an audit conducted in accordance with generally accepted auditing standards in Sweden will always detect actions or omissions that can give rise to liability to the company, or that the proposed appropriations of the company's profit or loss are not in accordance with the Companies Act.

As part of an audit in accordance with generally accepted auditing standards in Sweden, we exercise professional judgment and maintain professional skepticism throughout the audit. The examination of the administration and the proposed appropriations of the company's profit or loss is based primarily on the audit of the accounts. Additional audit procedures performed are based on our professional judgment with starting point in risk and materiality. This means that we focus the examination on such actions, areas and relationships that are material for the operations and where deviations and violations would have particular importance for the company's situation. We examine and test decisions undertaken, support for decisions, actions taken and other circumstances that are relevant to our opinion concerning discharge from liability. As a basis for our opinion on the Board of Directors' proposed appropriations of the company's profit or loss we examined whether the proposal is in accordance with the Companies Act.

The auditor's examination of the ESEF report

Opinion

In addition to our audit of the annual accounts and consolidated accounts, we have also examined that the Board of Directors and the Managing Director have prepared the annual accounts and consolidated accounts in a format that enables uniform electronic reporting (the Esef report) pursuant to Chapter 16, Section 4(a) of the Swedish Securities Market Act (2007:528) for Orexo AB for the financial year 2021.

Our examination and our opinion relate only to the statutory requirements.

In our opinion, the ESEF report #[4909e34e2c1a0ee74a2cd04816fa115a19119b860719238f2c2e13cc523fdbbe] has been prepared in a format that, in all material respects, enables uniform electronic reporting.

Basis for opinion

We have performed the examination in accordance with FAR's recommendation RevR 18 Examination of the ESEF report. Our responsibility under this recommendation is described in more detail in the Auditors' responsibility section. We are independent of Orexo AB in accordance with professional ethics for accountants in Sweden and have otherwise fulfilled our ethical responsibilities in accordance with these requirements.

We believe that the evidence we have obtained is sufficient and appropriate to provide a basis for our opinion.

Responsibilities of the Board of Directors and the Managing Director

The Board of Directors and the Managing Director are responsible for the preparation of the Esef report in accordance with Chapter 16, Section 4(a) of the Swedish Securities Market Act (2007:528), and for such internal control that the Board of Directors and the Managing Director determine is necessary to prepare the Esef report without material misstatements, whether due to fraud or error.

Auditor's responsibility

Our responsibility is to obtain reasonable assurance whether the Esef report is in all material respects prepared in a format that meets the requirements of Chapter 16, Section 4(a) of the Swedish Securities Market Act (2007:528), based on the procedures performed.

RevR 18 requires us to plan and execute procedures to achieve reasonable assurance that the Esef report is prepared in a format that meets these requirements.

Reasonable assurance is a high level of assurance, but it is not a guarantee that an engagement carried out according to RevR 18 and generally accepted auditing standards in Sweden will always detect a material misstatement when it exists. Misstatements can arise from fraud or error and are considered material if, individually or in aggregate, they could reasonably be expected to influence the economic decisions of users taken on the basis of the Esef report.

The audit firm applies ISQC 1 Quality Control for Firms that Perform Audits and Reviews of Financial Statements, and other Assurance and Related Services Engagements and accordingly maintains a comprehensive system of quality control, including documented policies and procedures regarding compliance with professional ethical requirements, professional standards and legal and regulatory requirements.

The examination involves obtaining evidence, through various procedures, that the Esef report has been prepared in a format that enables uniform electronic reporting of the annual and consolidated accounts. The procedures selected depend on the auditor's judgment, including the assessment of the risks of material misstatement in the report, whether due to fraud or error. In carrying out this risk assessment, and in order to design audit procedures that are appropriate in the circumstances, the auditor considers those elements of internal control that are relevant to the preparation of the Esef report by the Board of Directors and the Managing Director, but not for the purpose of expressing an opinion on the effectiveness of those internal controls. The examination also includes an evaluation of the appropriateness and reasonableness of assumptions made by the Board of Directors and the Managing Director.

The procedures mainly include a technical validation of the Esef report, i.e. if the file containing the Esef report meets the technical specification set out in the Commission's Delegated Regulation (EU) 2019/815 and a reconciliation of the Esef report with the audited annual accounts and consolidated accounts.

Furthermore, the procedures also include an assessment of whether the Esef report has been marked with iXBRL which enables a fair and complete machine-readable version of the consolidated statement of financial performance, financial position, changes in equity and cash flow.

Ernst & Young AB, Jakobsbergsgatan 24, 111 44, Stockholm, was appointed auditor of Orexo AB by the general meeting of the shareholders on 13 April 2021 and has been the company's auditor since 15 April 2016.

Stockholm 30 March 2022
Ernst & Young AB

Anna Svanberg
Authorized Public Accountant

Reconciliations and definitions of key figures

Group

Key figures and certain other operating infromation per share are reconciled as follows:

EBITDA SEK million	2021	2020
EBIT	–214.1	–19.9
Depreciation and amortization	53.0	38.9
EBITDA	**–161.0**	**19.0**
DTx EBIT	249.7	175.4
IP litigation and subpoena costs	59.6	16.8
EBITDA excluding DTx, IP litigation and subpoena costs	**148.3**	**211.3**

Return on shareholders' equity SEK million	2021	2020
Shareholders' equity beginning balance	558.5	706.4
Shareholders' equity ending balance	349.6	558.5
Average shareholders' equity	454.1	632.5
Net earnings	–223.5	–84.4
Return on shareholders' equity %	**–49.2**	**–13.3**

Operating expenses SEK million	2021	2020
Selling expenses	–280.4	–286.6
Administrative expenses	–151.5	–102.8
Research and development costs	–272.3	–224.9
Other operating income and expenses	4.0	–3.6
Operating expenses	**–700.2**	**–617.9**

Gross investments SEK million	2021	2020
Investments in tangible fixed assets	24.7	29.4
Investments in intangible fixed assets	28.1	160.3
Operating expenses	**52.9**	**189.8**

Key figures and certain other operating information per share are defined as follows:

Margins	Definition/calculation	Purpose
Gross margin	Gross profit divided by net revenues	Gross Margin is used to measure the relative direct profitability from sold products
Operating margin (EBIT margin)	Operating earnings as a percentage of net revenues	Operating profit margin is used for measuring the operational profitability

