






Develops and commercializes improved pharmaceuticals and digital therapies – with the aim of becoming a leader within the treatment of addiction



Capital Market Day, March 17, 2020

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

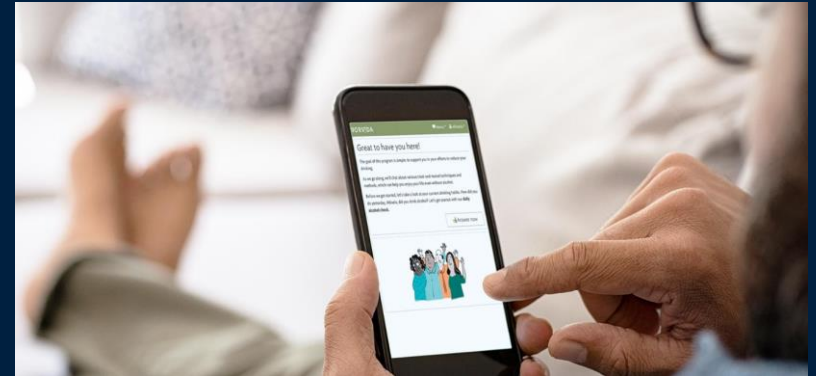
Agenda

Time <small>pm CET</small>	Topic	Presenter
Part 1 – Growth Strategy		
1:30 – 1:45	Strategy for short- and long-term growth	Nikolaj Sørensen, CEO and President
1:45 – 2:00	Growing the Zubsoolv® franchise	Robert DeLuca, President of Orexo US Inc. 
Part 2 – Pharma Pipeline		
2:00 – 2:20	A pipeline with significant future potential	Johannes Doll, EVP and Chief Commercial Officer
2:20 – 2:25	Q&A session	
2:25 – 2:35	Break	
Part 3 – Digital Therapeutics (DTx)		
2:35 – 3:05	DTx – new frontiers in patient care	Dennis Urbaniak, EVP Digital Therapeutics 
3:05 – 3:40	GAIA – a global leader in DTx	Dr. Mario Weiss, CEO and founder of GAIA AG 
3:40 – 3:55	Q&A session	
Part 4 – Outlook		Nikolaj Sørensen, CEO and President
4:00	Mingle and buffet	

Part 1 – Growth Strategy

Growing the Zubsoiv[®] franchise -
Nikolaj Sørensen, CEO and President

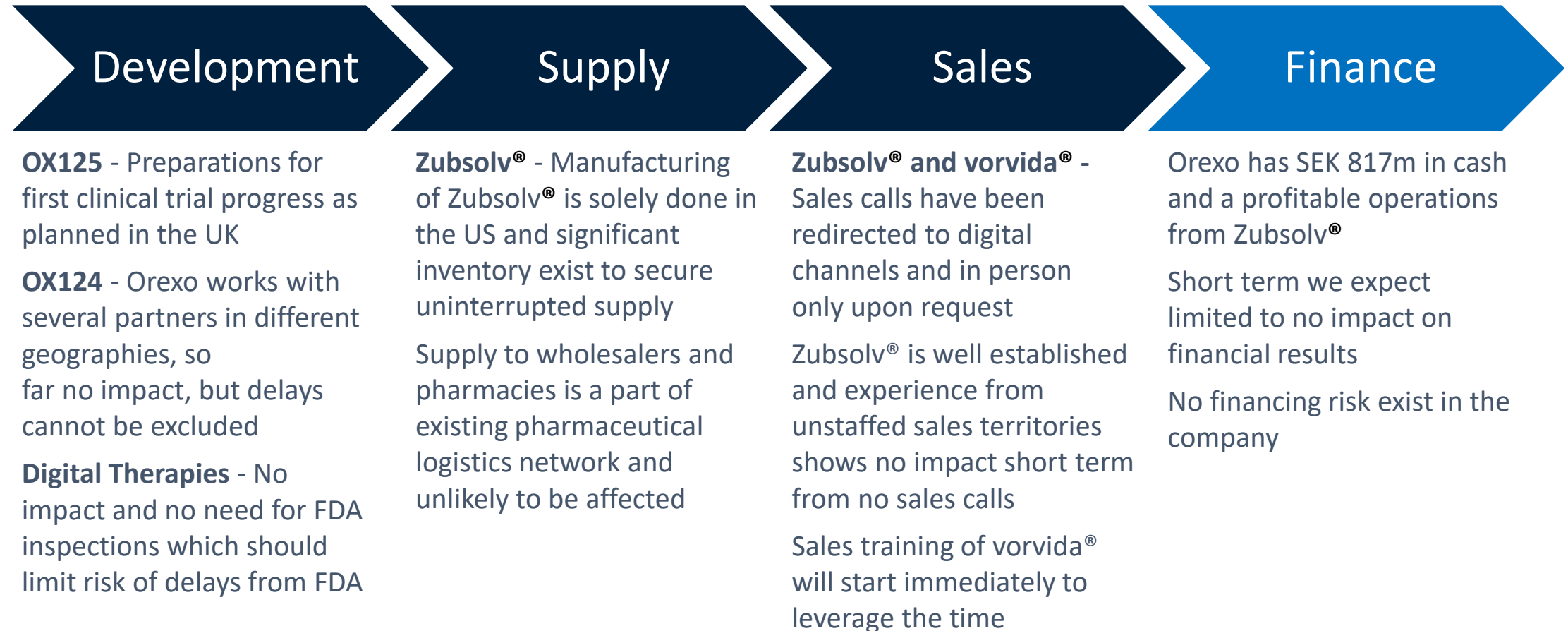
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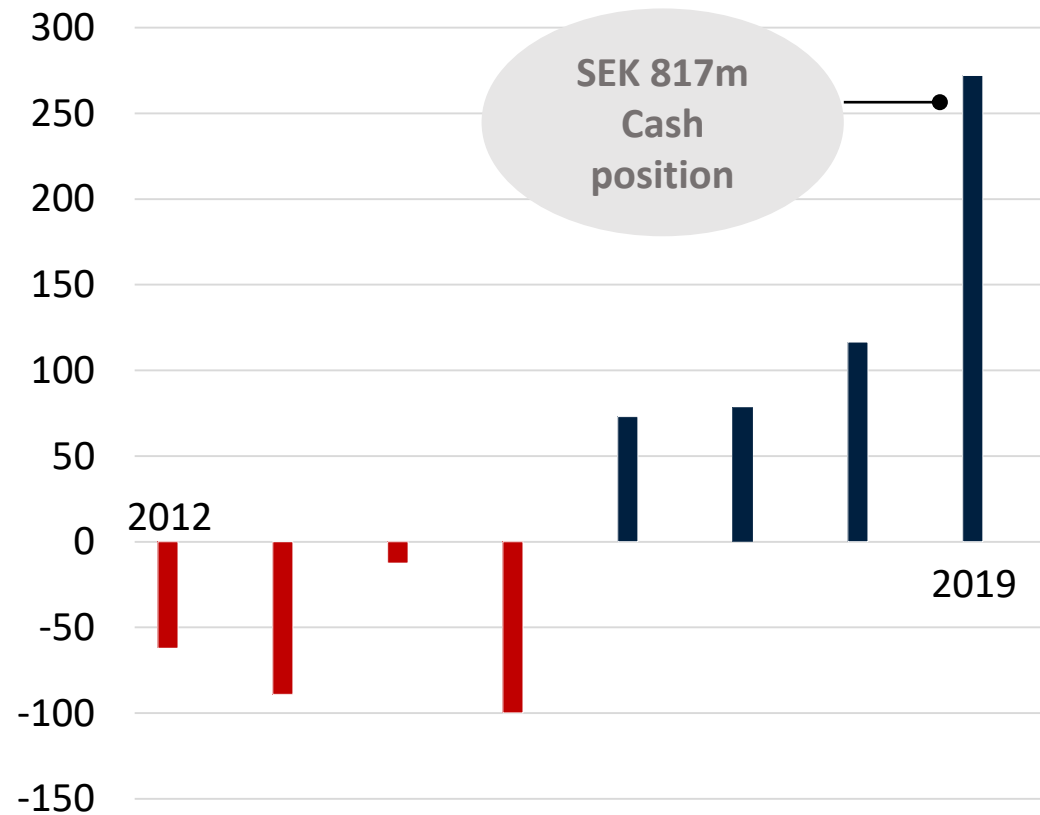
Limited impact from the COVID-19 virus currently¹



¹ This analysis assumes impact from COVID-19 is limited to H1 2020

2012 – 2019 successful strategic focus on building a solid foundation

EBITDA SEK m 2012-2019



Launch Zubsolv® in the US



First actions taken to broaden the US commercial platform



Secure profitability



Ensure a sustainable business model

2019 delivered the strongest financial results ever

Group net revenues SEK 845 m <i>85% from Zubsolv®</i>	Growth 8% <i>(Zubsolv® 16%)</i>
Group EBITDA SEK 272 m	Growth 133%
US EBIT SEK 351 m	Growth 77%
Cash position SEK 817 m	Positive net cash position SEK 527 m

The profit contributions from Zubsolv® enables investments in building a broader and stronger Orexo

Broaden...

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

Establish

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

Maintain

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

Launch

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



Objectives for the Capital Markets Day

What we would like to achieve today:

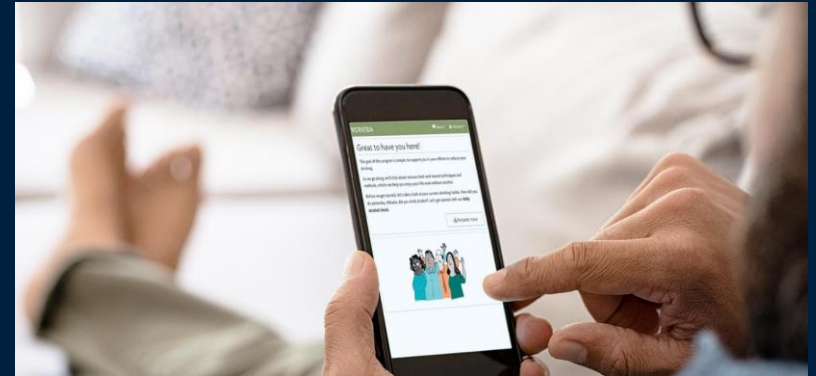
- Enable our shareholders and future investors to make a fair valuation of our pipeline
- Present why Orexo find Digital Therapeutics is a significant opportunity for the company and how it improve treatment outcome
- Create a confidence that Orexo is much more than Zubsolv® and is an exciting investment opportunity



Part 1 – Growth Strategy

Growing the Zubsoiv[®] franchise -
Robert DeLuca, President Orexo US Inc.

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Zubsolv® is well positioned to remain a strong profit contributor

>12 years of patent protection for Zubsolv® remains

...Zubsolv patents extend to Q4 2032 and Zubsolv® cannot be substituted by pharmacies with generic versions of Suboxone Tablet or Film

Zubsolv® continues to be a significant profit generator

...EBIT contribution from Orexo US of SEK 350m in 2019 and Orexo expects similar levels in 2020

...Zubsolv® net price has increased with 4 percentage points in Jan-Feb 2020 compared to same period last year¹ despite generic competition

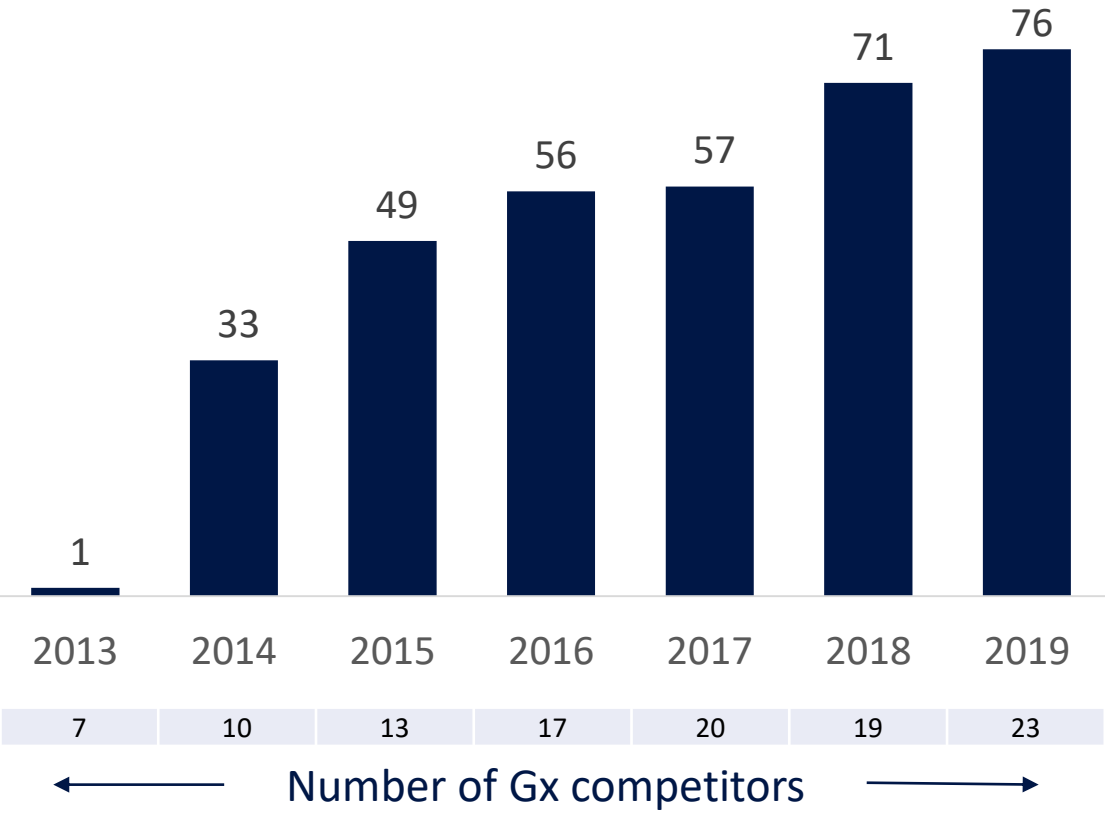


¹ Gross to net rate improvement due to price increase and more favorable payer mix

