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Develops improved pharmaceuticals and digital therapies addressing unmet needs within the growing space of substance use disorders and mental health

# Stockholm Corporate Finance 13th Life Science Seminar - March 23rd 2021

Nasdaq Stockholm: ORX US OTC Market: ORXOY (ADR)

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# Orexo in brief

- Developed **four commercial pharmaceutical products** with worldwide approval
- Addresses **unmet needs** within the growing space of **mental illness** and **addiction disorders**
- Broad product portfolio and development pipeline of traditional **pharma products** and **digital therapies**
- Strategic focus on **portfolio expansion** through development and licensing/M&A
- **Strong financial position** enables investment in future growth
- Top two largest shareholders[1]: **Novo Holdings** (27.8%) and **HealthCap** (10.2%)

**Corporate Headquarters**

(Uppsala, Sweden)
Corporate functions and Development

**US Commercial Platform**

Since 2013 direct presence in the US with a fully-owned sales force covering nearly all states

| Net revenues 2020 | EBITDA 2020 | Cash position 2020 |
|---|---|---|
| SEK 664 m | SEK 19 m | SEK 505 m |

[1] As of December 31, 2020
[2] Last Twleve Months

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# Strategic agenda to drive long-term growth

## Broadening…

…the portfolio of commercial products to be promoted by our US Pharma and Digital Therapeutics businesses

## Establishing…

…. a new revenue generating business area within DTx with three revenue generating products in the US market in 2021


## Maintaining…

.. ZUBSOLV® profit contribution and ensure it is sustainable and growing over time

## Launching…

….OX124, opioid overdose rescue medication in the US

# Products approved worldwide & pipeline of potential future assets

## Pharmaceuticals

| Product/ Project | Exploratory | Preclinical | Phase 1 | Phase 2 | Phase 3 | Registration | Approved and/or Launched US | Approved and/or Launched EU | Approved and/or Launched RoW |
|---|---|---|---|---|---|---|---|---|---|
| **ZUBSOLV®** Opioid Use Disorder<br>Partner: Accord Healthcare (EU market) | | | | | | | | | ▲ |
| **Abstral®** Breaktrough Cancer Pain<br>Partner: Kyowa Kirin (RoW) | | | | | | | | | |
| **Edluar®** Insomnia<br>Partner: Mylan (US & EU) | | | | | | | | | |
| **OX124** Naloxone, Opioid Overdose | | | | | | | | | |
| **OX125** Nalmefene, Opioid Overdose | | | | | | | | | |
| **OX338** Ketorolac, Moderate to moderately severe pain | | | | | | | | | |
| **OX-MPI** BI1029539, Microvascular Disease<br>Partner: Gesynta Pharma | | | | | | | | | |

▲ Approved in Australia

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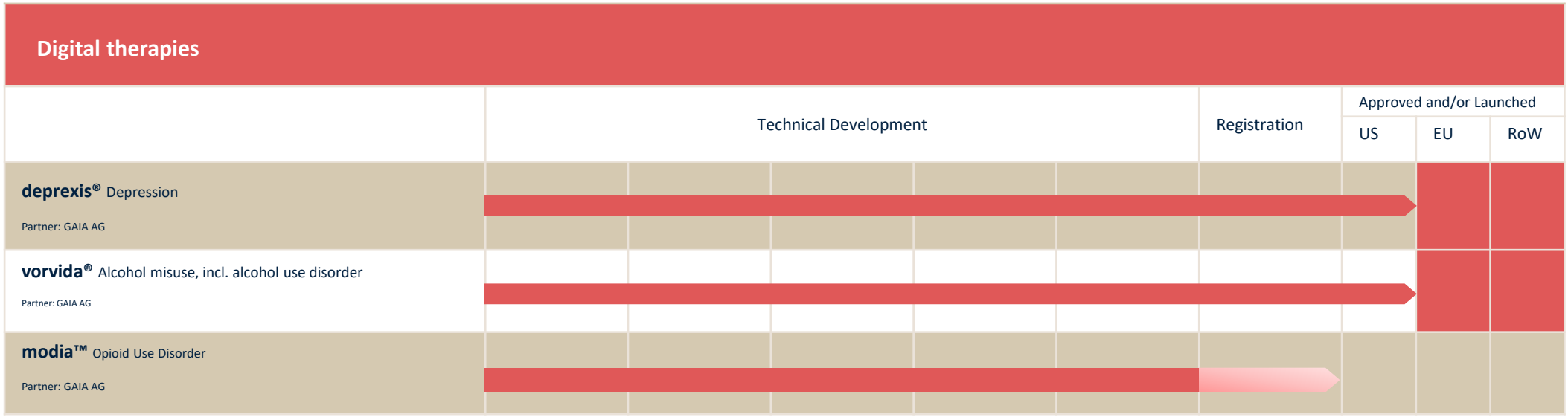
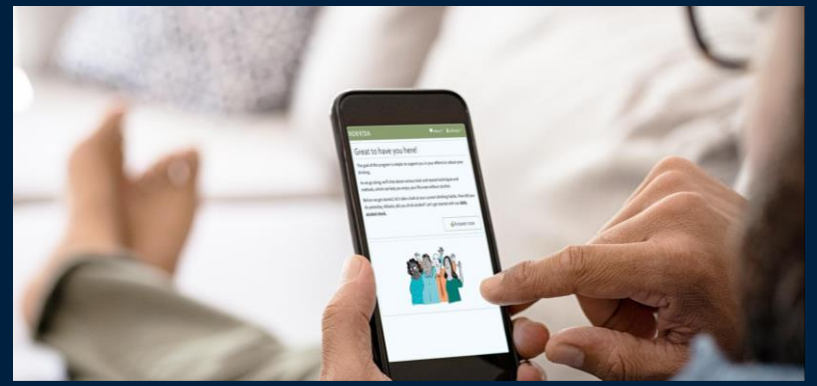
# Digital therapeutics to become an integral part of the healthcare landscape