Return	Definition/calculation	Purpose
Return on equity	Net earnings for the period as a percentage of average shareholders' equity	Return on equity is used to measure profit generation, given the resources attributable to the owners of the parent company

Capital structure	Definition/calculation	Purpose
Net Debt	Current and long-term interest-bearing liabilities including pension liabilities, less cash and cash equivalents	The net debt is used as an indication of the ability to pay off all debts if these became due simultaneously on the day of calculation, using only available cash and cash equivalents
Debt/equity ratio	Total liabilities divided by shareholders' equity	The debt/equity ratio measures how much debt a company is using to finance its assets relative to the amount of value represented in shareholder's equity.
Equity/assets ratio	Shareholders' equity as a percentage of total assets	This ratio is an indicator of the company's leverage used to finance the firm
Working capital	Current assets excluding cash and cash equivalents less current liabilities excluding interest bearing liabilities	Working capital is used to measure the company's ability, besides cash and cash equivalents, to meet current operational obligations
Capital employed	Interest-bearing liabilities and shareholders' equity	Capital employed measures the amount of capital used and serves as input for the return on capital employed
Gross investments	Value of investment before amortization	Gross investments is a measure of the company's investments in tangible and intangible fixed assets

Data per share	Definition/calculation	Purpose
Number of shares after dilution	Shares at the end of the period adjusted for the dilutive effect of potential shares	Is used to calculate earnings per share after dilution
Earnings per share, before dilution	Net earnings for the period after tax divided by the average number of shares outstanding before dilution during the period	The earnings per share before dilution measures the amount of net profit that is available for payment to its shareholders per share before dilution
Earnings per share, after dilution	Net earnings for the period after tax divided by the average number of shares outstanding after dilution during the period	The earnings per share after dilution measures the amount of net profit that is available for payment to its shareholders per share after dilution

Other definitions	Definition/calculation	Purpose
Gross Revenues	Grand total of all invoiced sales transactions reported in a period, without any deductions	Reflects the company's invoiced revenues without any deductions
Net Revenues	Gross Revenues less deductions for sales rebates, sales allowances, distribution, sales returns and other relevant deductions	Reflects the company's invoiced revenues after deductions
Gross to net ratio	Net Revenues divided by Gross Revenues	Reflects a relative portion of net revenue as percentage of gross revenue
Operating expenses	An expense incurred in daily operating activities. Expense related to financing is not considered part of daily operating activities.	Operating expenses reflect costs for selling, administration, research and development, depreciation and other operating income and operating expenses
EBIT	Earnings before net financial items and tax, the same as Operating earnings	This measure enables the profitability to be compared across locations where corporate taxes differ and irrespective the financing structure of the company
EBITDA	Earnings before interest, taxes, depreciation and amortization. EBIT plus depreciation	Profit measure which is more closely correlated with cash flow as non-cash items like Depreciation and Amortization are excluded
Earnings after financial items	Operating earnings (EBIT) plus financial income less financial expense	Earnings after financial items reflects earnings after, any results from participations in Group and associated companies, results from securities and receivables that fall within the type of fixed assets as well as interest expenses and interest income

Corporate governance

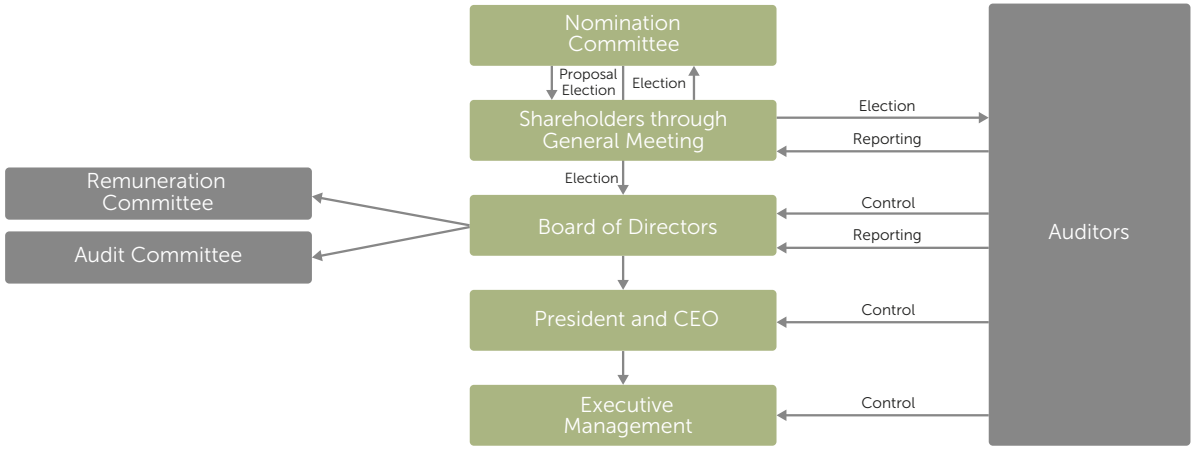
Photo: Jenny Lagerqvist.

Corporate governance report for Orexo AB (publ)

Orexo is a Swedish public limited liability company, with its registered office in Uppsala, Sweden. The company's shares are listed on Nasdaq (Mid Cap) Stockholm under the symbol ORX and with American Depositary Receipts (ADRs) traded on OTCQX under the symbol ORXOY. Corporate Governance in Orexo is based on applicable laws, rules and recommendations such as the Swedish Code of Corporate Governance ("the Code"), Orexo's articles of association and internal regulations and guidelines.

The aim of corporate governance at Orexo is to create a clear division of roles and responsibilities between shareholders, the Board of Directors and Management.

Internal governance, control and risk management concerning financial reporting are fundamental factors in Orexo's business control.



The governance, management and control of Orexo are divided between the General Meeting of Shareholders, the Board of Directors and the President.

Examples of external regulations influencing corporate governance

- Swedish Companies Act
- Regulations governing external reporting, such as the accounting law and the Annual Report law
- Nasdaq Stockholm rules for issuers
- OTCQX rules for companies trading ADRs on OTCQX
- Swedish Code of Corporate Governance (the Code, www.bolagsstyrning.se)

Examples of internal rules of significance for corporate governance

- Articles of Association
- Formal work plan for the Board of Directors (including terms of reference for Board Committees)
- Terms of reference for the President
- Guidelines for remuneration of senior executives
- Finance policy
- IR policy
- IT policy
- Financial guidelines
- HR guidelines
- Business Compliance and Ethics code

Shareholders

Orexo's share has been listed on Nasdaq Stockholm since 2005. At year-end, the total number of shares amounted to 34,710,639 (34,710,639), distributed among 7,272 shareholders (8,814).