Zubsolv® has grown Year-over-Year despite increasing competition

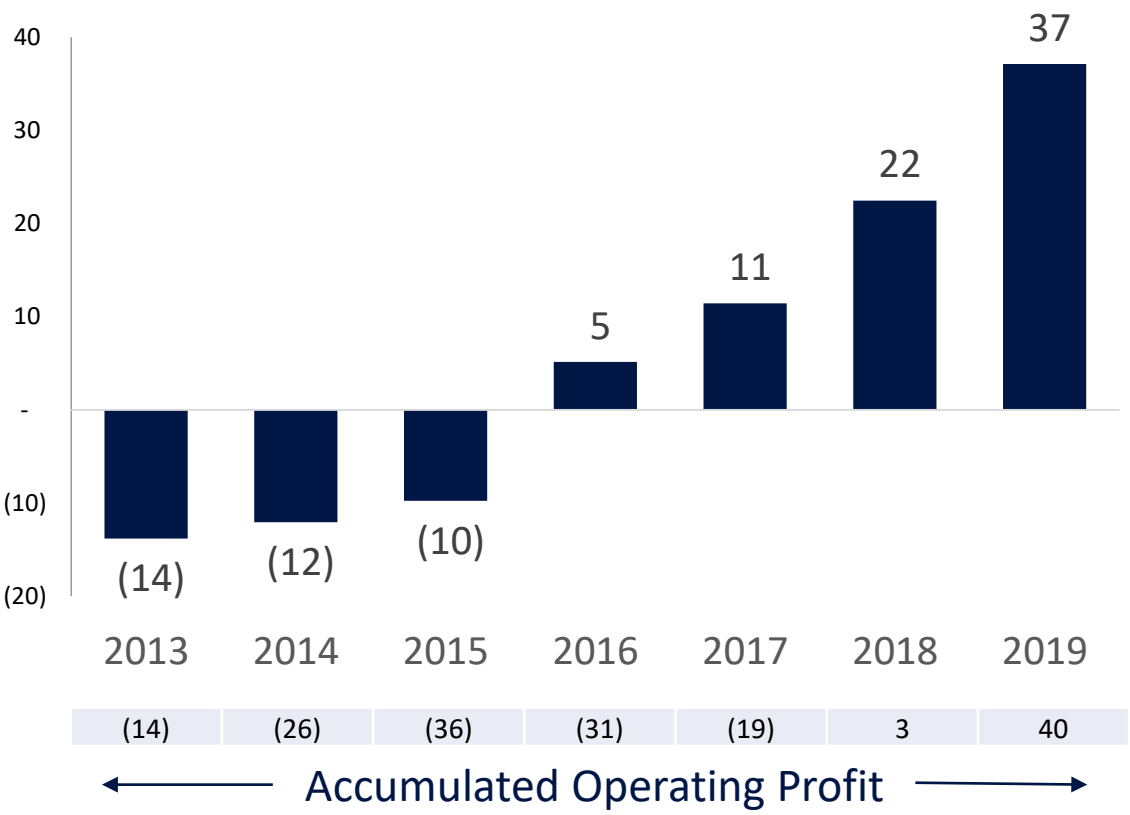
US Net Revenues

USD million



US Operating Profit

USD million



Source: Orexo Finance

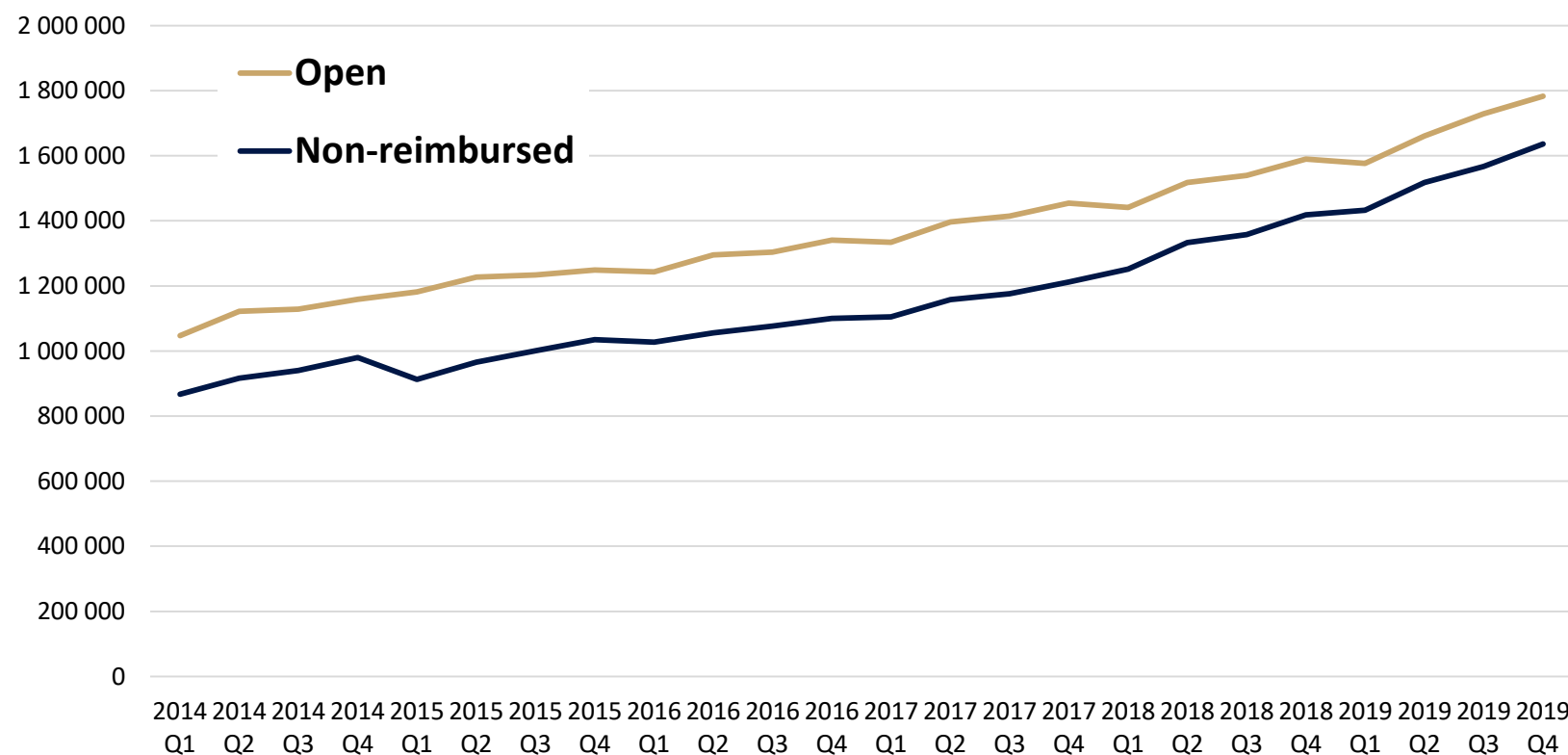


Full year market growth of 14% 2019 vs 2018 continues in Q1

New market definitions to be applied by Orexo

Market Volume Sales

Quarterly NTRx



Q1 YTD Growth

Total Market: +14%

By Segment

+14%

+13%

Definitions

Payers / Market Access

- **“Open”**
 - Market segments where Zubsolv® is reimbursed either exclusively or non-exclusively
- **“Non-Reimbursed”**
 - Market segments where Zubsolv® is not reimbursed

Note: NTRx = Total prescriptions adjusted to 30 tablet/film scripts
Source: IQVIA XPO

Zubsolv® growing in the open business, but overall volume declining from competition in former exclusive contracts

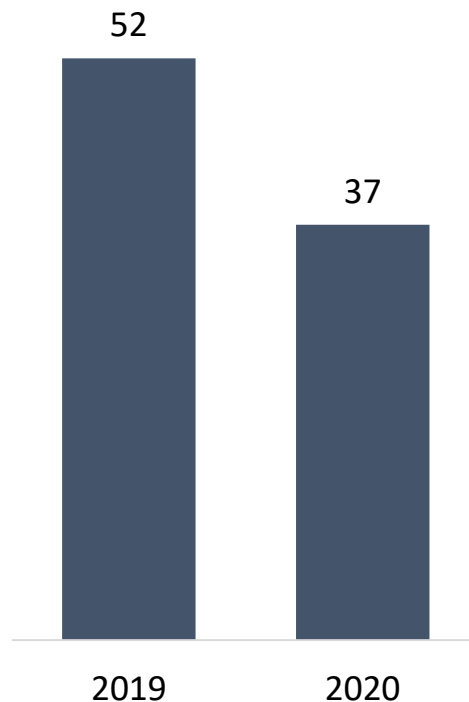
Open Market Access

Zubsolv NTRx YoY Q1TD (thousands)



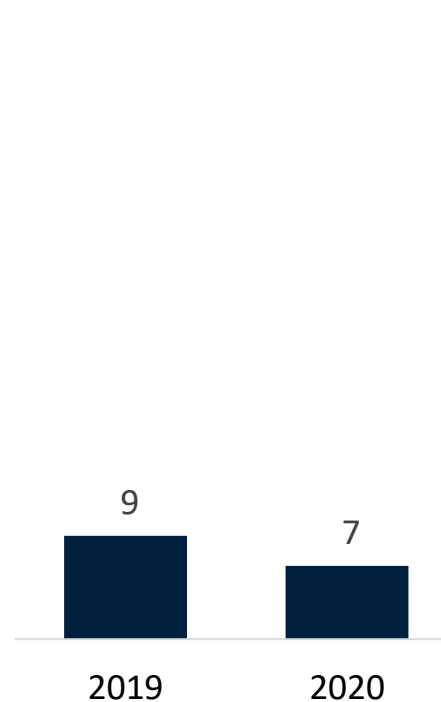
UHC/Humana/Cash

Zubsolv NTRx YoY Q1 TD (thousands)



Non-Reimbursed

Zubsolv NTRx YoY Q1TD (thousands)



Market Changes

From year 2019 to 2020

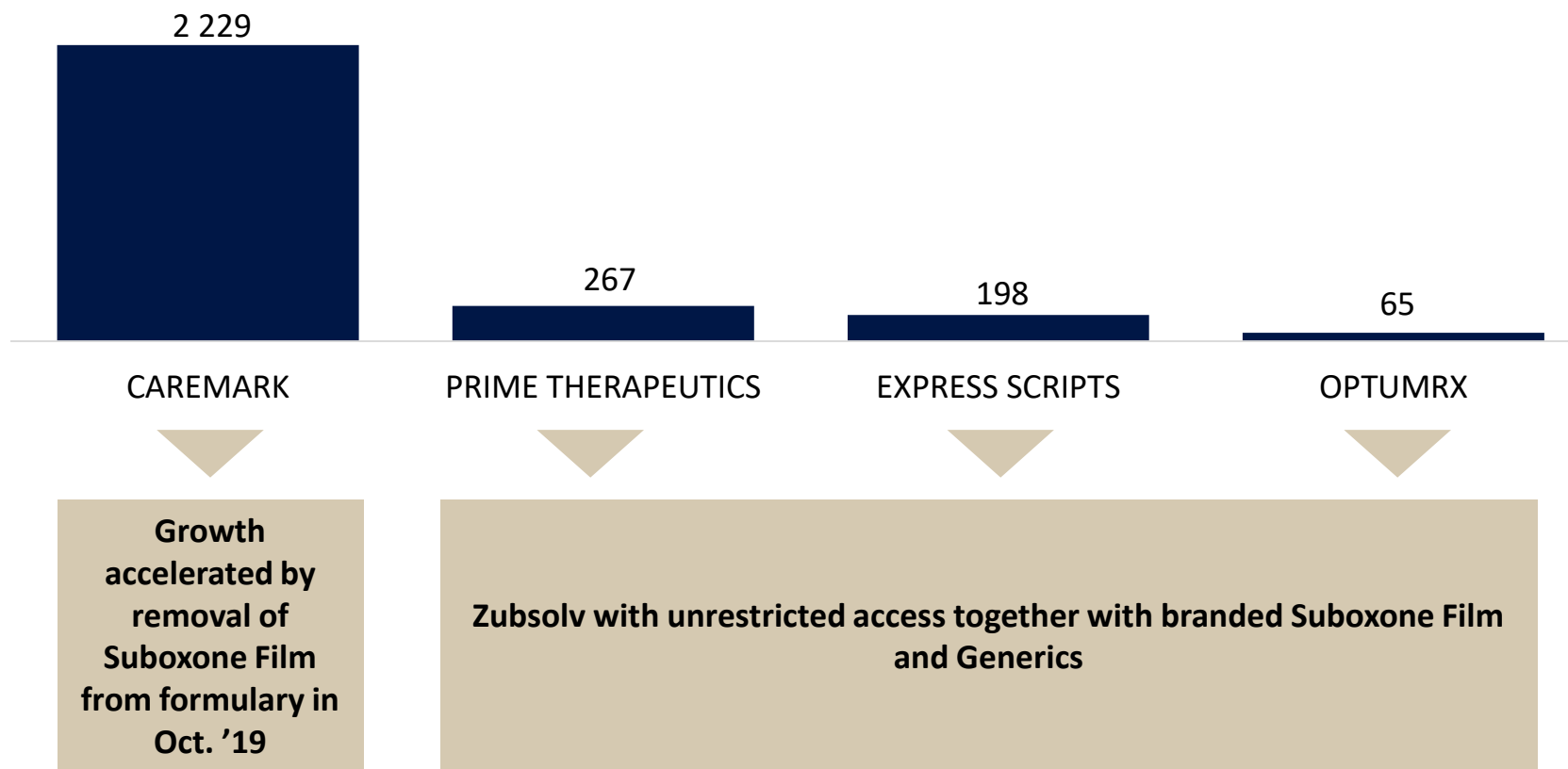
- **Generic film introduced late Feb 2019**
 - UHC/Humana add generics
- **2020 Public access lower by 3 %-point vs 2019**
- **2020 Commercial access increased 1 %-point vs 2019**