SUD and mental health issues are one of the main areas most in need of innovative ways to deliver treatment



# ZUBSOLV® - stable and strong EBIT, despite challenging market due to Covid-19

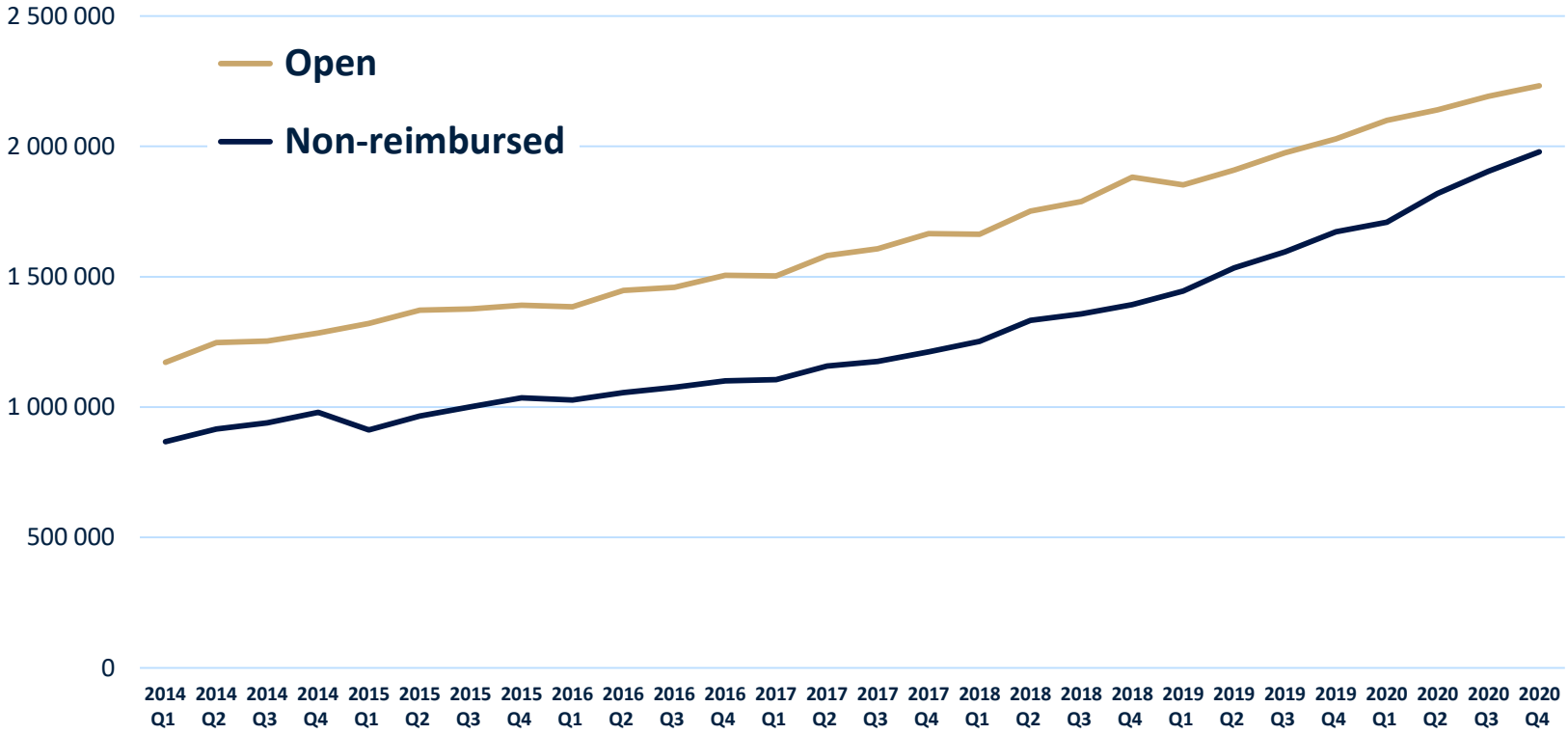
zubsolv® sublingual tablets
(buprenorphine and naloxone) CIII