The 10 largest shareholders held 58.3 percent (61.7) of the outstanding shares, management 0.4 percent (0.5) and other shareholders 41.3 percent (37.8). At December 31, 2021 one shareholder held shares representing 10 percent or more of the company – Novo Holding A/S, 27.8 percent. Non-Swedish shareholders accounted for approximately 43 percent (47) of the total number of shares. Institutions and industrial owners hold the majority of shares. At year-end, 74 percent (78) of the shares were held by legal entities, and 26 percent (22) by private individuals. Since November 13, 2013, the share is available in the US as an ADR on the OTCQX market.

Articles of Association

The Articles of Association are adopted by the General Meeting of Shareholders and outline a number of mandatory tasks of a fundamental nature for the company. Notification of the convening of the General Meetings is issued through an advertisement being placed on Orexo's website and in Post- och Inrikes Tidningar (Official Swedish Gazette). Confirmation that a General Meeting has been convened shall be announced in the Svenska Dagbladet newspaper. The Articles of Association state that Orexo shall conduct research and development, and manufacture, market and sell pharmaceuticals and diagnostic preparations. Orexo's Articles of Association also state that the Board of Directors shall have its registered office in Uppsala, Sweden, and shall consist of a minimum of three and a maximum of nine members, with a maximum of three deputies. The Articles of Association contain no special provisions on the appointment or dismissal of Board members. Amendments to the Articles of Association are made in accordance with the provisions of the Swedish Companies Act following a resolution of the General Meeting. The complete Articles of Association are available at www.orexo.com.

Annual General Meeting

Orexo's highest decision-making body is the General Meeting, at which every shareholder who is entered in the share register and who has provided notification of their attendance within the stipulated time is entitled to participate and vote for the amount of shares held. Shareholders can also be represented by proxy at General Meetings. One share entitles the holder to one vote at General Meetings, and there are no limits as to how many votes each shareholder can cast at a General Meeting. Resolutions at General Meetings are passed with a simple majority, unless the Companies Act stipulates a higher percentage of the shares and votes represented at the Meeting.

The Annual General Meeting elects members to the Board of Directors and sets Board fees. The other mandatory tasks of the Annual General Meeting include adopting the company's balance sheet and income statement, passing resolutions on the appropriation of earnings from operations, remuneration guidelines for senior executives and decisions concerning discharge from liability for Board members and the President. The Annual General Meeting also elects the company's auditor and sets the auditors' fees. In accordance with the Articles of Association, the Annual General Meeting shall be held in either Uppsala or Stockholm.

Annual General Meeting 2021

The Annual General Meeting was held on Tuesday, April 13, 2021 in Uppsala. At the Meeting:

- James Noble, Staffan Lindstrand, Henrik Kjaer Hansen, David Colpman, Kirsten Detrick, Mary-Pat Christie, Fred Wilkinson and Charlotte Hansson were re-elected as Board members.
- James Noble was re-elected as new Chairman of the Board.
- Ernst and Young Aktiebolag was re-elected as auditor.
- A resolution was adopted that fees for Board members should amount to SEK 3,550,000, with SEK 900,000 paid to the Chairman of the Board, SEK 300,000 to each of the other Board members, and a total of SEK 400,000 distributed between the members of the Audit Committee, so that the Chairman of the committee receives SEK 200,000 and SEK 200,000 is distributed between the other committee members for their work on the committee, and in total 150,000 to be allocated to the members of the remuneration committee in equal parts between the members of the committee, and that fees to the auditor should be paid against approved accounts.
- Further, the annual general meeting resolved on an additional board fee in accordance with the nomination committee's proposal to the board members James Noble, David Colpman, Kirsten Detrick, Fred Wilkinson, Mary Pat Christie and Charlotte Hansson of SEK 950,000, subject to (i) the board member's acquisition of shares in Orexo for the entire part (after taxes) of such additional board fee as soon as possible following the annual general meeting's resolution and the pay-out of the additional board fee, and (ii) the board member's commitment not to sell the shares during the board member's entire tenure on the Orexo board. The additional board fee is to be allocated as follows: SEK 450,000 to the chairman, corresponding to 50 percent of the ordinary board fee to the chairman, and SEK 100,000 to each of David Colpman, Kirsten Detrick, Fred Wilkinson, Mary Pat Christie and Charlotte Hansson, corresponding to 33 percent of the ordinary board fee to such board members. In the event that the board member, before the succeeding annual general meeting, is dismissed due to breach of his/her obligations as a board member or leaves the board at his/her own request, the board member must repay the entire additional board fee (after taxes).
- The Board's motion concerning guidelines for remuneration to the management was approved.
- The motion concerning the appointment of a Nomination Committee for AGM 2022 was approved.

- The balance sheet and income statement for the parent company and the Group for the 2020 fiscal year were adopted. It was resolved that there should be no dividend for 2020 and that the results of the company shall be carried forward.
- The Annual General Meeting granted Board members and the President discharge from liability for the 2020 fiscal year.
- A resolution was adopted in accordance with the Board's proposal concerning authorization of the Board to resolve to issue shares.
- A resolution was adopted in accordance with the Board's proposal concerning authorization of the Board to repurchase and transfer the company's own shares.
- A resolution was adopted in accordance with the Board's proposal concerning to adopt a long-term incentive program for senior executives and key employees within the Orexo group.
- The annual general meeting resolved, in accordance with the board's proposal, to make certain amendments to the articles of association as a result of statutory amendments and the annual general meeting's resolution to cancel all of the company's outstanding class C shares on 16 April 2020.
- The Board's motions concerning a long-term incentive program for senior executives and key employees and a long-term incentive program for for certain Global Management Team employees and US Leadership Team employees were approved.

Complete information about the 2021 Annual General Meeting can be found at www.orexo.com.

Annual General Meeting 2022

The Annual General Meeting of Orexo AB will be held on Tuesday, April 21, 2022. Full information about the Annual General Meeting can be found on the company's website, https://orexo.com/about-us/corporate-governance/.