Note: NTRx = Total prescriptions adjusted to 30 tablet/film scripts
Source: IQVIA XPO

Zubsolv® growth in open business explained by unrestricted access to all large national commercial PBMs

Prescription incremental growth to major national PBMs

Zubsolv NTRx YoY Q1TD (thousands)



Total increase of 2,759 NTRx year-to-date

Opportunity to continue to grow business and to translate successes to other payers as well

Additional removal of Suboxone Film from formularies likely to drive additional growth

Growth in commercial formularies expected to increase after Q1 due to declining deductibles

Note: NTRx = Total prescriptions adjusted to 30 tablet/film scripts
Source: IQVIA XPO

Several possible triggers for Zubsolv® growth in 2020 and beyond



Continued improved market access

- ...Orexo continues to aggressively pursue expanding market access in Medicare and Medicaid
- ...Largest branded competitor likely to lose reimbursement over time

Competition from “the preferred” authorized generic of Suboxone Film will end

- ...Supply of authorized generic has ceased from the manufacturer (Indivior) and product will disappear when inventories are depleted
- ...Market share of authorized generic has dropped from >50% to 28% last week

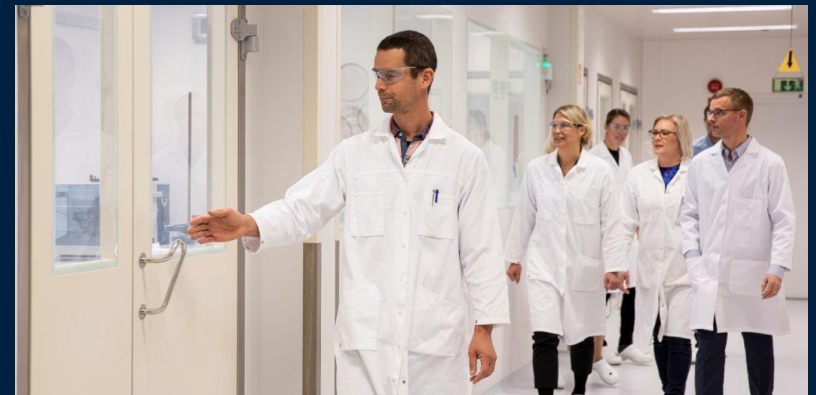
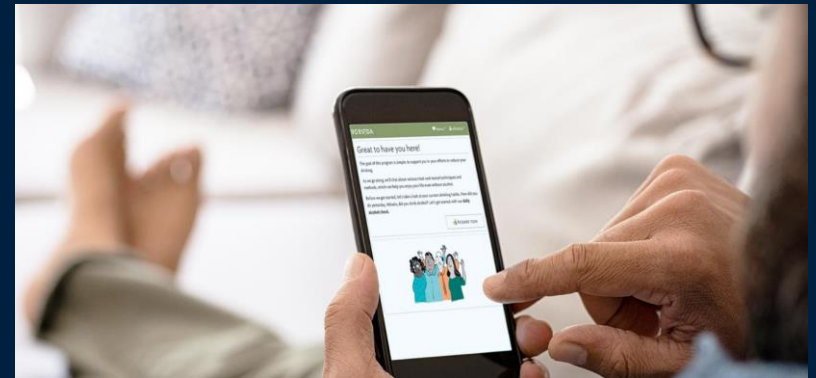
Orexo will be the only pharmaceutical company promoting a Buprenorphine product to most prescribers

- ...Sublocade and other depot formulations primarily promoted to larger institutions
- ...Orexo has an expanding pipeline addressing the most urgent concerns in the industry

Part 2 – Pharma Pipeline

A pipeline with significant future potential -
Johannes Doll, EVP and Chief Commercial Officer

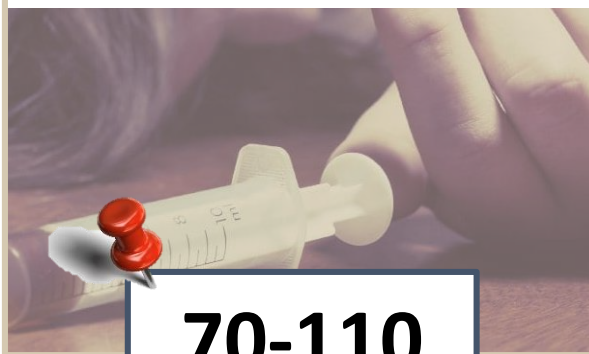
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3 convincing development assets addressing critical unmet needs

OX124 – opioid overdose

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



70-110

MUSD net sales potential (US)

OX125 – opioid overdose

A rescue medication to reverse opioid overdoses, developed for situations where very long-lasting effect is required

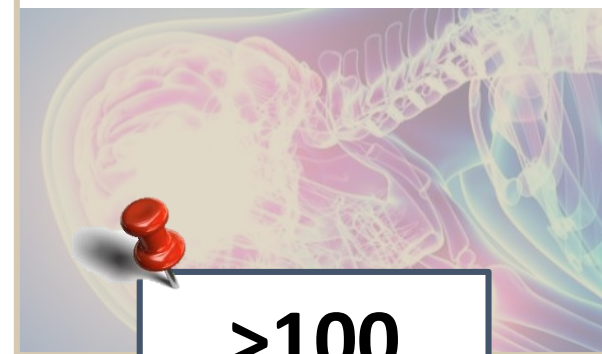


40-60

MUSD net sales potential (US)

OX338 – non-opioid pain

A non-opioid pain killer with opioid-level efficacy for short-term pain (up to 5 days), but without the risk of addiction



>100

MUSD net sales potential (US)

Orexo R&D pipeline

- OX124 – nasal naloxone rescue drug
- OX125 – nasal nalmefene rescue drug
- OX338 – oral ketorolac

OX124 at a glance

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

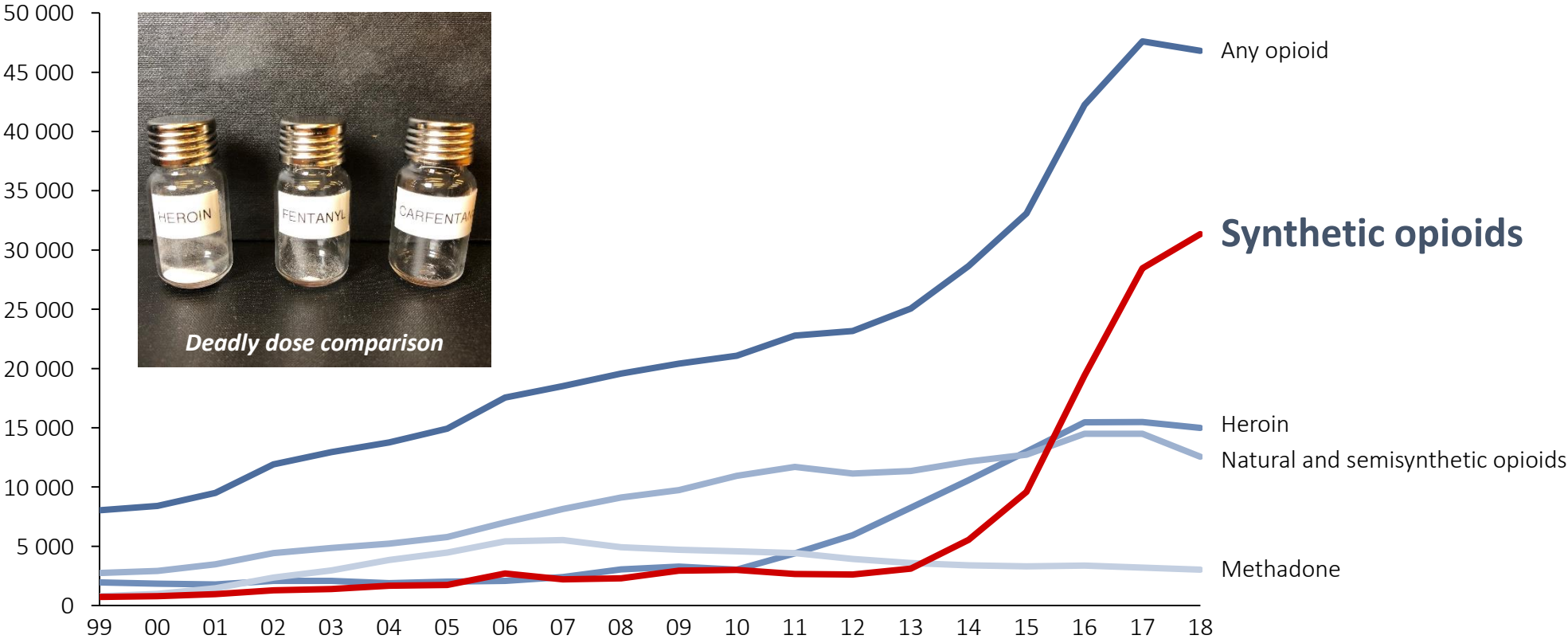
million USD net sales (US market)



While overall deaths from opioid overdoses showed a slight decline in 2018, deaths from synthetic opioids continue to rise

Deaths from opioid overdose

By type of opioid, United States



Source: Hedegaard H, et al. NCHS DATA Brief 356 - Drug Overdose Deaths in the United States, 1999-2018. NCHS, National Vital Statistics System, Mortality. Jan 2020.

The market for rescue drugs – key figures

47

thousand

Deaths from opioid
overdoses¹

1-2

million

Doses of naloxone rescue
medications administered²

~10

million

Doses of naloxone rescue
drugs distributed

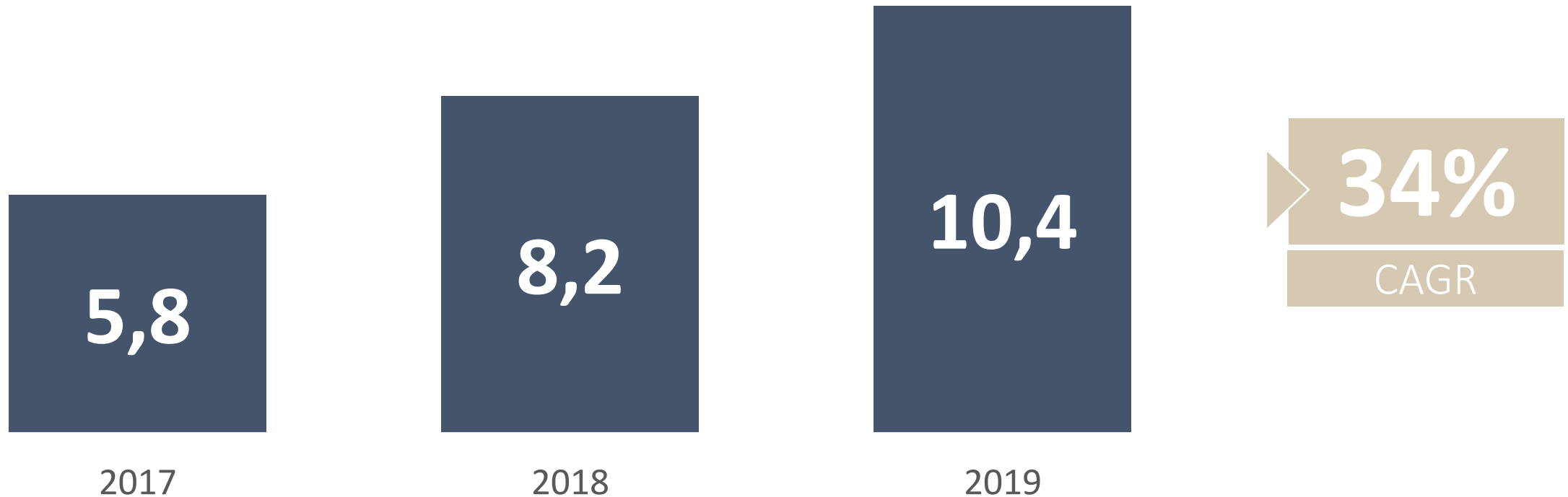
¹ Year 2018, NCHS, National Vital Statistics System, Mortality. Jan 2020