# 2020 market volume showed strongest growth rate since ZUBSOLV® launch

New market definitions applied by Orexo

**Market Volume Sales,** Quarterly NTRx




**Q4 2020 vs Q4 2019 Growth**

Total Market: +13%

**By Segment**

+10%

**+18%**

**Definitions**

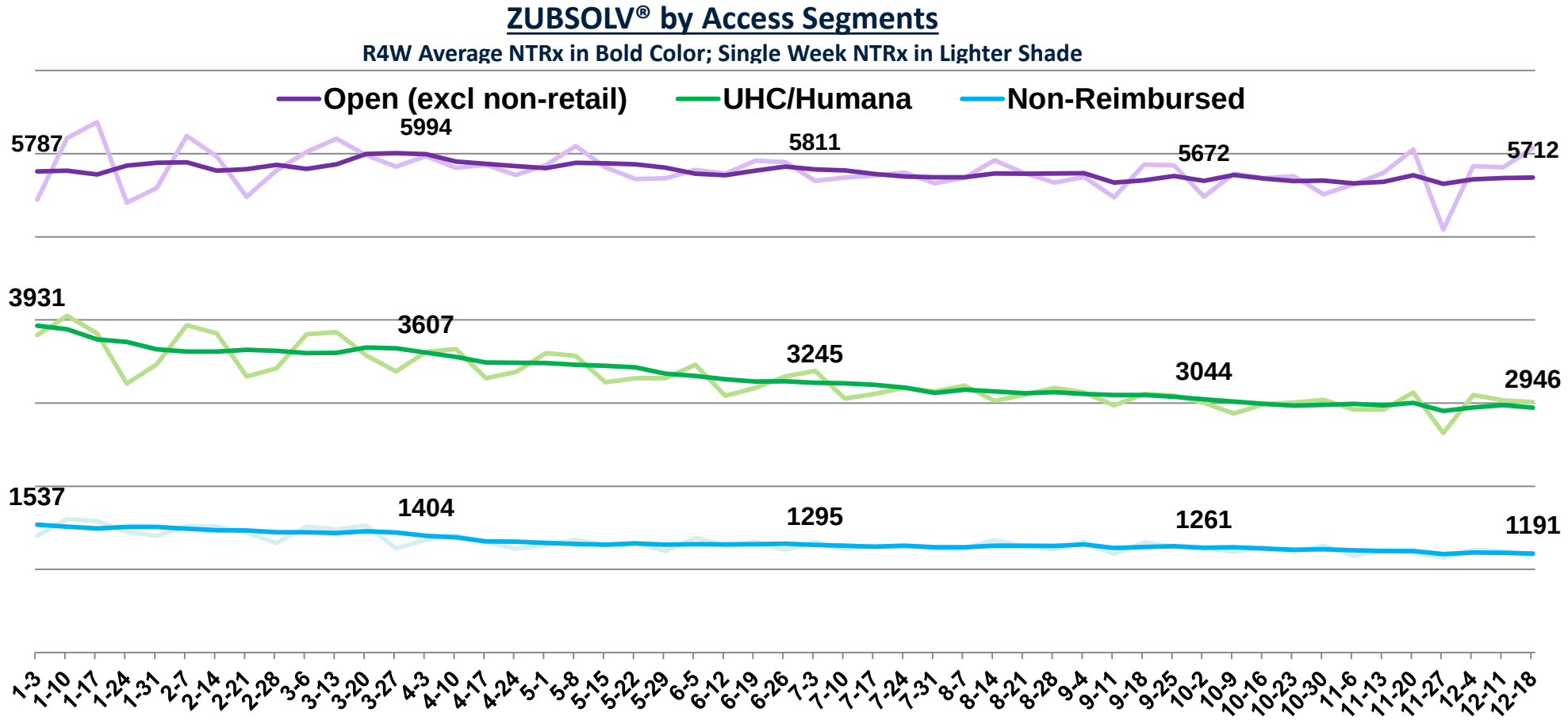
Payers / Market Access

- **"Open"**
  - Market segments where ZUBSOLV® is currently reimbursed either exclusively or non-exclusively
- **"Non-Reimbursed"**
  - Market segments where ZUBSOLV® is currently not reimbursed