Nomination Committee

The 2021 Annual General Meeting adopted a resolution that the Company should have a Nomination Committee. The Nomination Committee represents the company's shareholders. It is tasked with creating the best possible basis for the General Meeting's resolutions regarding the election of Board members and Board fees and with submitting proposals concerning, for example, the appointment of auditors and auditors' fees. The Nomination Committee comprises representatives of the three largest shareholders in terms of voting rights as per September 30, 2021, in addition to the Chairman of the Board. The composition of the Nomination Committee was announced on Orexo's website and in a press release on November 1, 2021. The Committee held 2 (11) meeting during the year.

Through the Chairman of the Board, the Nomination Committee reviewed the evaluation of the Board's work and received information regarding developments in the company. The principal requirements to be imposed on the Board of Orexo and the importance of independent Board members were discussed.

No special remuneration was paid for participation in the Nomination Committee.

Nomination Committee for the Annual General Meeting 2021:

Name	Representatives
Christian Salling	Novo Holding A/S, and Chairman of the Nomination Committee
Patrik Walldov	Representantative for Anders Walldov (incl. indirect holding via Brohuvudet AB)
Claus Berner Møller	Arbejdsmarkedets Tillaegspension (ATP)
James Noble	Chairman of the Board of Orexo

Combined, the Nomination Committee represents about 38 percent of the number of shares and votes in the company, based on shareholder data at the time of appointment.

Composition of the Board

Name	Function	Independent	Elected	Present at Board meetings	Present at Remuneration Committee	Present at Audit Committee
James Noble	Chairman of the Board	■	2020	16/16	2/2	4/4
David Colpman	Board member	■	2015	16/16	2/2	–
Charlotte Hansson	Board member	■	2020	16/16	–	4/4
Henrik Kjaer Hansen	Board member	■	2018	16/16	–	4/4
Mary-Pat Christie	Board member	■	2019	16/16	–	–
Staffan Lindstrand	Board member	■	2002	16/16	2/2	–
Fred Wilkinson	Board member	■	2019	15/16	–	–
Kirsten Detrick	Board member	■	2016	16/16	–	–

■ Independent in relation to Orexo and its management
■ Independent in relation to Orexo, its management and the company's largest shareholders

Board of Directors

The Board of Directors have a responsibility to the shareholders for the Group's management and organization. They monitor the president's work and continuously follows the business development and the reliability of the internal control within the company. The Board's responsibility is regulated in the Companies Act and the formal work plan that is established annually. The formal work plan establishes the division of the Board's work between the Board in its entirety and the Board's various committees and between the Board and the President. It also sets out the items to be addressed at Board meetings and the manner in which the President provides the Board with information and reports. The Board has appointed Audit and Remuneration Committees from within its ranks.

At year-end, Orexo's Board of Directors consisted of Chairman James Noble and Board members David Colpman, Staffan Lindstrand, Henrik Kjaer Hansen, Charlotte Hansson, Kirsten Detrick, Mary-Pat Christie and Fred Wilkinson. For a more detailed description of Board members, please refer to page 108.

The work of the Board

The Board's formal work plan establishes the items to be addressed at the scheduled Board meetings. Following presentations by the Audit Committee and President, the Board reviews all interim reports prior to publishing. The company's long-term targets and strategy and its budget are evaluated and approved by the Board. At each Board meeting, the President or another senior executive reports on the business situation and the status of relevant projects.

In addition to the statutory Board meeting, at least six scheduled Board meetings must be held. At the Board meeting during which the annual audit is to be considered, the Board meets with the auditors without the participation of the company's management.

It is incumbent upon the Board to ensure that the guidelines for remuneration to senior executives approved by the Annual General Meeting are followed and that the Annual General Meeting proposes guidelines for remuneration to senior executives.

Each year, the Board's work is evaluated by way of discussions and through external assessment. The results of the evaluation are presented to the Board and Orexo's Nomination Committee and form the basis for proposals for Board members. In matters concerning ownership Orexo is represented by the Chairman of the Board.

During the year, the Board held 16 (14) meetings, of which 16 (14) were telephone conferences or meetings by circulation. The Board mainly addressed and resolved on issues concerning the company's strategic direction, the status of projects, the follow-up of financial performance, financing, investment matters, external reporting, budget planning and follow-up. These issues are addressed by the Board in its entirety.

Remuneration of the Board

The 2021 Annual General Meeting resolved that Board fees should amount to SEK 3,550,000, of which SEK 900,000 was to be paid to the Chairman of the Board, SEK 300,000 to each of the other Board members, and a total of SEK 400,000 to be divided among the members of the Audit Committee, so that the Chairman of the committee receives SEK 200,000 and the other committee members share SEK 200,000, and in total 150,000 to be allocated to the members of the remuneration committee in equal parts between the members of the committee. Further, the annual general meeting resolved on an additional board fee in accordance with the nomination committee's proposal to the board members James Noble, David Colpman, Kirsten Detrick, Fred Wilkinson, Mary Pat Christie and Charlotte Hansson of SEK 950,000, subject to (i) the board member's acquisition of shares in Orexo for the entire part (after taxes) of such additional board fee as soon as possible following the annual general meeting's resolution and the pay-out of the additional board fee, and (ii) the board member's commitment not to sell the shares during the board member's entire tenure on the Orexo board. The additional board fee is to be allocated as follows: SEK 450,000 to the chairman, corresponding to 50 percent of the ordinary board fee to the chairman, and SEK 100,000 to each of David Colpman, Kirsten Detrick, Fred Wilkinson, Mary Pat Christie and Charlotte Hansson, corresponding to 33 percent of the ordinary board fee to such board members. In the event that the board member, before the succeeding annual general meeting, is dismissed due to breach of his/her obligations as a board member or leaves the board at his/her own request, the board member must repay the entire additional board fee (after taxes).

Composition of the Board

Board members, their positions and whether or not they are considered to be independent in relation to Orexo, its management and the company's largest shareholders are stated in the table on page 104. Orexo's Board of Directors is deemed to have satisfied the requirements of the Code in respect of independence, as all members elected by the Meeting have been deemed to be independent in relation to Orexo and its management and all of these members, with the exception of one, have also been deemed to be independent in relation to the company's largest shareholders.