² Clarion Healthcare analysis, Year 2018

³ Year 2019, IQVIA National Sales Perspective, adjusted for est. NarcanDirect sales (not captured by IQVIA)

The market for rescue medications has seen a significant increase

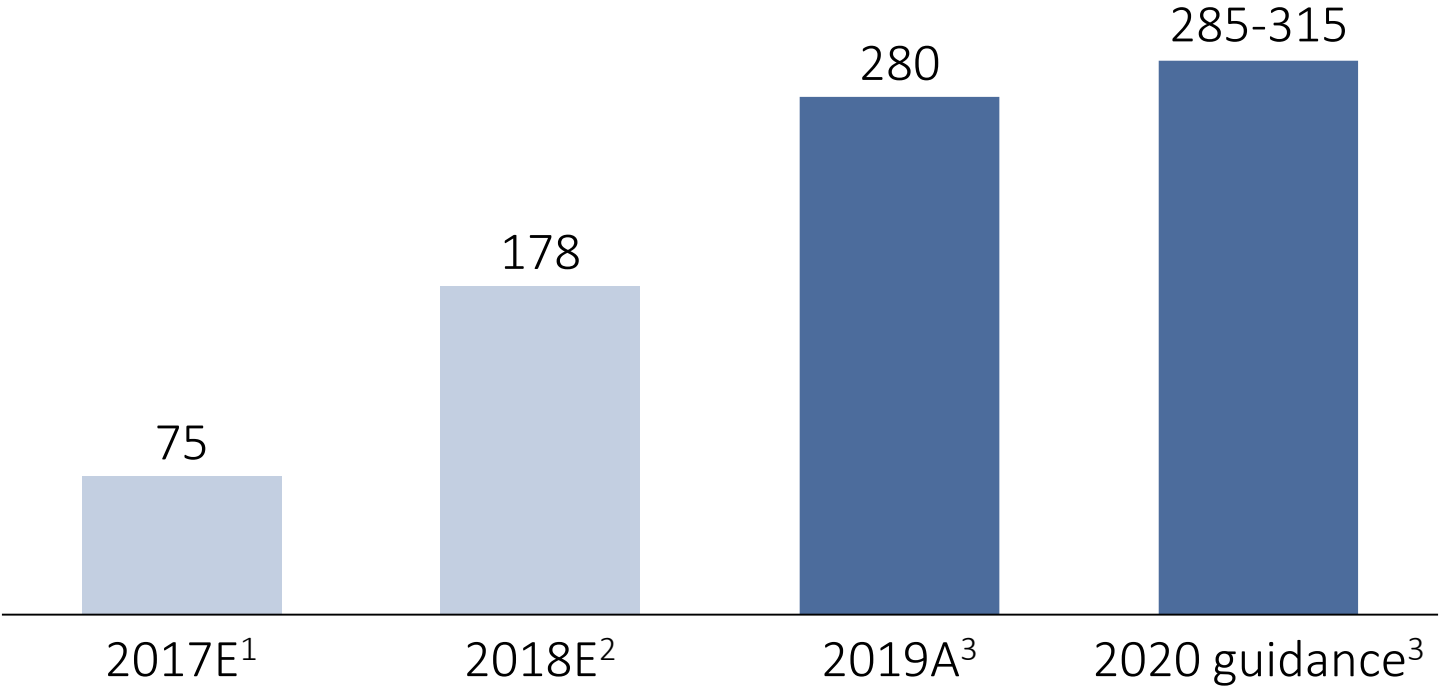
Naloxone Sales Volume
Million Units



Source: IQVIA National Sales Perspective, adjusted for est. NarcanDirect sales (not captured by IQVIA)

Narcan Nasal Spray is currently dominating the branded market

Narcan Nasal Spray Net Sales
USD Million



¹ Year 2017 estimated based on royalty payments to Opiant

² Year 2018 Zacks Small Cap Research

³ Emergent Biosolutions Reports

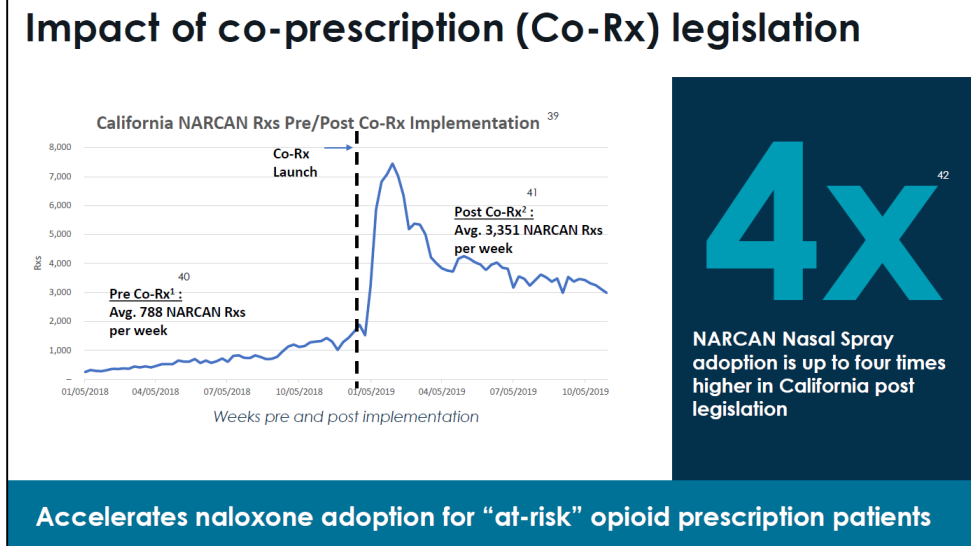
Mandatory coRx in more states could further accelerate market growth

Mandatory coRx...












- 15-20 million patients at risk of accidental overdose due to high-dose opioids for pain
- 9 states have implemented legislation to make rescue medication mandatory for these patients
- Further upside from remaining states

... leading to further upside

From Emergent Biosolutions' investor presentation:



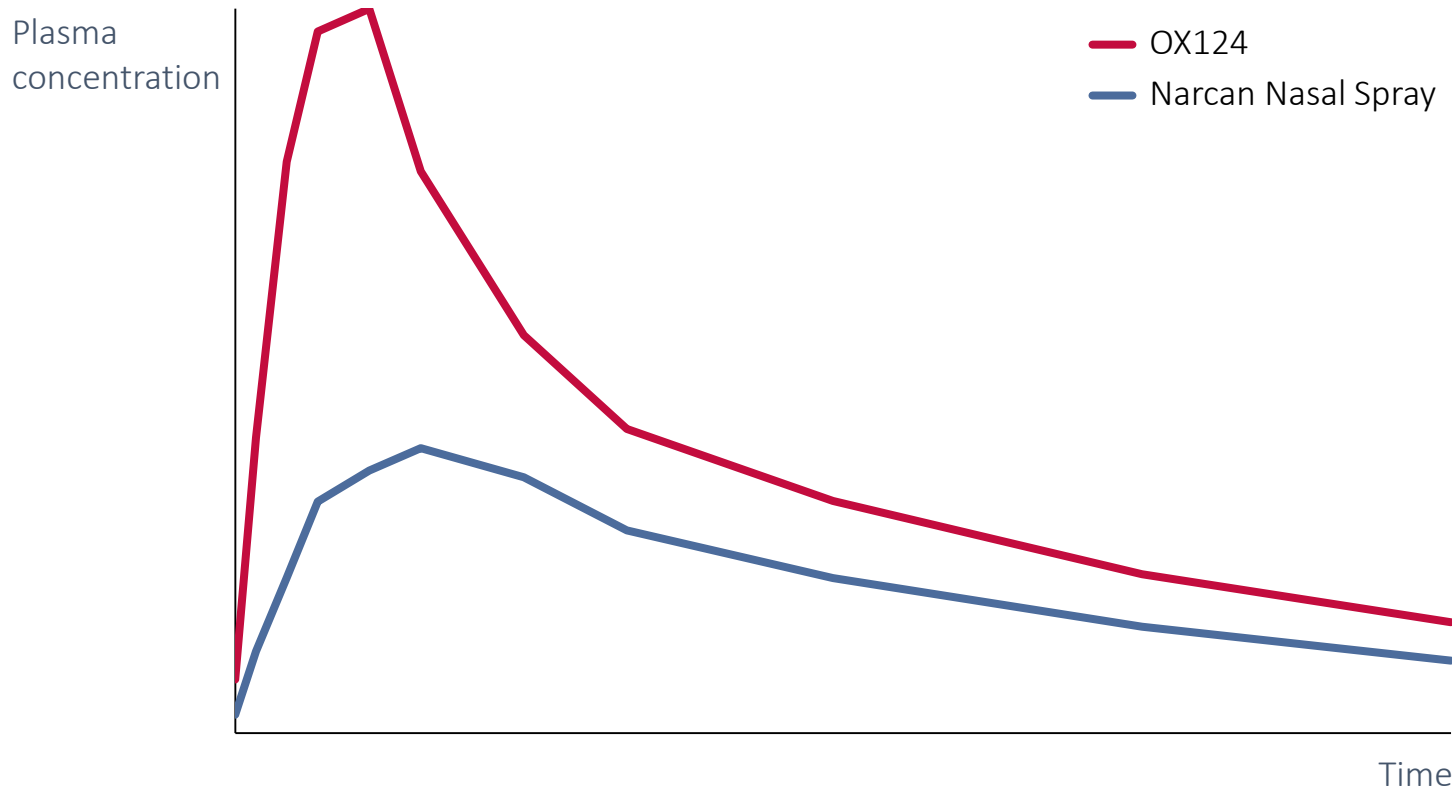
Pipeline overview – several development projects are underway

	Pre-clinical	Clinical	NDA filed	Approved
Nasal		 OX124, Planned NDA '21	 NDA filed Q3 '19 (8mg)	 Narcan, launched '16
		 Multi-dose, Possible NDA '20		 Narcan generic, Approved Apr '19, Ongoing litigation
Injectable	 Long-Acting injectable 24 hrs.	 Pre-filled syringe	 Zimhi, injectable, CRL Nov '19	 Evzio, auto-injector, launched '14
				 Vials and Pre-filled syringes, multiple companies
Other	 Buccal co-gel			
	 Buccal film			

We have 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

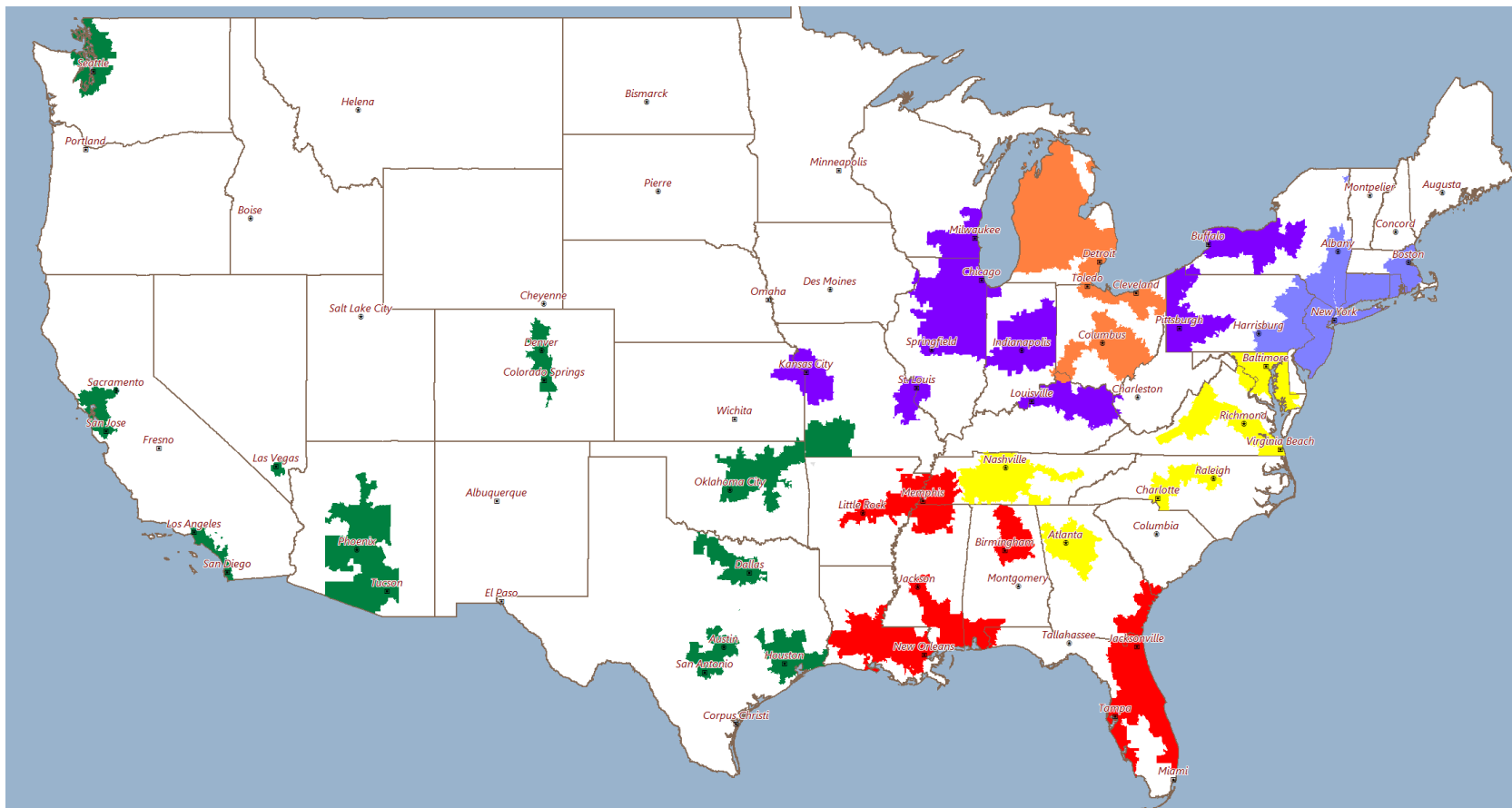


Expected patient benefit

- 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)