Note: NTRx =Total prescriptions adjusted to 30 tablet/film scripts
Note: Historical figures may slightly vary due to IQVIA recategorization
Source: IQVIA XPO

# Open segment resilient throughout 2020 despite market challenges

UHC/Humana continue to decline, but the decline is fading during Q4




Source: IMS XPO
NTRx =Total prescriptions adjusted to 30 tablet/film scripts
Open: Market segments where ZUBSOLV®® is reimbursed either exclusively or non-exclusively
Note: Historical figures may slightly vary due to IQVIA recategorization
Non-Reimbursed: Market segments where Zubsolv® is not reimbursed

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# Several possible triggers for ZUBSOLV® growth in 2021

**Continued improvement in ZUBSOLV® market access**

…ESI & Cigna have now listed ZUBSOLV® as the only preferred branded product on their Commercial and Medicare formularies.

…Commercial access increased to 99%

**Strong bi-partisan support to increase access to MAT**

… The former US administration recently paved the way for all US physicians to prescribe medical-assisted treatment(MAT) for opioid dependence

…such a change will likely drive sustained strong market growth

…the opioid crisis will remain a key priority for the new Administration

**Orexo Sales Force office access gradually improving**

…Q4 2020 has had better office access than Q3 2020 and should continue to improve in 2021 as restrictions begin to ease post-vaccine roll out

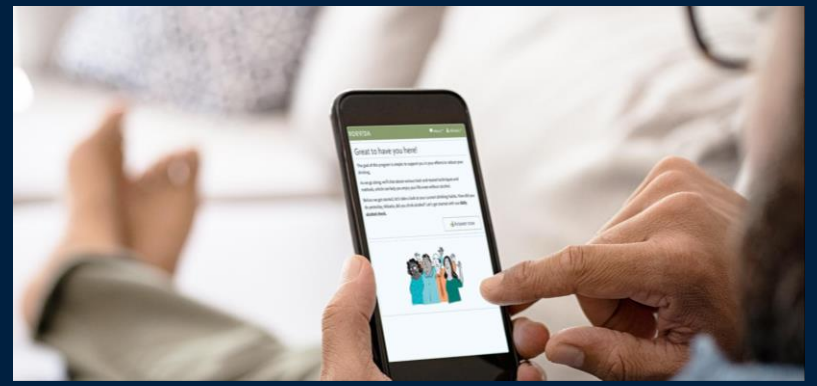
…Orexo to continue to develop new selling methods to overcome barriers

**DTx offer new customer value proposition and synergies**

…sales meetings including vorvida® get significantly more time from health care providers

…modia™ will provide patients, physicians and payers with a complete offering of both medication and psychological support

# OX124 - overdose rescue medication, on track to file mid-2022




# OX124 - a new stronger rescue medication with naloxone

Expected launch in the US in 2023

## The unmet need

Available rescue medications have been developed for heroin overdoses, but most patients are dying from synthetic opioids like fentanyl today

## Our aim

A rescue medication that is stronger and longer-acting, and thus effective in reversing overdoses caused by synthetic opioids

## The potential

**70-110** million USD net sales (US market)

# OX124 will enter a >USD 300 million market

## Recent market development

- **Covid-19 making the unmet need even more severe**:
  - According to estimated numbers 83,000 Americans died of an overdose in 2020, an increase of 21 percent[1]
  - Synthetic opioids are now representing 76 percent of opioid related deaths[1]
- **US market leader Narcan® sales at record level[2]**:
  - USD 311 m for the full year of 2020, YoY increase of 11 percent
  - 2021 guidance: USD 305-325 m
  - Co-prescription legislation and standing orders at pharmacys will fuel growth going forward
- **New FDA requirements increase hurdle for new entrants**:
  - Competitor with high dose auto-injector received complete response letter and other competitors appear to be delayed