Audit Committee

Orexo's Audit Committee is primarily concerned with ensuring compliance with established principles for financial reporting and internal controls. The Audit Committee must also remain informed about the audit of the Annual Report and consolidated accounts, inspect and monitor the impartiality and independence of the auditor, paying particularly close attention to instances where the auditor provides the company with services outside the scope of the audit, and assist in the

preparation of proposals to the General Meeting in respect of auditor selection. The Audit Committee presents the final version of Orexo's interim reports and of the Annual Report to the Board for approval and publication. The Audit Committee meets prior to the publication of each interim report, in connection with the auditor's review of the internal control over the financial reporting and when otherwise necessary. The aforementioned issues are addressed by the Committee and the Board makes resolutions on the basis of the proposals produced. Orexo's auditor attends the meetings of the Audit Committee before the publishing of the interim reports and to present the outcome of the review of the internal control. Matters addressed in the Audit Committee is reported to the Board on a regular basis and the minutes are distributed to the Board.

During the year, the Audit Committee was convened on 4 (4) occasions. At least one of the members of the Committee must be independent in relation to the company and Executive Management, and also be independent in relation to the company's largest shareholders and have accounting or auditing expertise. The Committee is currently made up of Charlotte Hansson (Chairman), James Noble and Henrik Kjaer Hansen.

Remuneration Committee

The Remuneration Committee is tasked with addressing matters concerning salaries and other terms of employment, pension benefits and bonus systems, including any allocation of employee stock options and share awards under the terms of approved incentive programs for the President and the senior executives and managers, as well as remuneration issues of principle nature. The Committee shall meet as often as required. The above issues are addressed by the Committee and the Board makes resolutions on the basis of the proposals from the Committee.
The Committee should possess the required knowledge and expertise to deal with issues related to the remuneration of senior executives. The Remuneration Committee comprises James Noble (Chairman), David Colpman and Staffan Lindstrand. During the year, the Remuneration Committee was convened on 2 (4) occasions and managed other issues with written communication.

Evaluation of the Board's and President's work

The work of the Board, similar to that of the President, is evaluated annually in a systematic and structured process. The Nomination Committee is informed of the results of the evaluation.

Auditors

Orexo's auditors is the auditing firm EY, with Authorised Public Accountant Anna Svanberg as auditor in charge. At the Annual General Meeting 2021 EY was re-elected as auditors until the Annual General Meeting 2022. The external auditors discuss the external audit plan and risk management with the Audit Committee. The auditors perform a review of the interim report for the third quarter, and audit the annual accounts and consolidated financial statements. The auditors also express an opinion on whether this Corporate Governance Report has been prepared in accordance with, and whether certain disclosures herein are consistent with, the annual accounts and consolidated financial statements. The auditors report the results of their audit of the annual accounts and consolidated financial statements, their review of the Corporate Governance Report in the auditor's report, and a separate opinion on the Corporate Governance Report, in a presentation to the AGM. In addition, the auditors present detailed findings from their reviews to the Audit Committee three times per year, and to the Board in its entirety once per year.

For information regarding fees for the company's auditors, see Note 29.

President and the Management

The President leads the work of the Management Team and makes decision in consultation with them. At the end of 2021 the Management Team consisted of six persons in addition to the President. The Management Team hold regular meetings under the supervision of the President. For a more detailed description of the CEO and the management, see page 110.

Board of Directors' Report on Internal Control and Risk Management regarding Financial Reporting

The aim of Orexo's risk management systems and processes is to ensure that the shareholders can have the utmost confidence in the financial operation and presented reports, including the information given in this Annual Report and all interim reports. Orexo has established a methodology for developing, implementing, driving and evaluating internal controls and risk management in respect of all parts of the company, including financial reporting.

This methodology conforms to internationally established standards in the industry and comprises a framework with five principal components: control environment, risk assessment, control activities, information and communication, and follow-up and evaluation.

Control environment

Pursuant to the Swedish Companies Act, the Board of Directors is responsible for the internal control and governance of the company. To maintain and develop a functional control environment, the Board has implemented a process of risk mapping and established a number of basic control documents and procedures that are of importance to financial reporting. These include the formal work plan for the Board of Directors and the terms of reference for the President, which are reviewed and approved annually by the Board.

In addition, the control environment is continuously updated and secured by means of continuous monitoring and regular evaluations of risk profiles within various functions.

Responsibility for the daily work of maintaining the control environment is primarily incumbent on the President. He reports regularly to the Board of Directors and the Audit Committee pursuant to established procedures. In addition, the Board also receives regular reports directly from the company's auditor. Company managers have defined authorities, control functions and responsibilities within their respective areas for financial and internal controls.

Risk assessment

Orexo regularly conducts evaluations of financial risks and other risks that may impact financial reporting. These reviews extend to all parts of the company and are carried out to ensure that there is no significant risk of errors occurring in financial reporting. There are several areas where the control of financial information is particularly important, and Orexo has established a risk map that highlights a number of key potential risks in the financial reporting system.

The company continuously monitors and evaluates these areas and regularly examines other areas in order to create a set of control procedures that will minimize the risks and impact in these areas. In addition, new and existing risks are identified, addressed and regulated through a process of discussion in forums such as the Management Team, The Board of Directors and Audit Committee.

Control activities

In light of the risks identified on the risk map, and the continuous monitoring of the methods used to manage financial information, Orexo has developed control activities that ensure good internal control of all aspects of financial reporting. A number of policy documents and procedures have been applied throughout the year to manage reporting and accounting. Standard procedures, attestation systems, financial guidelines and the risk map are examples of such policy documents.

The finance and controller functions are responsible for ensuring that financial reporting is correct, complete and timely. Orexo strives to continually improve its internal control systems and has, on occasion, engaged external specialists when validating these controls.

Information and communication

Orexo is a listed company in one of the most regulated markets in the world – healthcare. In addition to the highly exacting requirements that Nasdaq Stockholm and the supervisory authorities impose on the scope and accuracy of information, Orexo also employs internal information and communication control functions designed to ensure that correct financial and other corporate information is communicated to employees and other stakeholders.

The Board receives monthly reports concerning financial performance, commercial performance and the status of Orexo's development projects and other relevant information.

The corporate intranet provides detailed information about applicable procedures in all parts of the company and describes the control functions and how they are implemented.