We are currently the only player with a presence in the retail segment (doctors' offices)

Orexo field force – US sales territories

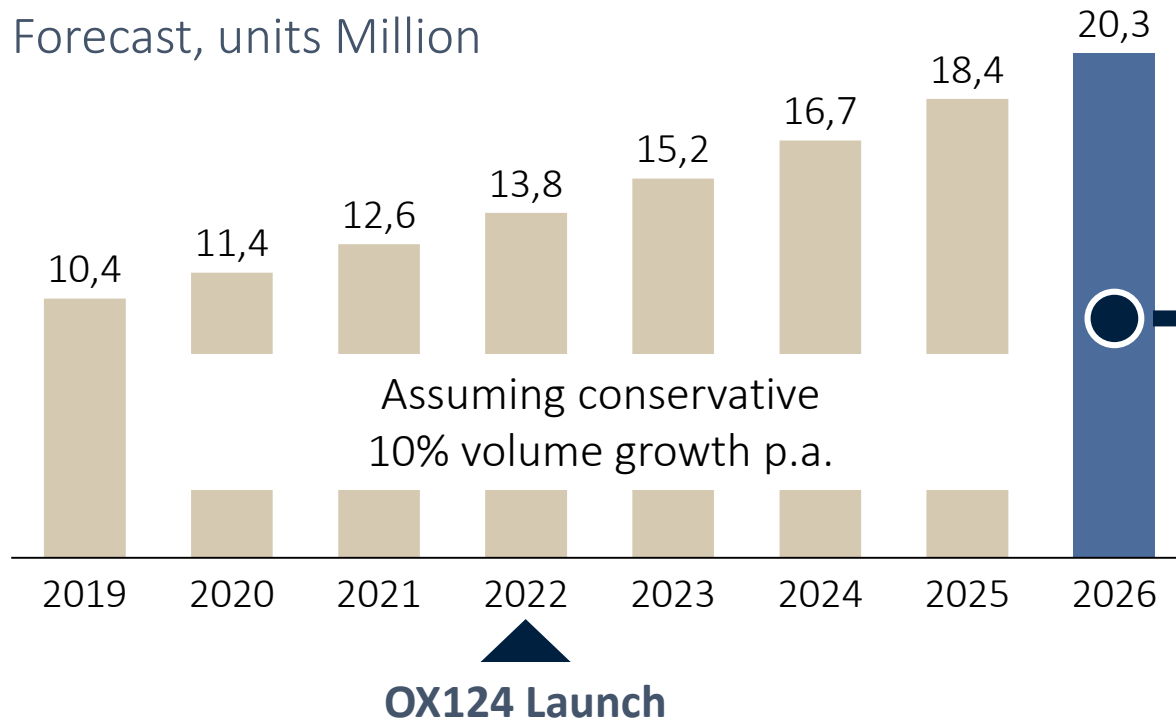


- Retail is the fastest growing segment
- Orexo's field force already covers most relevant geographies in the US
- Currently 51 sales territories organized in 6 regions
- Promoting Zubsolv® to 3,500 addiction specialists
- Flexibility to extend to pain practices to capture coRx opportunities

We are anticipating OX124 net sales of USD 70-110 million

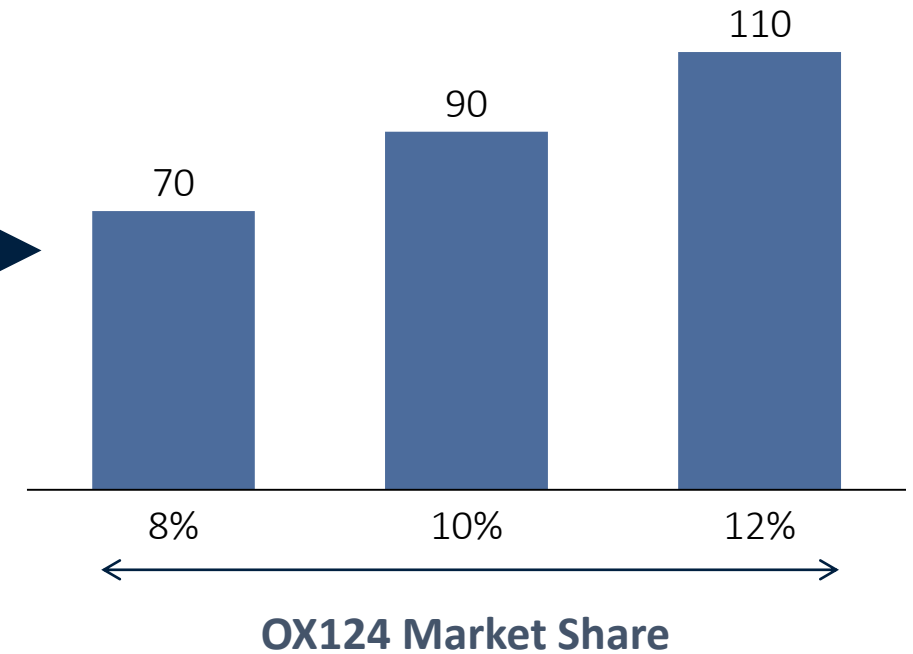
Rescue drugs market development

Forecast, units Million



OX124 Net Sales 5 years post launch

Forecast, USD Million



- Recent market growth >30% p.a.
- Continued increase of opioid addicted patients
- Growing awareness
- Upside from further states introducing mandatory coRx

- Differentiated profile (faster, stronger and longer-acting)
- Existing retail field force with track record to fight for market share in competitive market

We are currently preparing for the pivotal trial in Q4 of this year



¹ Assumes FDA fast track designation

Orexo R&D pipeline

- OX124 – nasal naloxone rescue drug
- **OX125 – nasal nalmefene rescue drug**
- OX338 – oral ketorolac

OX125 at a glance

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 powerful rescue medication for situations where very long-lasting effect is required, e.g., in remote areas, as response to long-acting drugs or for anti-terror stockpiling

The potential

40-60

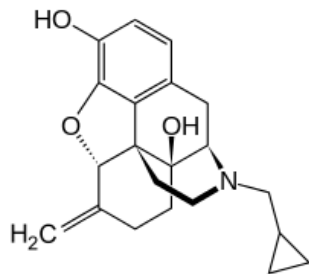
million USD net sales (US market)



While we expect naloxone to remain the dominant rescue drug, there are distinct areas where nalmefene may be better suited

Nalmefene

- Opioid antagonist (like naloxone)
- More potent than naloxone (higher μ receptor affinity)
- Longer half-life than naloxone (8 hours vs. 2 hours)



Where it may be better suited than naloxone



Rural areas

- Long acting rescue drug optimal for areas with long travel time to the closest hospital



Response to long-acting illicit drugs

- Recent emergence of illicit oral fentanyl tablets with longer effect in Philadelphia



Narco-terrorism

- Safety stock for potential terror attacks involving fentanyl or other synthetic opioids

Competition for nalmefene products is more limited



Note: Pipeline does not include 6 month nalmefene implant (Titan / Opiant, Proneura technology) intended for prevention of relapse following detox or Emergent’s SR Injection to treat opioid use disorder

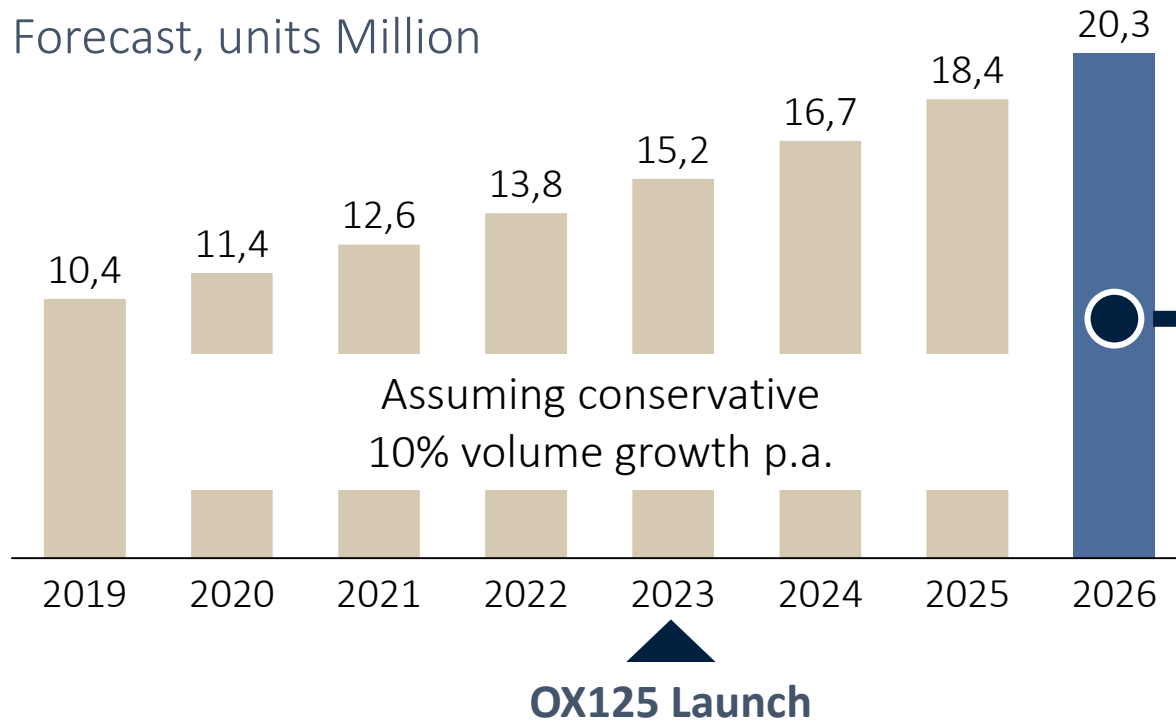
¹ Purdue has communicated intention to develop pre-filled syringe, vial and auto-injector including nalmefene for opioid overdose reversal

Sources: GlobalData, Company Webpages and Press-Releases, FDA webpage

We are anticipating OX125 net sales of USD 40-60 million

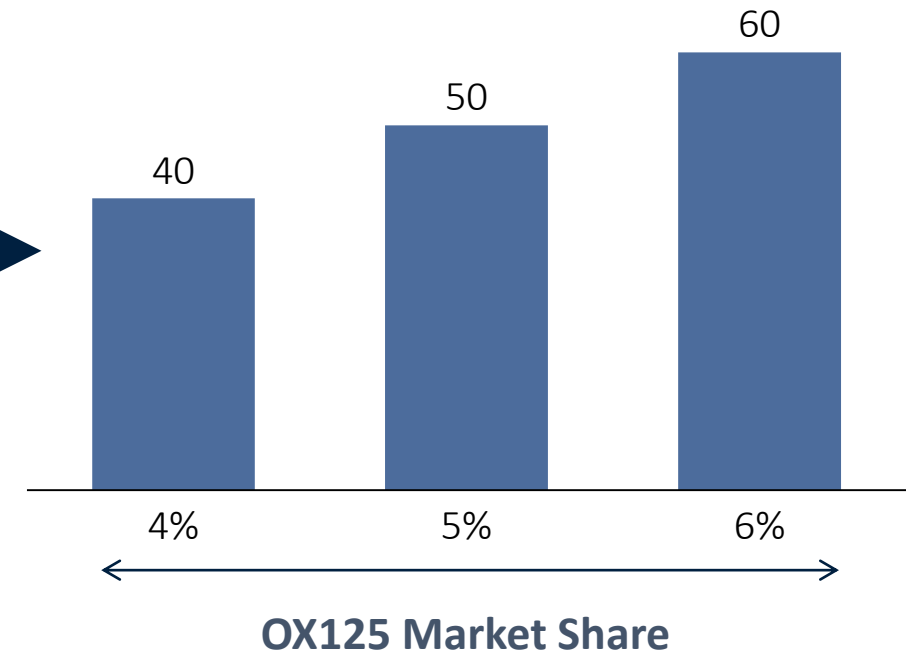
Rescue drugs market development

Forecast, units Million



OX125 Net Sales 5 years post launch

Forecast, USD Million



- Recent market growth >30% p.a.
- Continued increase of opioid addicted patients
- Growing awareness

- Differentiated profile (longer-acting than naloxone-based products)
- Existing retail field force with track record to fight for market share in competitive market

The first clinical trial in humans for OX125 is about to start



Orexo R&D pipeline

- OX124 – nasal naloxone rescue drug
- OX125 – nasal nalmefene rescue drug
- OX338 – oral ketorolac

OX338 at a glance

The unmet need

Opioids are still used unnecessarily in many situations, further fuelling the opioid crisis

Our aim

Opioid-level pain relief for short-term pain (up to 5 days) without the risk of addiction