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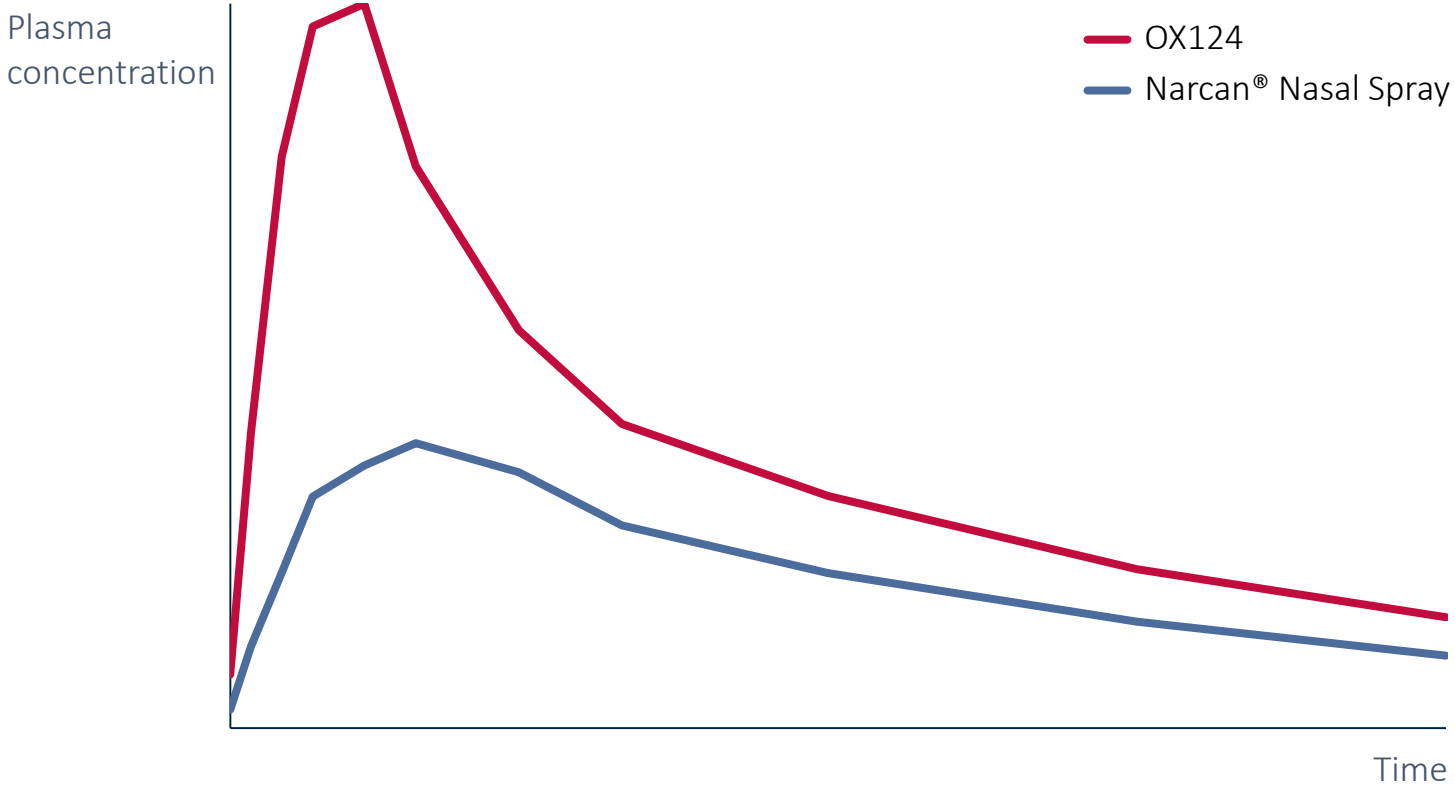
[1] June 2019 – June 2020 vs. June 2018 – June 2019 (https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm#dashboard)
[2] Emergent BioSolutions

# OX124 has shown better PK profile than Narcan® Nasal Spray

## Faster, stronger and longer-acting vs Narcan® Nasal Spray

Results from exploratory PK study in healthy volunteers, 2019




## Expected patient benefit

- Rescue more patients with the first dose (~34% of overdose patients require more than one dose of Narcan)
- Avoid ”second overdoses” thanks to longer duration (Fentanyl has a half life of 8-10 hours vs. 2 hours for naloxone)

# Strong progress with the aim to launch in the US in 2023

| Q4 progress | 2021-2022 |
| --- | --- |
| ✓ Established the full commercial supply chain of both devices and the API (Naloxone) | Q2-Q3 Perform the pivotal bridging study |
| ✓ Received positive feedback from FDA on the investigational new drug (IND) application | Mid-22 File the New Drug Application with FDA* |
| ✓ Improved IP protection | '23 Launch in the US* |

* Assumes Fast Track Designation, without fast track designation, the filing will be delayed 6 months

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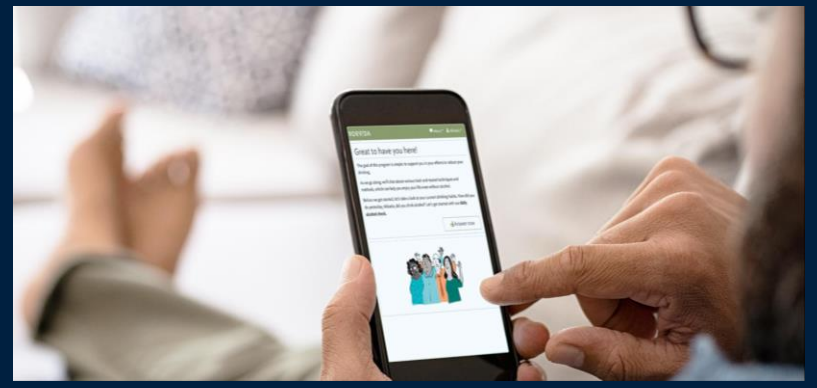
# Digital Therapeutics - expanding the commercialization model