The security of all information that may affect the market value of the company and mechanisms to ensure that such information is communicated in a correct and timely fashion are the cornerstones of the company's undertaking as a listed company. These two factors, and the procedures for managing them, ensure that financial reports are received by all players in the financial market at the same time, and that they provide an accurate presentation of the company's financial position and performance. These procedures are continuously updated to secure compliance with the EU Market Abuse Regulation (MAR).

Follow-up

Orexo's management conducts bi-weekly performance follow-up, with an analysis of deviations from the budget and plans. Orexo's controller function also conducts monthly controls, evaluations and follow-ups of financial reporting. Because much of the company's product development is carried out in project form, this is followed up on a continuous basis from a financial perspective. Routines and reporting is implemented to secure continuous follow-up on all aspects of the ZUBSOLV® business, e.g. manufacturing, sales performance, wholesaler orders, sales force performance, inventory levels etc. The Board of Directors and the Audit Committee review the Annual Report and interim reports prior to publication. The Audit Committee discusses special accounting policies, internal control framework, risks and other issues associated with the reports. The company's external auditor also participates in these discussions.

Internal audit

Orexo has no separate internal audit function. The Board annually evaluates the need for such a function and, considering the size and structure of the company, has found no basis for establishing a separate internal audit function. The Board of Directors monitors the internal control over financial reporting through regular follow-ups by the Audit Committee and the Board.

Further information about Orexo's corporate governance

The following information is available at www.orexo.se (in Swedish) and www.orexo.com (in English):

- Articles of Association
- Information about the Swedish Code of Corporate Governance
- Information from General Meetings of previous years
- Information from the Nomination Committee
- Information about remuneration principles for senior executives
- Corporate governance reports from 2009 onwards
- Information for the 2022 Annual General Meeting (convening notice, Nomination Committee proposals, presentation of the work of the Nomination Committee, etc.).

Board of directors

James Noble

Chairman of the Board of directors since 2020.
M.A. from the University of Oxford.

Other assignments
Board member of Adaptimmune and Chairman of the Board of two private UK-based cancer research companies

Previous experience
Co-founder and CEO of Adaptimmune and Immunocore. Board member and Deputy Chairman of GW Pharmaceuticals until its acquisition by Jazz Pharmaceuticals. Chairman and CEO of Avidex, which was acquired by Medigene. Other positions as Board member include companies, such as Medigene, PowderJect Pharmaceuticals and CuraGen Corporation.

Holdings 2021
9,500 shares, and bonds of a nominal value of SEK 2,500,000.

Staffan Lindstrand

Board member since 2002.
M.Sc. in Engineering.

Other assignments
Partner of HealthCap since 1997, Board member of HealthCap AB, Doctrin AB, Elsa Science AB, GET.ON Institut für Online Gesundheitstrainings GmbH, and The Swedish Association of Exchange-listed companies.

Previous experience
Ten years in investment banking.

Holdings 2021
881 shares.

Charlotte Hansson

Board member since 2020.
MSc. in Business Administration from Handelshögskolan at the University of Gothenburg.

Other assignments
CFO at Tele 2 AB.

Previous experience
CFO at Systembolaget AB, CFO & Executive VP at Cision AB, CFO at Addici AB and various positions within business controlling at Modern Times Group.

Holdings 2021
2,500 shares.

Henrik Kjaer Hansen

Board member since 2018.
BSc. in Business Administration and a MSc. in Applied Economic and Finance at Copenhagen Business School.

Other assignments
Senior Director, Principal Investments, Novo Holdings A/S. Board member of Xellia Pharmaceutical.

Previous experience
Senior Vice President in Moelis & Co. in London, focusing on healthcare M&A transactions. Other previous employments include Deutsche Bank and ABN AMRO, all in London.

Holdings 2021
Does not hold any shares. Dependent in relation to major shareholders in the company.

David Colpman

Board member since 2015.
B.Sc. Pharmacy.

Other assignments
Director of Colpman Consulting Ltd. Member of the Royal Pharmaceutical Society. Board member of HRA Pharma and Forendo Pharma Ltd.

Previous experience
Head of Global Business Development 2012–2014, Senior Vice President of Business Development at Shire plc 1999–2012. Various business development and commercial positions at Glaxo Wellcome, Novo Nordisk and Boots Pharmaceuticals.

Holdings 2021
4,379 shares.

Kirsten Detrick

Board member since 2016.
MBA.

Other assignments
Managing Director at Takeda Austria GmbH and Takeda Osteuropa Holding GmbH.

Previous experience:
Vice President Global Marketing, Therapeutic Area Commercial Lead – GI at Takeda Pharmaceuticals, Executive Director positions within US as well as Global Marketing and Commercialization at Amgen Inc. 2004–2013, Various marketing and commercial positions at Bristol-Myers Squibb 1991–2004. Former member of the Board of Southern California Biomedical Council and member of Healthcare Businesswomen's Association.

Holdings 2021
1,500 American Depository Receipts, listed in USD.

Mary Pat Christie

Board member since 2019.
MBA.

Other assignments
Board member of Hackensack Meridian Health's Carrier Clinic and Restaurant Technologies.

Previous experience
Managing Director at Angelo Gordon & Co., where she focused on business development of new fund strategies and new strategic alliances. Prior to that at Cantor Fitzgerald as an Institutional Salesperson and was an original partner at the Seaport Group. Christie was also the founder of Mendham Capital Management. Her career also includes high level roles at JP Morgan, Donaldson, Lufkin & Jenrette, and Fleet Bank.

Holdings 2021
1,150 American Depository Receipts, listed in USD.

Fred Wilkinson

Board member since 2019.
MBA., B.Sc. Pharmacy.

Other assignments
Board member of Alter Pharma Group.

Previous experience
Chief Executive Officer and Board member of Impax Laboratories, Inc., President of the Specialty business at Watson Pharmaceuticals, Inc. (currently Allergan), President of Duramed Pharmaceuticals, Inc., Chief Executive Officer of Columbia Laboratories, and multiple positions at Sandoz Pharmaceutical Corporation, Inc.

Holdings 2021
2,100 American Depository Receipts, listed in USD.

Management

Nikolaj Sørensen

President and CEO since 2013.
B.Sc., and M.Sc., Copenhagen Business School, Denmark.