The potential

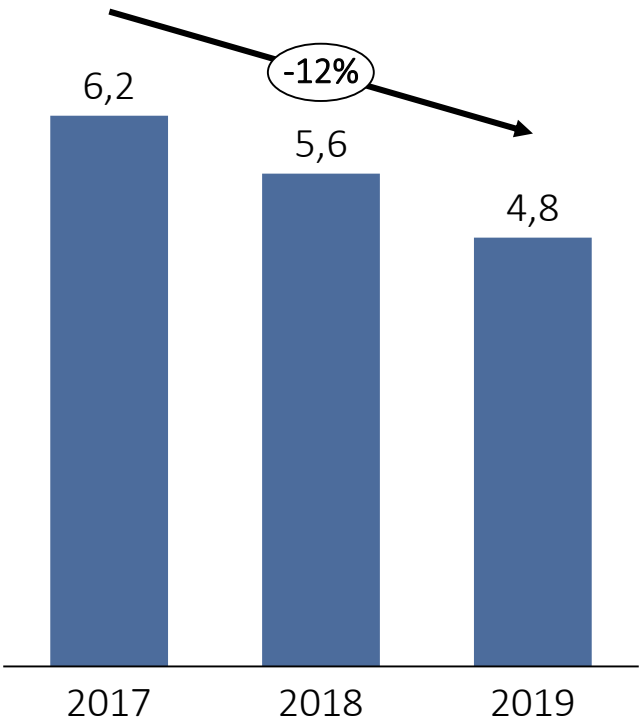
>100

million USD net sales (US market)



Despite some decline, the opioid market is still massive – and opioids continue to be used unnecessarily in many situations

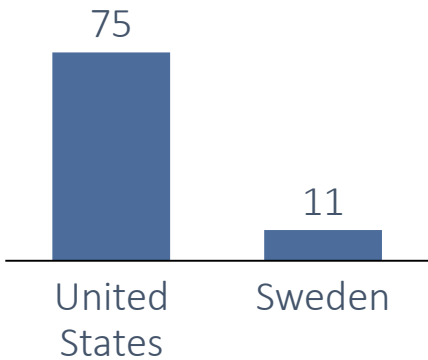
Opioid market United States¹
USD billion



Evidence for opioid over-prescribing
United States



Share of patients with an opioid prescription upon discharge post-surgery²



~6% of adolescents and young adults who have received opioids after wisdom teeth removal were diagnosed with opioid abuse within 12 months³

¹ IQVIA National Sales Perspective (Average Selling Prices)

² JAMA Netw Open. 2019; 2(9): e1910734, based on four frequently performed procedures: surgery to remove the appendix, surgery to remove the gallbladder, a minimally invasive procedure to treat a torn meniscus cartilage in the knee and a procedure to remove a breast lump

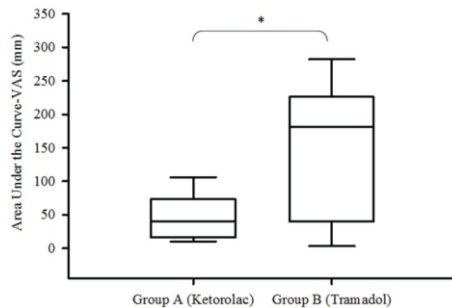
³ JAMA Intern Med. 2019: 145-152

Ketorolac is proven to be as effective as opioids

Examples for ketorolac's proven efficacy

MEDICINA ORAL PATOLOGÍA ORAL Y CIRUGÍA BUCAL

Third Molar surgery



“...this study suggests that **10 mg of oral ketorolac had superior analgesic effect than 50 mg of tramadol** when administered before a mandibular third molar surgery.”

Isiordia-Espinoza et al. 2016. Med Oral Patol Oral Cir Bucal

BMJ British Medical Journal

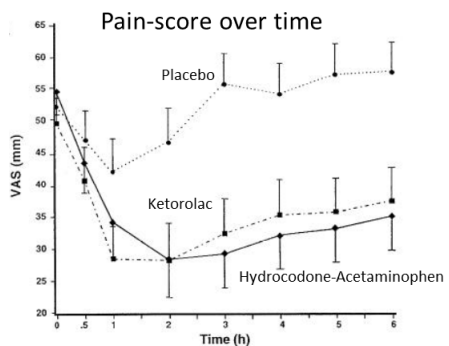
Painful injuries

“Ketorolac proved to be **as effective as morphine in relieving pain and did so just as quickly**. It seemed to have advantages over morphine in relieving pain associated with activity.”

Jelinek. 2000. British Medical Journal
(ER injuries included e.g., fractures of the femur, tibia, and fibula)

ANESTHESIA & ANALGESIA

Artroscopic surgery procedures



“In conclusion, there was **no difference in the efficacy between oral ketorolac and hydrocodone-acetaminophen combination** in controlling pain after outpatient arthroscopic surgery procedures.”

White et al. 1997. Anesthesia & Analgesia

PHARMACOTHERAPY The Journal of Human Pharmacology and Drug Therapy

Surgeries

“Ketorolac 10 and 30 mg were **as effective as morphine 12 mg** during the entire 6-hour observation period, and ketorolac 90 mg was **more effective than morphine 12 mg** during the entire 6 hours.

Yee et al. 1986. Pharmacotherapy
(Surgeries included e.g., cholecystectomy and abdominal hysterectomy, tendon and ligament repairs)

We are aiming at clearly differentiating OX338 vs. SPRIX and Generics

SPRIX Nasal Spray

- Only branded product on the market
- Complicated storage and dosing instructions
- Administration site reactions/discomfort and bad taste
- High \$1,600 list price



OX338 is expected to...









- ... be much easier to administer and have less patient discomfort
- ... not require the first dose to be given as an injection

Ketorolac Generics

- First dose must be given as an IM or IV injection
- Oral Gx are only indicated for continuation therapy after the injection
- Complicated dosing



There is limited activity in the ketorolac pipeline, especially for oral products

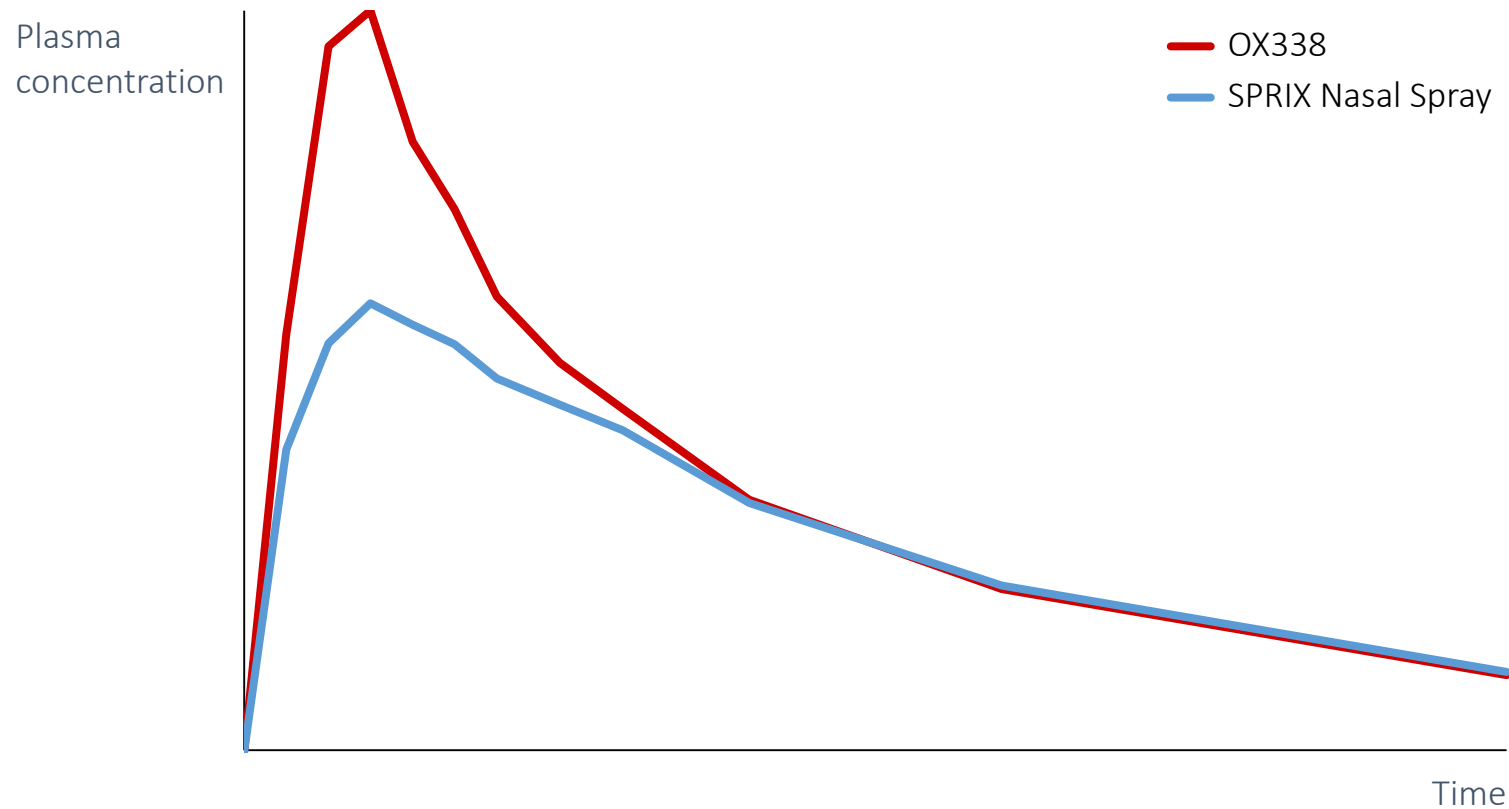
	Pre-clinical	Clinical	NDA filed	Approved/launched
Oral		 OX338, Planned NDA '22		 Toradol Oral Tablets
Other	 Intrathecal injection	 Patient-Controlled Analgesia	 Pre-mixed bag	 Toradol IV/IM injection
		 PatchPump, unclear status following acquisition by United Therapeutics		 Sprix nasal spray, approved '10

Note: Other projects which have been assumed inactive: Elliptical Therapeutics (Transdermal Patch); Insys Therapeutics (Sublingual Spray); Oxford Pharmascience Group (Oral tablets); PLx Pharma (Oral Capsules)
Sources: GlobalData, Company Webpages and Press-Releases

We have shown better PK profile than SPRIX® Nasal Spray

Faster uptake and higher peak vs. SPRIX® Nasal Spray

Results from exploratory PK study in healthy volunteers, 2019 (n=19)

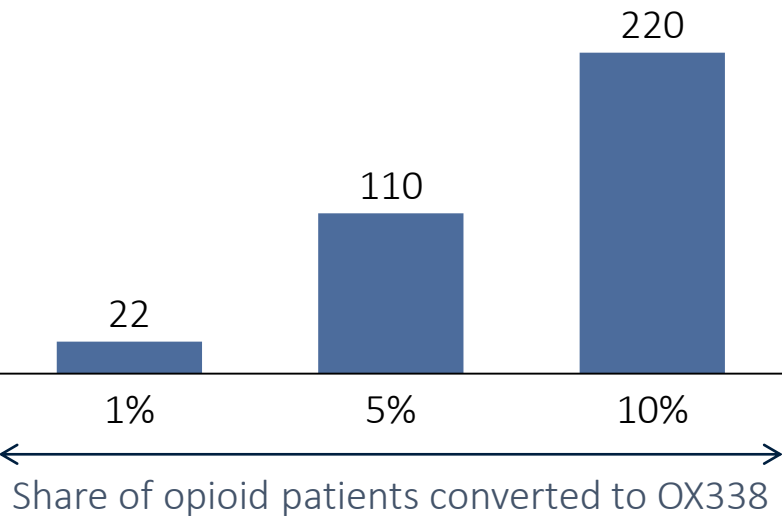


We see significant potential from converting unnecessary opioid prescriptions to OX338

Dental procedures

~11 million patients p.a. receive opioids after a dental procedure

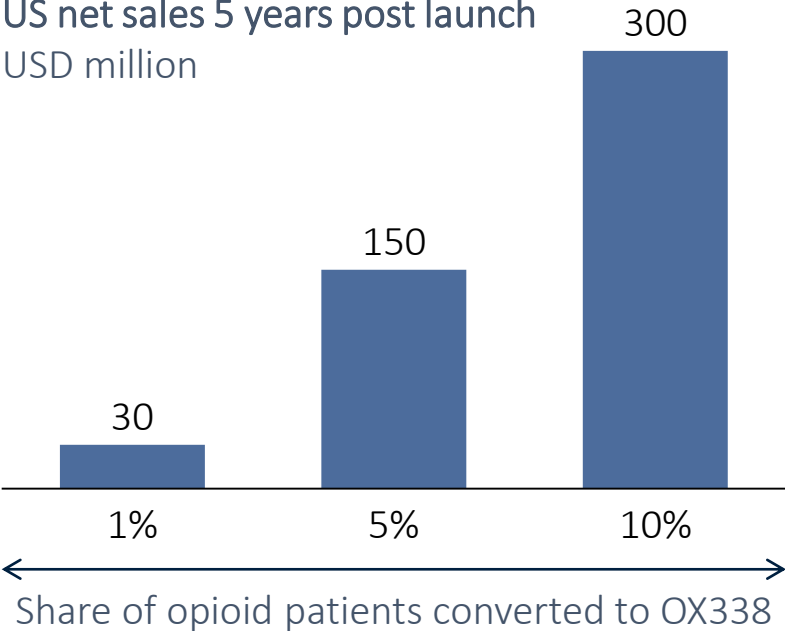
US net sales 5 years post launch
USD million