VORV!DA®

deprexis®

modia



# With 3 digital therapies, Orexo is well positioned to take a leading role addressing unmet needs within SUD and mental health issues

## deprexis®

deprexis® is a fully automated digital therapy to help patients manage their symptoms of mild to severe depression with extensive clinical evidence

**> 150-225**
MUSD net sales potential in the US

## vorvida®

A fully automated digital therapy scientifically proven to reduce troublesome drinking patterns in adults suffering from alcohol misuse incl. alcohol use disorder (AUD)

**120-200**
MUSD net sales potential in the US

## OXD01/modia™

"Digitizing" counselling at scale to offer with ZUBSOLV®, a full medication assisted therapy (MAT) solution for opioid use disorder (OUD) patients in need

**150-225**
MUSD net sales potential in the US

# Digital therapeutics is in its infancy - while the potential is significant, several hurdles need to be addressed before the market takes off

**Commercialization**
- Optimal pathways to commercialize and scale DTx are still unchartered

**Reimbursement**
- Many payors still to establish payment and reimbursement processes

**Pricing**
- Entry barriers are low for offerings without clinical evidence, and thus payors need to establish appropriate assessment criteria to enable price differentiation

**Disruptive technology**
- While digital therapies have been proven clinically, speed of adoption is still unknown as for any new therapeutic approach

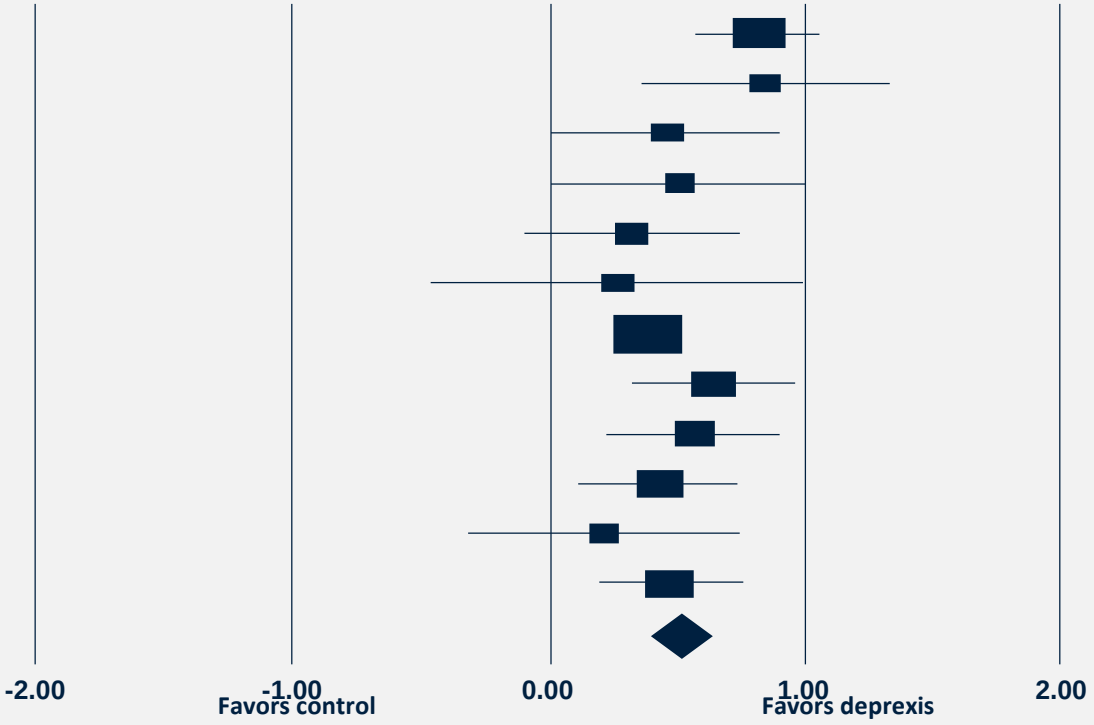
**Orexo will continue to assess the business model, the potential and the investment levels required to capture new opportunities at the appropriate time**