Other assignments
Member of the Board, Bioservo Technologies AB and Moberg Pharma AB.

Previous experience
Senior management positions at Pfizer Inc. with a focus on commercialization in Europe and Chairman of the Board and Managing Director at Pfizer AB. Prior to Pfizer management consultant at Boston Consulting Group (BCG), leading several projects within M&A, commercial transformation, and turn-arounds.

Holdings 2021
88,865 shares and stock options/share awards entitling to 192,960 shares.

Joseph DeFeo

EVP and Chief Financial Officer since 2018.
B.Sc. in accounting. Clarion University, US, and a MBA in finance, St. Joseph's University, US.

Previous experience
Vice President, Finance & Administration at Orexo US Inc., 2013–2017. Prior to joining Orexo, Head of International Treasury and led finance for the commercial operations in the US for two major pharmaceutical companies.

Holdings 2021
4,969 shares and stock options/share awards entitling to 99,032 shares.

Robert Rönn

SVP and Head of R&D since 2019.
MSc in Chemical Engineering and PhD in Medicinal Chemistry, Uppsala University, Sweden.

Previous experience
Head of Pharmaceutical Development & IP at Orexo AB since 2016 and prior to that extensive experience of drug discovery and development, as well as patent prosecution and litigation, from various key positions at Biolipox AB and Orexo AB.

Holdings 2021
2,805 shares and stock options/share awards entitling to 70,922 shares.

Robert A. DeLuca

President of Orexo US Inc. since 2013.
R. Ph.

Other assignments
Member of the St. John's College of Pharmacy Dean's Advisory Board, American Society of Addiction Medicine, Academy of Managed Care Pharmacy and the American and New Jersey Pharmacists Associations.

Previous experience
Extensive experience establishing commercial operations in the US with a combined background in market access, marketing, and sales. Has held leadership positions at multinational pharmaceutical companies including Sanofi-Aventis, Schering Plough, Berlex and Pharmacia, and most recently served as Chief Commercial Officer at Archimedes Pharmaceuticals.

Holdings 2021
8,586 shares and stock options/share awards entitling to 99,854 shares.

Dennis Urbaniak

EVP Digital Therapeutics since 2019.
Monmouth University, US, BS Business Administration/ Marketing/English.

Other assignments
Member of HIMSS[1]

Previous experience
Chief Digital Officer, Havas Health & You, Chief Executive Officer, Havas Health Plus. Prior to Havas Health & You, Managing Director Accenture Digital Life Sciences Analytics and Janssen Client Account Lead. Before joining Accenture, twenty years at Sanofi in various sales and marketing roles.

Holdings 2021
10,000 shares and stock options/share awards entitling to 84,700 shares.

Cecilia Coupland

SVP and Head of Operations since 2019.
MSc in Chemical Engineering, Uppsala University, Sweden.

Previous experience
Head of Supply Chain & Planning at Orexo since 2014 and prior to that extensive experience of global pharmaceutical manufacturing and supply chain management, as well as drug development and project management, from various key positions at AstraZeneca and Orexo AB.

Holdings 2021
4,419 shares and stock options/share awards entitling to 71,410 shares.

Michael Sumner

Chief Medical Officer since 2013.
MB BS, MRCP (UK), MBA.

Other assignments
Scientific Advisory Board FirstString Research Inc.

Previous experience
Extensive experience within the pharmaceutical industry from Novartis Pharmaceuticals, Aventis Behring, Novo Nordisk and prior to joining Orexo held the position of Vice President Clinical and Medical Affairs at Shire.

Holdings 2021
29,120 shares and stock options/share awards entitling to 78,792 shares.

[1] Healthcare Information and Management Systems Society.

Auditor's report on the corporate governance report

To the general meeting of the shareholders of Orexo AB,
corporate identity number 556500-0600.

Engagement and responsibility

It is the Board of Directors who is responsible for the corporate governance statement for the year 2021 on pages 101–112 and that it has been prepared in accordance with the Annual Accounts Act.

The scope of the audit

Our examination has been conducted in accordance with FAR's auditing standard RevU 16 *The auditor's examination of the corporate governance statement*. This means that our examination of the corporate governance statement is different and substantially less in scope than an audit conducted in accordance with International Standards on Auditing and generally accepted auditing standards in Sweden. We believe that the examination has provided us with sufficient basis for our opinions.

Opinions

A corporate governance statement has been prepared. Disclosures in accordance with chapter 6 section 6 the second paragraph points 2–6 the Annual Accounts Act and chapter 7 section 31 the second paragraph the same law are consistent with the annual accounts and the consolidated accounts and are in accordance with the Annual Accounts Act.

Stockholm, Sweden, March 30, 2022
Ernst & Young AB

Anna Svanberg
Authorized Public Accountant

Shareholder information

2022 Annual General Meeting

The Annual General Meeting (AGM) of Orexo AB will be held on Thursday, April 21, 2022 16.00 CET at Rapsgatan 7E in Uppsala, Sweden.

Orexo's Nomination Committee for the AGM 2022

Prior to the AGM in 2022, Orexo has appointed a Nomination Committee which represents approximately 38 percent of the number of votes in the company as of September 30, 2021.

The Nomination Committee comprises:

- Christian Salling, Novo Holdings A/S, also Chairman of the Nomination Committee
- Claus Berner Møller, ATP
- Patrik Walldov, representative for Anders Walldov (incl. indirect holding via Brohuvudet AB)
- James Noble, Chairman of the Board of Orexo.

The Nomination Committee will prepare proposals to the AGM regarding Chairman of the Meeting, Chairman of the Board, Board members, Board member fees, any remuneration for committee work, and fees to the auditor, as well as principles for the composition of the Nomination Committee.

The Nomination Committee's proposals are presented in the Notice of the AGM and on Orexo's website, https://orexo.com/about-us/corporate-governance/

Registration, advance voting etc.

Shareholders who wish to participate in the meeting must be recorded in the share register maintained by Euroclear Sweden AB on April 11, 2022, and notify Orexo of their intention to attend the meeting not later than April 13, 2022, by post to Orexo AB, P.O. Box 303, SE 751 05 Uppsala, Sweden, by telephone +46 (0) 18 780 88 00, or by e-mail to lena.wange@orexo.com.

