### orexo

Improves lives for people suffering from mental illness and addiction disorders



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

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# Introduction & strategic agenda









### 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<sup>1</sup>: **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 LTM<sup>2</sup> Q320

EBITDA LTM<sup>2</sup> Q320 Cash position Q320

SEK **742** m

SEK 104 m

**SEK 593** m

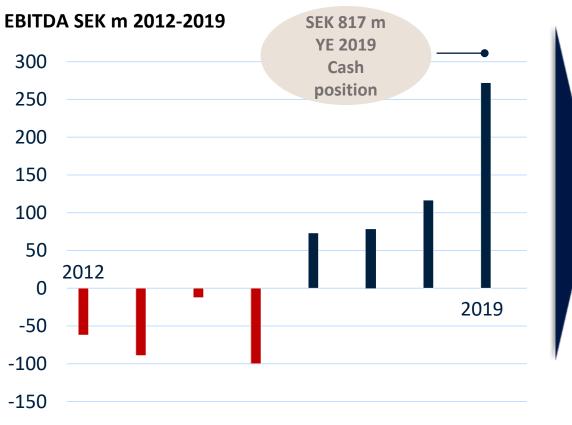
<sup>&</sup>lt;sup>2</sup> Last Twleve Months



<sup>&</sup>lt;sup>1</sup> As of October 30, 2020

# 2012 – 2019 successful strategic focus on building a solid foundation for investments in future growth drivers

### Strong cash position and cash flow from ZUBSOLV®...



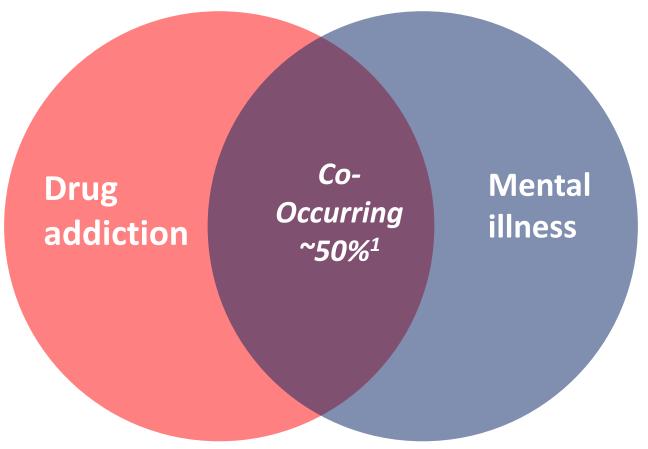
### ..has enabled investments in future growth

- Acquired US rights to the digital therapies vorvida® and deprexis®
- Developed a digital therapy for opioid use disorder
- Developed a distribution and reimbursement platform for digital therapies
- Advanced the pharma pipeline in opioid addiction and pain treatment



### Entering closely related therapeutic areas with large unmet needs.....

....and which are expected to be significantly impacted by the on-going Covid-19 pandemic



- Globally opioids continue to cause the most harm, accounting for two-thirds of the deaths attributed to drug addiction<sup>1</sup>
- Only about half of individuals with co-occurring mental health and drug addiction received treatment in 20182
- In the US approx. 16.6 m are heavy alcohol users and yearly, > 88,000 people die from alcohol misuse making it the third leading preventable cause of death in the country<sup>3 4</sup>
- Depression is the leading cause of disablility worldwide and in 2017, an estimated 17.3 million US adults (7.1% of all adults) in had at least one Major Depressive Episode (MDE)<sup>5</sup>

<sup>&</sup>lt;sup>5</sup>National Institute of Mental Health. Major Depression. Retrieved from: https://www.nimh.nih.gov/health/statistics/major-depression.shtml



<sup>&</sup>lt;sup>1</sup>Substance Abuse and Mental Health Services Administration <sup>2</sup> World Drug Report <sup>3</sup> Substance Abuse and Mental Health Services Administration <sup>4</sup> Sacks, J.J.; Gonzales, K.R.; Bouchery, E.E.; Tomedi, L.E.; and Brewer, R.D. 2010 National and state costs of excessive alcohol consumption. American Journal of Preventive Medicine49(5):e73–e79, 2015