# Clinical evidence is critical for DTx to gain traction in health care

## deprexis® demonstrates consistent clinical effect across multiple settings

Meta-analysis of 12 RCTs demonstrated the effectiveness of deprexis for reducing depressive symptoms with a moderate effect size ($g$ = 0.51, 95% CI: 0.40–0.62) and low heterogeneity ($I^2$= 26 %)

| | Study Statistics | | | | Sample Size | |
|---|---|---|---|---|---|---|
| **Study** | **Hedge's *g*** | **LL** | **UL** | ***p*-value** | **Control** | **Deprexis** |
| Beevers (2016) | 0.81 | 0.57 | 1.06 | 0.00 | 91 | 285 |
| Berger (2011) | 0.84 | 0.36 | 1.33 | 0.00 | 26 | 50 |
| Berger (2018) | 0.46 | 0.02 | 0.90 | 0.04 | 47 | 51 |
| Bücker (2018) | 0.51 | -0.01 | 1.02 | 0.06 | 69 | 71 |
| Fischer (2015) | 0.32 | -0.09 | 0.74 | 0.12 | 45 | 45 |
| Fuhr (2018) | 0.27 | -0.47 | 1.00 | 0.48 | 13 | 14 |
| Klein (2016) | 0.39 | 0.26 | 0.51 | 0.00 | 504 | 509 |
| Meyer (2009) | 0.64 | 0.33 | 0.94 | 0.00 | 76 | 320 |
| Meyer (2015) | 0.57 | 0.22 | 0.91 | 0.00 | 85 | 78 |
| Moritz (2012) | 0.43 | 0.13 | 0.73 | 0.01 | 105 | 105 |
| Schröder (2014) | 0.22 | -0.30 | 0.73 | 0.41 | 40 | 38 |
| Zwerenz (2017) | 0.47 | 0.20 | 0.74 | 0.00 | 110 | 109 |
| **OVERALL** | **0.51** | **0.40** | **0.62** | **0.00** | **1108** | **1409** |




Twomey C, et al. PLoS One. 2020; 30;15(1): e0228100.

# Agreement with Magellan Rx Management to complete a Real World Evidence study of modia™ is a major step forward for Orexo

**Magellan is a leading US payer**

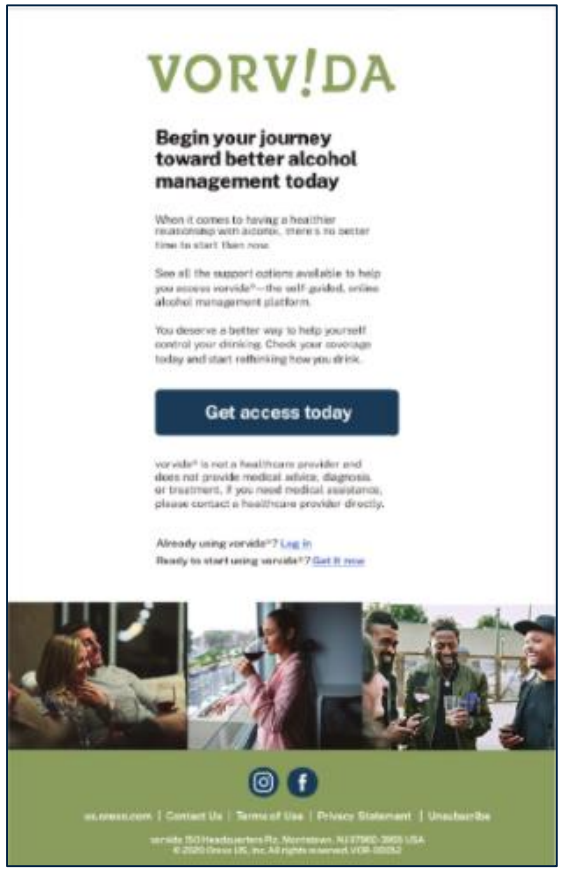
- **Behavioral Health Management & Specialty Health Solutions covers 49.9 million lives**
- **The leading payer in Medicaid in the US, both in total number of lives and in Medication Assisted Treatment (MAT i.e. buprenorphine)**
- **Third largest payer in MAT (after CVS Caremark and Express Script)**
- **Magellan has already included two insurance companies in the RWE study**
- **Announcement of the RWE study reached 39M readers**

**Magellan and ApexB.io will work with Orexo to define a study meeting the requirements of payers in the US**

- Study end-points will be defined in collaboration between the parties
- Magellan will leverage network to payers to provide insights into information required to cover DTx and to general issues and concerns with regards to DTx
  - Together with plan structure, clinical outcome data, lack of RWE is the leading concern