Ambulatory surgeries

~15 million patients p.a. receive opioids after an ambulatory surgery

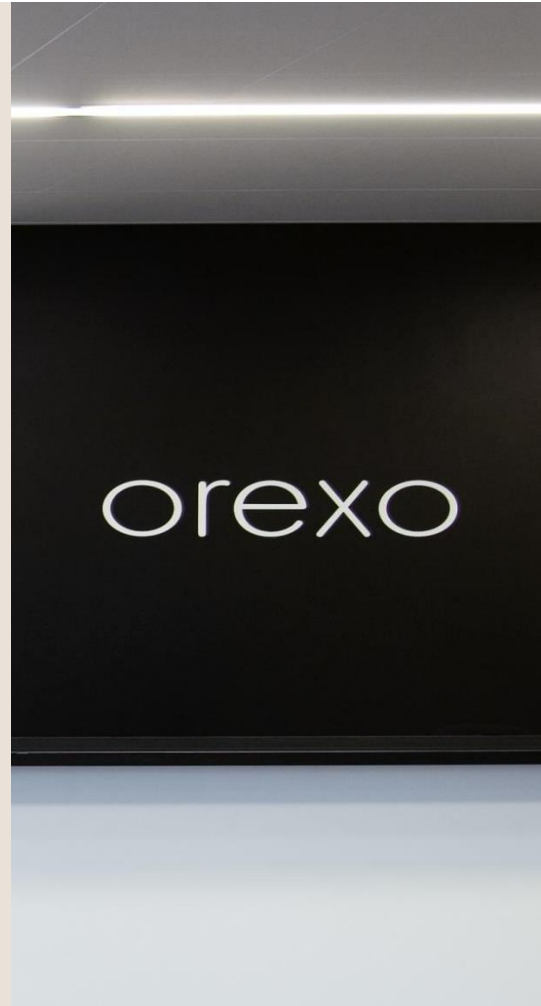
US net sales 5 years post launch
USD million



Key take-aways



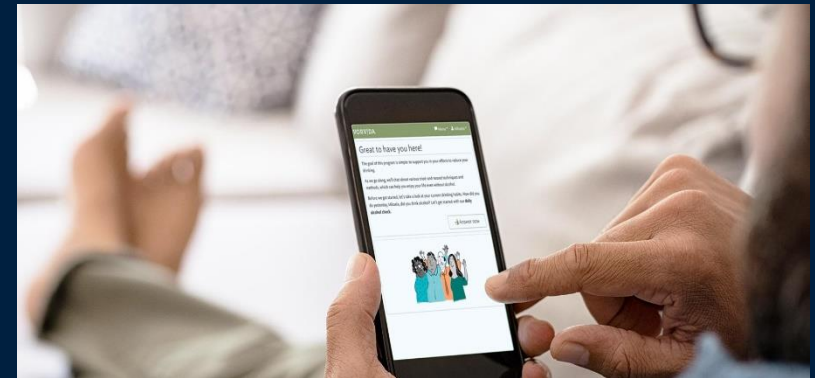
- **3 late-stage development assets** aiming at building the leading addiction company
- All in areas with **high unmet need** and with **clearly differentiated** product characteristics
- Highly **complementary with Zubsolv®** and our **existing commercial infrastructure** in the US
- All **successfully tested in humans** or about to enter clinical trial in humans, **first launch in 2022**
- Realistic opportunity to achieve **multiples of today's Zubsolv® sales**



Part 3 – Digital Therapeutics

DTx – new frontiers in patient care -
Dennis Urbaniak, EVP Digital Therapeutics

orexo



The COVID-19 global situation demonstrates the benefits of digitization of healthcare

Hospitals stress at unprecedented levels

Patients are flooding to virtual clinics and online medical councils

Companies are boosting their digital strategy on the back of the coronavirus

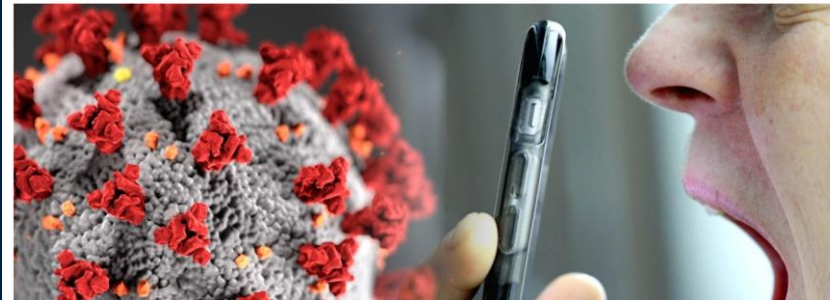
Digital and delivery services thrive on the coronavirus outbreak

As Italy's Hospitals Overwhelmed by Coronavirus, Top Health Official Says 'Worst Is Yet Come' for US

"We will see more cases and things will get worse than they are right now."

Patienter strömmar till nätläkarna efter corona

Av [JOHANNES KARLSSON](#) | onsdag 11 mars 2020 kl. 20:19 | johannes.karlsson@di.se | [@Karlsson_J](#)



Coronavirus' biggest winners: From Netflix to fitness bike maker Peloton

The COVID-19 virus has battered global markets and threatens to worsen the global economic slowdown. But not everyone is losing money even as the fast-spreading epidemic wipes out trillions from global markets.

Stay home, stay connected

Shares in teleconferencing startup Zoom Video have soared nearly 50% since February as investors bet on a rise in remote workplaces amid fears of the coronavirus spreading further. The company has already added more active users this year — 2.22 million — than it did in all of 2019, Bernstein Research analysts said. ⁴⁷

In a few months....

Patients

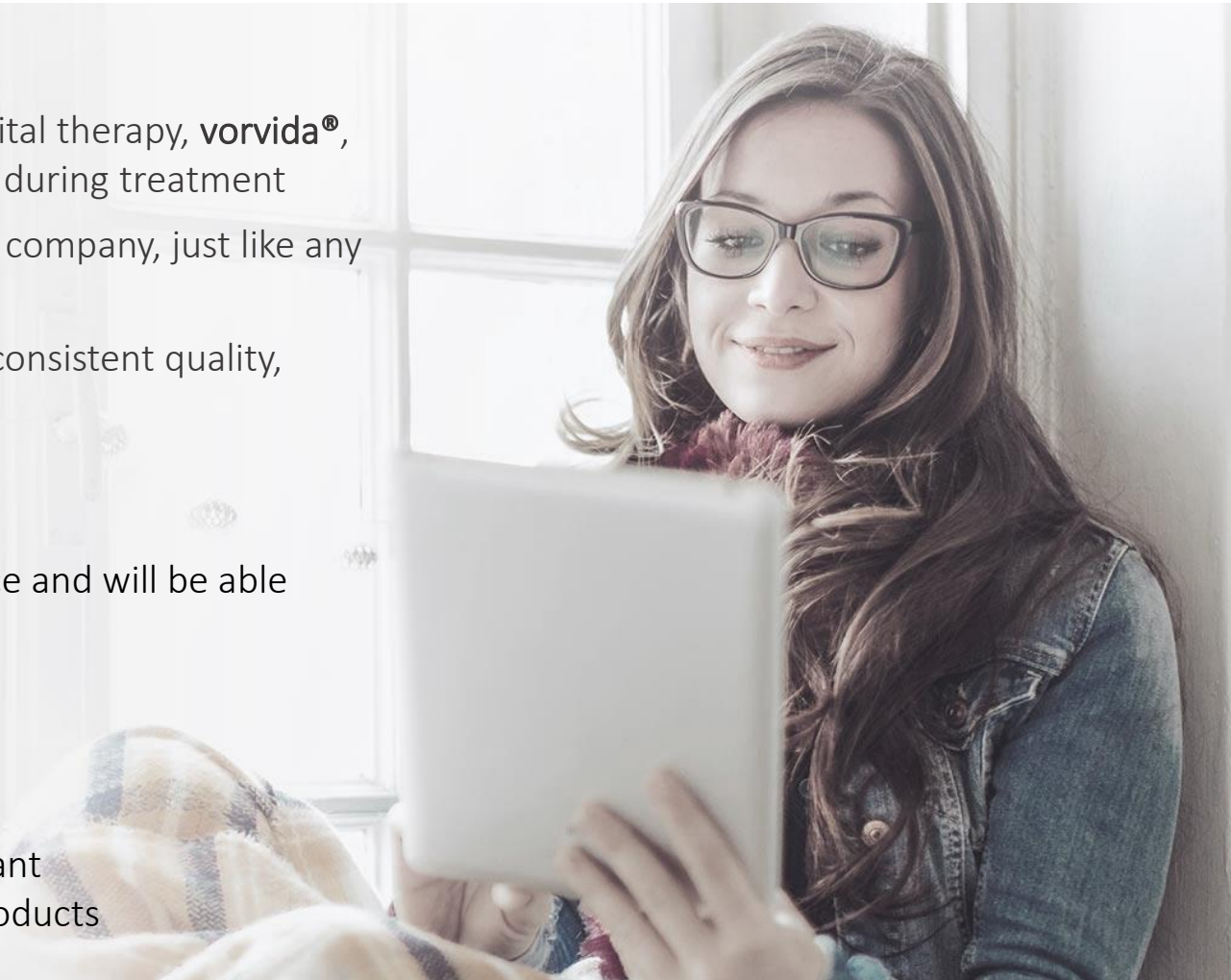
- ...suffering from alcohol misuse will have access to a new digital therapy, **vorvida**®, which replaces the need for frequent visits to a counsellor during treatment
- ...will get their digital therapy reimbursed by their insurance company, just like any other medical intervention
- ...will have access to gold standard behavioral therapy with consistent quality, when they have time and in their own privacy

Healthcare Professionals

- ...will have access to a treatment with strong clinical evidence and will be able to prescribe **vorvida**® like any other treatment available
- ...will be able to treat more patients with less efforts

Orexo

- ... will expand into a new adjacent disease area with significant unmet patient need and with a completely new type of products



Digital Therapeutics (DTx) is a sub-category of Digital Health



Source: DTx Alliance (Oct '18): "DTx: Combining Technology & Evidence-based Medicine to Transform Personalized Pt Care"

The regulatory and payer landscape is starting to adopt digital therapy ...

Significant movement in both US and Europe



The Digital Health Software Pre-certification (Pre-Cert) Program is part of an effort by the FDA to develop a future regulatory model that will provide more streamlined and efficient regulatory oversight of software-based medical devices.²



The Bundestag recently passed the German Digital Care Act (DVG), which requires public health insurance companies to cover the costs of certain health technology applications.¹

The two largest PBMs are reducing barriers for DTx



Express Scripts is placing companies, offering cutting-edge treatments, into a "formulary" of recommendations for insurance plans and doctors in order to ease commercial traction.³



CVS Caremark has launched a platform for digital therapies, enabling payers to formalize the reimbursement and distribution and allowing CVS to capitalize on booming interest in digital health treatments.⁴

Source: 1. Frontiers <https://www.frontiers.health/german-digital-healthcare-act/> 2. <https://www.fda.gov/medical-devices/digital-health/digital-health-software-precertification-pre-cert-program> 3. CNBC <https://www-cnbc-com.cdn.ampproject.org/c/s/www.cnn.com/amp/2019/12/12/express-scripts-to-add-digital-health-treatments-like-livongo-omada.html> 4. Business Insider <https://www.businessinsider.com/cvs-caremark-launches-digital-therapeutics-platform-2019-6?r=US&IR=T>

... but digital therapy is in its infancy

Commercialization

- Optimal pathways to commercialize and scale DTx are still uncharted

Pricing

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

Reimbursement

- Many payers 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



Establishing a pricing and payer model is critical for future success in digital therapy

Alternative Payer Models

Orexo sees several alternatives for future payer models and will not apply a traditional one-fits-all Rx model

Pharmaceutical Model

- Reimbursement similar to pharmaceuticals or other medical benefits by insurance companies and employers