# The profit and cash contributions from ZUBSOLV® enables continued investments in building a broader and stronger Orexo

**Orexo objectives** 

### Broadening...

..the portfolio of commercial products to be promoted by our existing US organization in 2020

### Maintaining...

..ZUBSOLV® profit contribution in 2020 and ensure it is sustainable and growing over time

### Establishing...

..a new revenue generating business area within Digital Therapeutics (DTx) and launch first new product in 2020

### Launching...

..a new pharmaceutical product from Orexo's development pipeline within the next two years



# Digital therapeutics branch out









# Digital therapeutics will become an integral part of the future healthcare landscape



- Almost all industries have been transformed or are under transformation by digitalization; healthcare is not an exception
- To meet increased demand from an aging population, health care delivery needs to be transformed to drive efficiency
- Digital therapeutics have the potential to significantly improve the efficiency and quality of multiple disease spaces and in particular within mental health
- Quality of digital therapeutics are improving and payors are starting to finance digital therapies along with traditional treatments

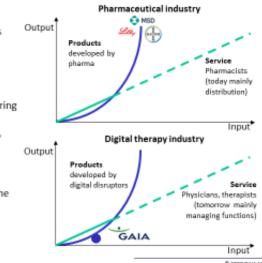
Physician consultation time is high in demand but limited in supply: Digital therapy is disrupting the service paradigm by providing 24/7 unlimited access to consultation.

Past: Physicians prescribed a "recipe" (Rx) that instructed pharmacists to mix certain ingredients for the patient. "Drug production" was a service performed by pharmacists.

Entrepreneurial pharmacists and smart chemical suppliers disrupted this service paradigm by offering standardised machine-produced products. This marked the birth of the pharmaceutical industry, making high quality drugs available to the mass market.

Today: Computer technology allows disrupting the next large service block in healthcare: Physician - patient interaction

GAIA is leading this transformation



Strong synergies with the current US commercial platform with a focus on opioid use disorder and treatment with ZUBSOLV® (bup/nal) and R&D pipeline

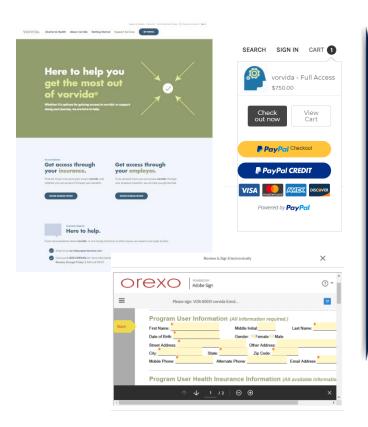


Our ambition is become a leader in digital therapeutics, leveraging our existing commercial infrastructure and new technical platforms to scale up

### **Enter DTx**



### **Establish the platform**



### **Expand presence and portfolio**





# 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

### **Pricing**

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

#### Reimbursement

 Many payors still to establish payment and reimbursement processes

### **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



# 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



### vorvida®

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



### 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





# The scientific evidence for DTx is comprehensive e.g. 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	<i>p</i> -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



# Pharma products and projects under development









ZUBSOLV® resilient and strong cash contributor in a challenging market

environment

### **ZUBSOLV** – treatment of opioid dependence

ZUBSOLV® is a product for the treatment of opioid dependence.