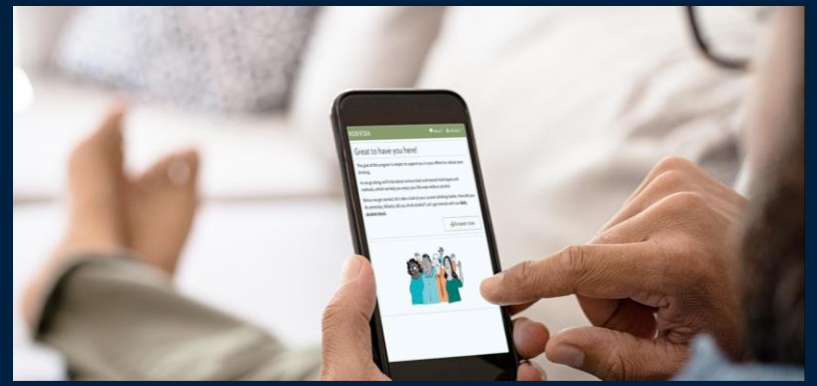
1 Abbreviated New Drug Application

# High expectations to 2021 for the Digital Therapeutics business




- Piloting of reimbursement pathways and commercialization concepts continues during Q1
- With positive outcome, Orexo's financial strength enables rapid acceleration of commercial efforts
- Partnership with larger health care providers anticipated with positive outcome of pilot testing reimbursement pathways
- Expectations to announce partnership with payers for either reimbursement or pilot programs to test one or more of the products in real world settings during Q1
- Positive experience with Trinity Health as an employer has triggered increased focus on large employers in the US and partnership with employers is expected to be announced during Q1 or early Q2

# Financial information




# 2020 – A transformative year building for future growth

Numbers reflects loss in Abstral® royalty due to patent expiration and investments in the build-up of DTx venture

| | |
|---|---|
| Group net revenues 2020 [1,2]<br>**SEK 664 m** (USD 77 m) | US Pharma net revenues 2020 [1]<br>**USD 68 m** |
| Group EBITDA 2020 [1,2]<br>**SEK 19 m** (USD 2 m) | US Pharma EBIT 2020 [1]<br>**USD 36 m** |
| Cash position Q4 2020[2]<br>**SEK 505 m** (USD 59 m) | US Pharma EBIT Margin<br>**53 %** |
| Net Cash position Q4 2020[2]<br>**SEK 281 m** (USD 33 m) | Investments in DTx 2020 (OPEX)<br>**SEK 171 m** (USD ~20 m) |

Denomination currency is SEK

[1] Last Twelve Months [2] 8.6 USD/SEK, Q4 average

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# No changes in the two ongoing legal processes in Q4, except new patent issued for ZUBSOLV® in Dec. and listed in Orange book in January

## Subpoena

- On July 14, 2020 Orexo US received subpoenas to provide US Authorities with certain information with regards to ZUBSOLV® and other buprenorphine products. Orexo has no knowledge of the background to the requests.
- Orexo has engaged a US counsel to advice the company and prepare for any further requests or actions from the authorities

**No further information or requests have been received from the authorities after July 14th 2020.**

## Patent infringement litigation against Sun Pharma

- Orexo on September 13 filed a patent infringement action in the US District Court for the District of New Jersey, against Sun Pharmaceuticals. The filing statutorily precludes FDA from approving Sun's ANDA for 30 months, or until a district court decision finds ZUBSOLV's patents to be invalid or not infringed, whichever occurs first
- Orexo currently has six patents listed in the Orange Book with expiration dates from Dec. 2027 to Sep. 2032

**Orexo has previously successfully defended the ZUBSOLV® patents and is well prepared for a new process with Sun**

1 Abbreviated New Drug Application

# Value drivers for long-term growth 1 - 5

1 **Product portfolio addressing large and growing markets**

Focusing on becoming a leader in the large and growing space of substance use disorders and mental health. In parallel, Orexo is also addressing the ongoing opioid epidemic, one of the largest health crises to take place in the US and increasingly a growing global concern.

2 **Entering digital therapeutics, a new evidence-based frontier in patient care**

Digital therapeutics can increase access to treatment and improve treatment outcomes and is set to become an integral part of the global healthcare landscape. Substance use disorder and mental health are areas where it is most needed.

# Value drivers for long-term growth 1 - 5

3 **Strong cash conversion to support growth**

Lead product ZUBSOLV®, for the treatment of opioid use disorder, is a strong cash and profit contributor, enabling continued investment in on-market products and R&D.

4 **Leveraging our US commercial excellence**

Strategic focus on leveraging its commercial excellence and strong market access network in the US, by adding more products to the US commercial platform.

5 **Expanding pipeline targeting unmet medical needs**

Continue to build on the strong experience of developing products with worldwide approval by expanding the pipeline with multiple short-time to market assets based on innovative drug delivery technologies and digital therapies, addressing unmet medical needs in our key therapeutic areas.

# Thank You

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