The notification shall set forth the name, personal/corporate identity number, the number of shares held, telephone number (daytime) and, where applicable, number of assistants (not more than two) that the shareholder intends to bring to the meeting. Shareholders to be represented by proxy should submit a power of attorney (original document) and a certificate of registration or equivalent together with the notification of attendance. A proxy form is available at www.orexo.com.

Shareholders whose shares are registered in the name of a nominee/custodian must temporarily re-register their shares in their own names to be entitled to participate in the meeting. Shareholders must inform their nominee/custodian of such reregistration well before April 13, 2022, by which date such re-registration must have been executed.

Full information about the AGM can be found on the company's website, https://orexo.com/about-us/corporate-governance/

Contact Investor Relations
+46 (0)18 780 88 00
ir@orexo.com or
lena.wange@orexo.com

Financial Calendar 2022

2022 Annual General Meeting	April 21, 2022
Interim Report Q1 2022	April 28, 2022
Interim Report Q2 2022	Juli 14, 2022
Interim Report Q3 2022	November 3, 2022
Full Year Report 2022, incl. Q4	January 26, 2023

Glossary

Abbreviated New Drug Application, ANDA
An Abbreviated New Drug Application (ANDA) is an application for a US generic drug approval for an existing licensed medication or approved drug.

American Depositary Receipt, ADR
An instrument that is issued by a depositary bank that represents ownership of a company's underlying shares. ADR programs are created to facilitate US investors to hold shares in non-US companies and trade them in the same way as US securities.

Artificial intelligence, AI
Artificial intelligence (AI) is the simulation of human intelligence processes by machines, especially computer systems.

AUD
Abbreviation of Alcohol Use Disorder

B2C
Abbreviation of Business to Consumer

B2B
Abbreviation of Business to Business

Breakthrough pain
A short, intensive period of pain that occurs in addition to chronic levels of long-term pain even though these are treated by regular painkillers.

Broca®
GAIA's proprietary intelligence system, based on artificial intelligence, underpins the development of digital therapies targeting multiple therapy areas.

Buprenorphine
A potent opioid partial agonist first used as a pain-relieving substance, but now most commonly used to help patients withdraw from more addictive opioid drugs such as morphine.

Cash payer segment
One of three payer segments in the US market for treatment of opioid dependence. In this segment, the patient is paying for the prescriptions out of pocket.

Clinical studies/Clinical trials
Studies of the safety and efficacy of a drug in human beings.

Cognitive behavioral therapy techniques, CBT
Cognitive behavioral therapy techniques, CBT are used to alter mal- adaptive thought patterns. The cognitive behavioral therapy is used in the treatment of various disorders related to mood, personality, anxiety, substance abuse, etc.

Commercial payer segment
One of three payer segments in the US market for treatment of opioid dependence. The commercial segment is funded by private insurances or employers.

CMO
Abbreviation of Contract Manufacturing Organisation

Digital health
Digital health is the convergence of digital technologies with health and healthcare to enhance the efficiency of healthcare delivery and make medicine more personalized and precise.

Digital therapeutics, DTx
Digital therapeutics, a subset of digital health, are evidence-based therapeutic interventions driven by high quality software programs to prevent, manage, or treat a medical disorder or disease.

Drug delivery
The process through which a pharmaceutical may be introduced to the patient that enables the active compound to function as intended.

Food and Drug Administration, FDA
The United States Food and Drug Administration is a federal agency of the Department of Health and Human Services, HHS. The FDA is responsible for protecting and promoting public health through the control and supervision of food safety, tobacco products, pharmaceuticals and other medicinal products.

IP
Abbreviation of Intellectual Properties.

Ketorolac
Ketorolac is a nonsteroidal anti-inflammatory drug (NSAID) used to treat moderate to severe pain.

Medication assisted treatment, MAT
Medication assisted treatment (MAT) is the use of medications, in combination with counseling and behavioral therapies, to provide a "whole-patient" approach to the treatment of substance use disorders.

Naloxone
An opioid antagonist used to counter the effects of opioids.

New Drug Application, NDA
The NDA application is the vehicle through which drug sponsors formally propose that the FDA approve a new pharmaceutical for sale and marketing in the US.

Non-steroidal anti-inflammatory drugs, NSAIDs
Non-steroidal anti-inflammatory drugs which are active against pain, inflammation and fever.

Open market
ZUBSOLV's total business where the pharmaceutical is reimbursed and competes with other products in the market both branded and/or generics. Open formulary business excludes recent formulary changes in United Health Group and Humana, the cash payer segment, and payers where it is not reimbursed.

Opioids
Collective term for compounds that act via opioid receptors on nerve cells, mainly in the central nervous system.

OUD
Abbreviation of Opioid Use Disorder

Pharmacokinetic study, PK study
A clinical study investigating the absorption, distribution, metabolism and elimination of a drug by the body. Pharmacokinetics (PK) is the study of how an organism affects a drug, whereas pharmacodynamics (PD) is the study of how the drug affects the organism. Both together influence dosing, benefit, and adverse effects, as seen in PK/PD models.

Preclinical development/Preclinical studies
Studies of the safety and efficacy of a drug prior to evaluation in humans. Can be performed on animals and in various cell systems.

Proof of Concept studies
A Proof of Concept study is performed to get a first indication of an idea's practical feasibility.

Public payer segment
One of three payer segments in the US market for treatment of opioid dependence. The public segment covers state and federal funded reimbursement programs i.e. Managed Medicaid, FFS Medicaid, Medicare Part D.

Randomized controlled trial, RCT
A randomized controlled trial, RCT is a clinical trial aims to reduce certain sources of bias when testing the effectiveness of new treatments; this is accomplished by randomly allocating subjects, treating them differently, and then comparing them with respect to a measured response.

Reimbursement
Contribution from the state or insurance company in order to reduce the price of drugs / treatment for the patient.

Rest of World, RoW
Rest of World, RoW refers to countries or territories other than United States (US) and European countries (EU).

Sublingual
Under the tongue

SUD
Abbreviation of Substance Use Disorder

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 main market today is the American market for buprenorphine/naloxone products, where Orexo commercializes its lead product ZUBSOLV for treatment of opioid use disorder. Total net sales for 2021 amounted to SEK 565 million and the number of employees was 121. 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.

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

Production Solberg, photo by Jenny Lagerqvist on page 6, 11, 21, 29, 31, 37, 39, 41, 62, and 101.