### Product advantages include:

- Higher bioavailability
- Fast dissolve time
- Preferred menthol flavor
- Broadest range of dose strengths



### Recent developments

### Continued strong market growth of 13% year over year

- Covid-19 led to increased relapse of opioid dependent patients
- Market growth is driven by Medicaid, while commercial segment has decreased during 2020 due to increased unemployment

### • ZUBSOLV® sales stable in "open segment" and profitability increase

- Overall sales declining due to increased competition in previously exclusive contracts with United Health Group and Humana
- ZUBSOLV® sales in "open<sup>1</sup>" segment is growing YoY and has been stable during Covid-19 pandemic
- EBIT margin above 50% expected for 2020

### • Improved market access in 2021 will support ZUBSOLV® sales:

- Significant market access win in ESI & CIGNA, where is ZUBSOLV® now the only preferred branded product
- ZUBSOLV® remains the only branded product on top three US Commercial PBMs



### OX124 continues to be an attractive opportunity

### OX124 - opioid overdose

A powerful rescue medication, designed to reverse opioid overdoses, including those from synthetic opioids like fentanyl



### Recent market developments

### Covid making the unmet need even more severe:

- Overdose deaths in the US will reach an all-time-high this year, with a projected increase of 13%<sup>1</sup>, now trending to >76,000 deaths for 2020<sup>1</sup>
- Synthetic opioids are now representing 76%¹ of opioid related deaths
- In July, Millennium Health analyzed 500,000 urine drug tests and found a 32% increase in the national usage of non-prescribed Fentanyl<sup>2</sup>

### • US market leader Narcan® sales at record level3:

- USD 89 m in Q3 '20 highest reported quarter ever (up from USD 75 m in '19)
- USD 234 m for first nine months '20 (up from USD 214 m in '19)
- 2020 Guidance: USD 295-315 m (up from USD 280m in '19)

### 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



<sup>&</sup>lt;sup>1</sup> April 2019 – April 2020 vs. April 2018 – April 2019 (<a href="https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm#dashboard">https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm#dashboard</a>)

<sup>&</sup>lt;sup>2</sup> Comparing March 13, 2020 to May 13, 2020 (millenniumhealth.com/news/signalsreportcovid/)

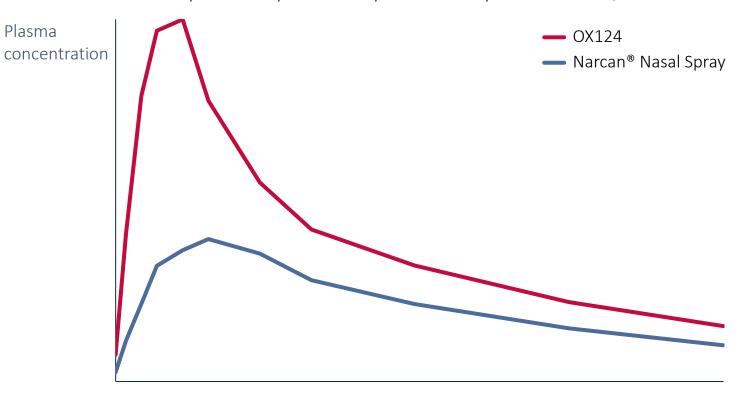
<sup>&</sup>lt;sup>3</sup> Emergent BioSolutions Q3 2020 Report

### OX124 - We have shown better PK profile than Narcan® Nasal Spray

Time

### 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)



# Financial & Legal



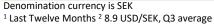




### Strong financial position to drive future growth

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

Group net revenues LTM <sup>1,2</sup>	Growth YoY
SEK 742 m (USD 83 m)	-11%
Group EBITDA LTM <sup>1,2</sup>	
SEK 104 m (USD 12 m)	-55%
US Pharma EBIT (ZUBSOLV® US) LTM <sup>1</sup>	
SEK 331 m (USD 37 m)	6%
Cash position Q3 2020 <sup>2</sup>	Positive net cash position <sup>2</sup>
SEK 593 m (USD 67 m)	SEK 369 m (USD 41 m)





### Two legal processes emerged during July and August 2020

### 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 14<sup>th</sup> 2020.

### Paragraph IV notice from Sun Pharmaceutical Industries Ltd ("Sun")

- 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 five 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



# Summary







### Summary - Strong value drivers for long-term growth

# Future value drivers

Product portfolio addressing large and growing markets Strong cash conversion to support growth

- Leveraging our US commercial excellence
- Expanding pipeline targeting unmet medical needs
- Entering digital
   therapeutics, a new
   evidence-based frontier
   in patient care



# Thank You