Framework agreement models

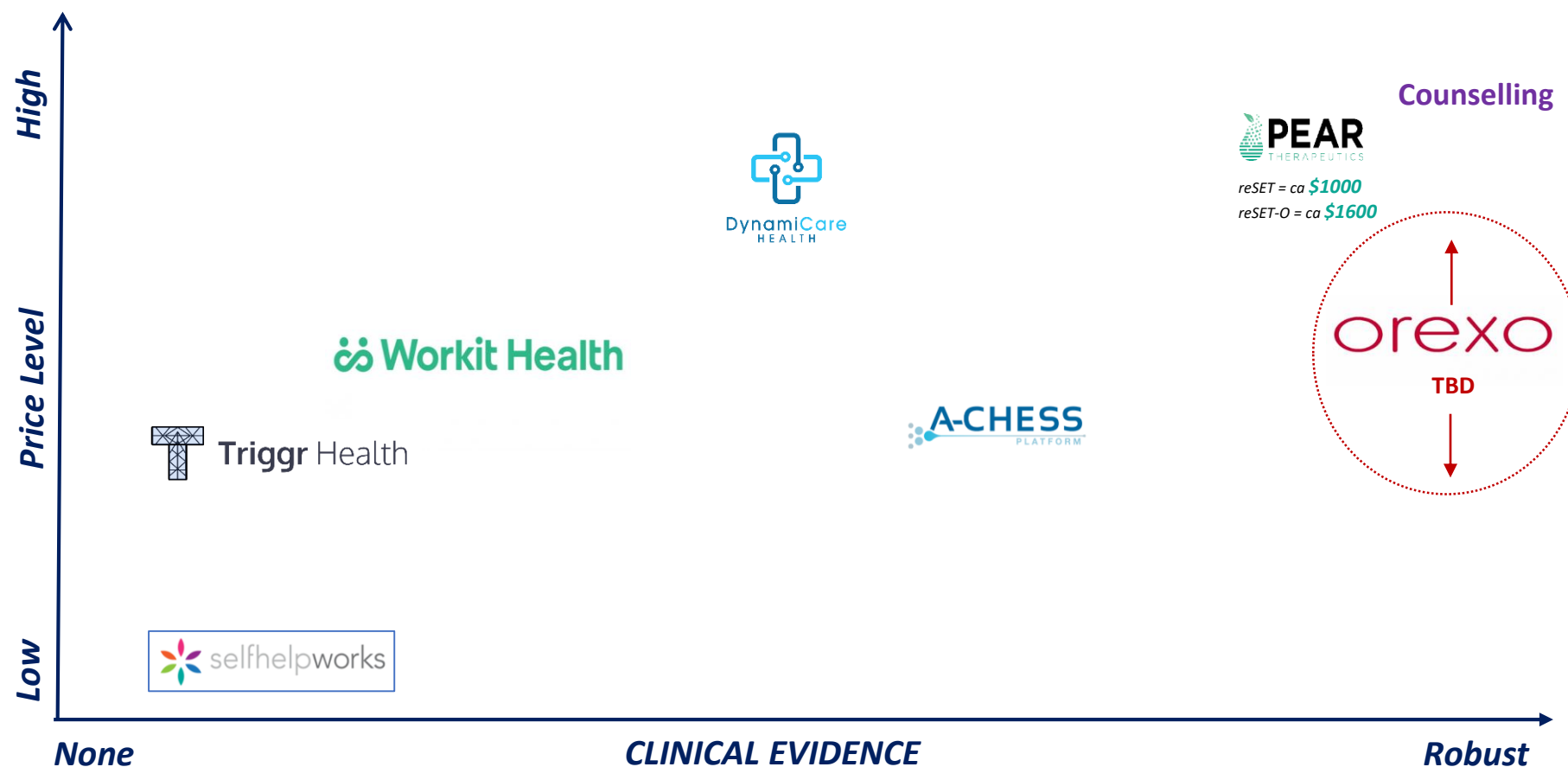
- Agreements with specific insurance companies to cover all customers
- Agreement with institutional health care providers

Patient model

- Patients paying for the therapy out-of-pocket

Payer models are evolving continuously, but no established standard has emerged

The pricing of digital therapy is scattered, with significant differences driven by sophistication and clinical evidence



Pricing of Orexo DTx expected in the range of USD 600-1,000 per treatment

Digital therapy has the potential to become a very important tool in the treatment of addiction

The unmet need

Addiction is a highly stigmatized behavioural disease requiring a multi-faceted approach to treatment with both pharmaceutical and behavioural therapy

Our aim

Orexo will become the leading provider of clinically proven digital therapy for addiction treatment in the US. Leveraging our unique position with field force in all large cities in the US

The value to patients





Patients can access a gold standard behavioural therapy with consistent and quality therapeutic intervention, when they need the interactions the most

The value to healthcare

Orexo enables physicians and counsellors to treat more patients, more efficiently with significantly better monitoring of patient treatment progress



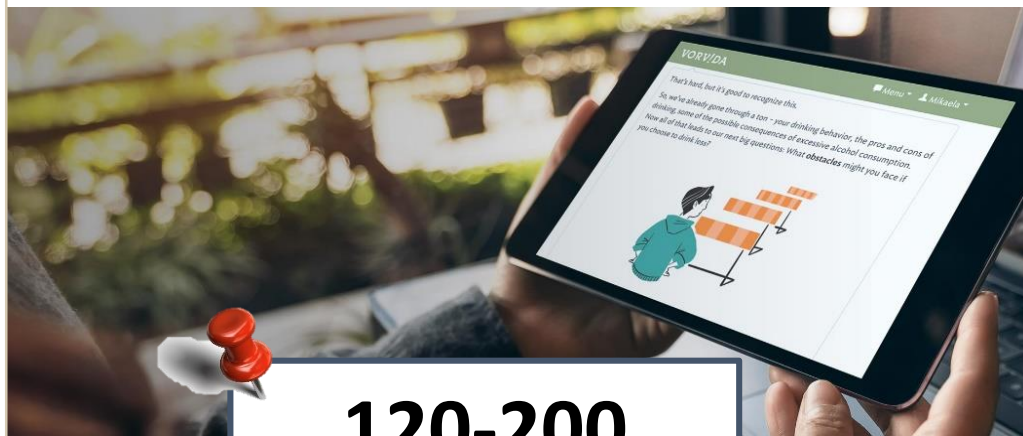
How we define our playing field

	Description	Orexo position
 <div>Aspect of patient journey</div>	<ul style="list-style-type: none">Digital therapy products cover the full patient journey, ranging from Wellness and Prevention, symptom onset and seeking care, diagnosis, condition monitoring to treatment	<ul style="list-style-type: none">Our focus is on products that treat a disease with measurable outcomes
 <div>Scientific evidence</div>	<ul style="list-style-type: none">Most digital offerings have no scientific data or have data that lacks scientific depth and rigor	<ul style="list-style-type: none">We will only consider products with sound scientific evidence from well-run clinical studies
 <div>Regulatory oversight</div>	<ul style="list-style-type: none">A small number of digital therapy offerings seek involvement/oversight from FDA	<ul style="list-style-type: none">We will seek different levels of FDA involvement depending on the product in order to open reimbursement pathways and establish relevant price points
 <div>Therapy area</div>	<ul style="list-style-type: none">Digital therapies are spread over different therapy areas with a focus on CNS	<ul style="list-style-type: none">We will focus our digital therapy efforts in those areas that provide synergies to our existing portfolio and future assets

Two digital therapies with the potential to disrupt the current treatment of substance use disorder in the US

vorvida®

A fully automated digital therapy scientifically proven to reduce trouble-some drinking patterns in adults with AUD

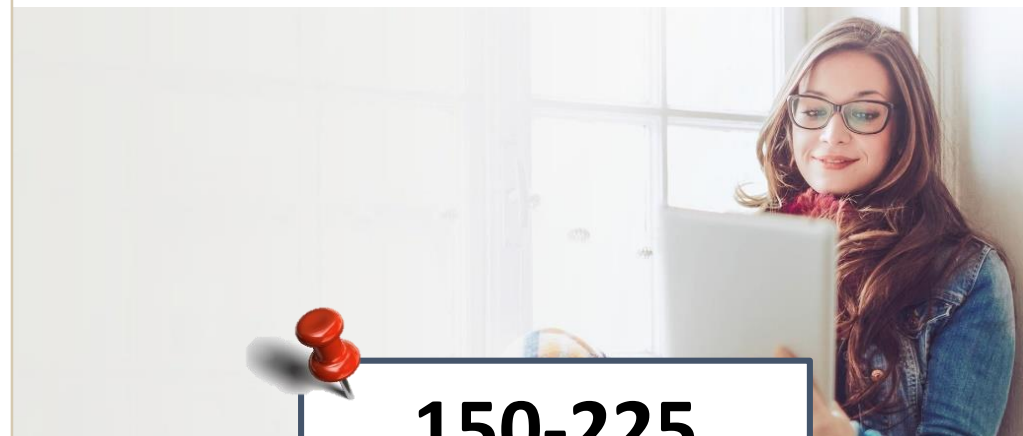


120-200

MUSD net sales potential in the US

OXD01

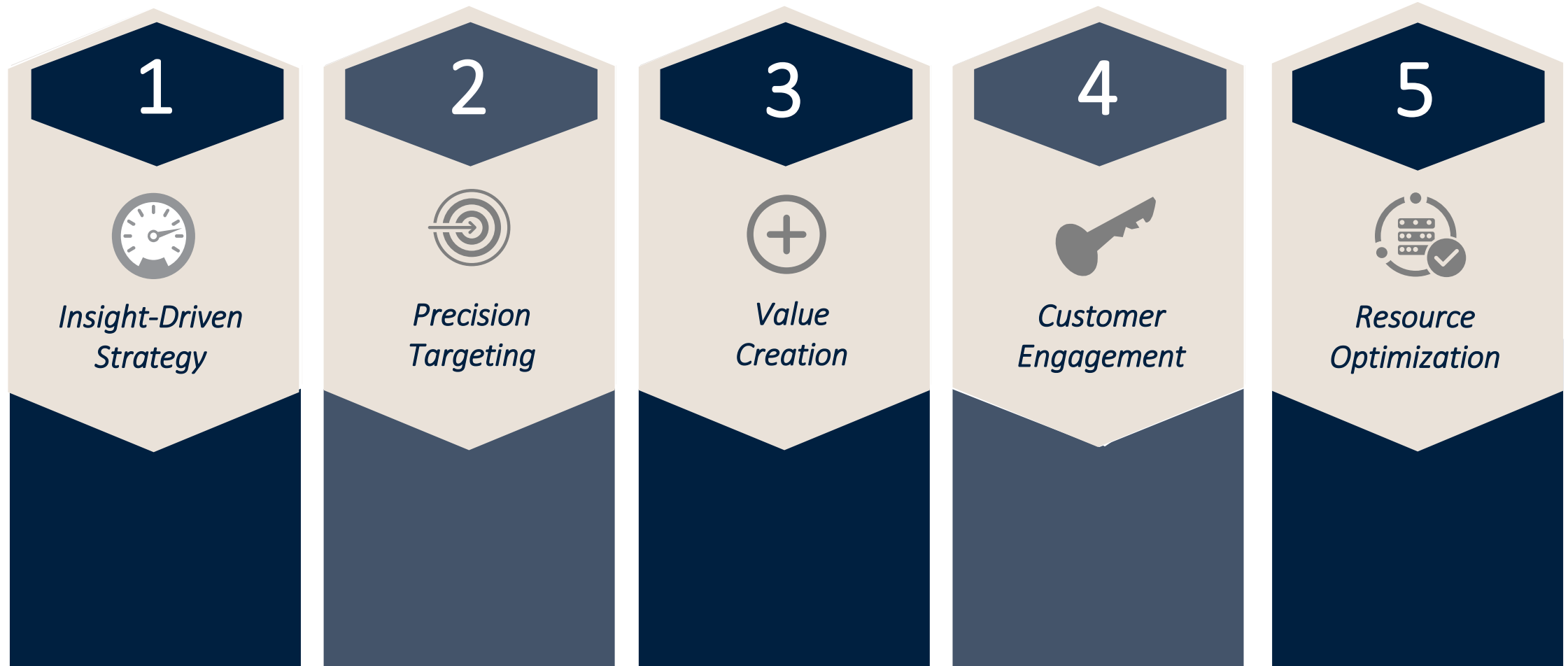
“Digitizing” counselling at scale to offer with Zubsolv®, a full medication assisted therapy (MAT) solution for so many opioid use disorder (OUD) patients in need.



150-225

MUSD net sales potential in the US

A cohesive philosophy underpins the DTx commercial approach



Limited investments required to establish Digital business unit



The Orexo/GAIA partnered digital therapies – vorvida

- vorvida® – digital therapy of alcohol misuse
- OXD01 – digital therapy of opioid use disorder

vorvida® at a glance

The unmet need

Alcohol misuse is a highly stigmatized, only few people seek professional help, and those who seek help will have issues finding quality support

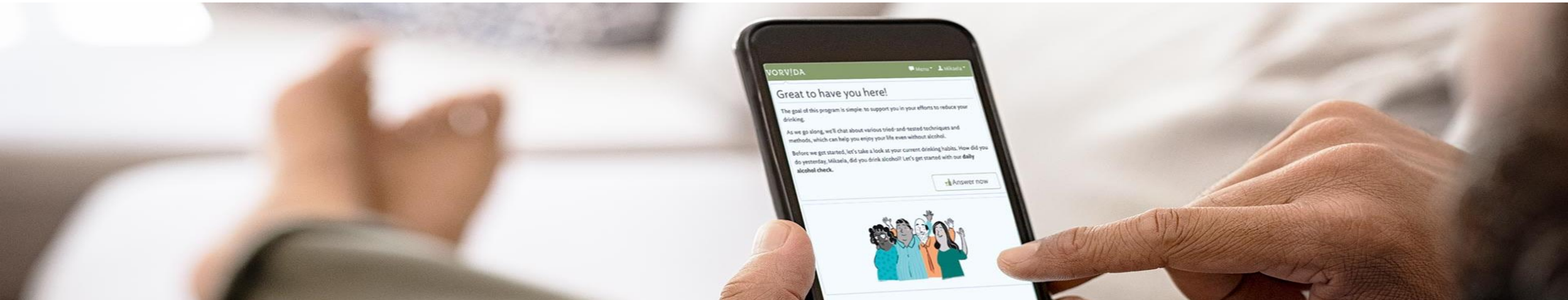
Our aim

Establish vorvida® as the leading digital therapeutic for people suffering from alcohol misuse

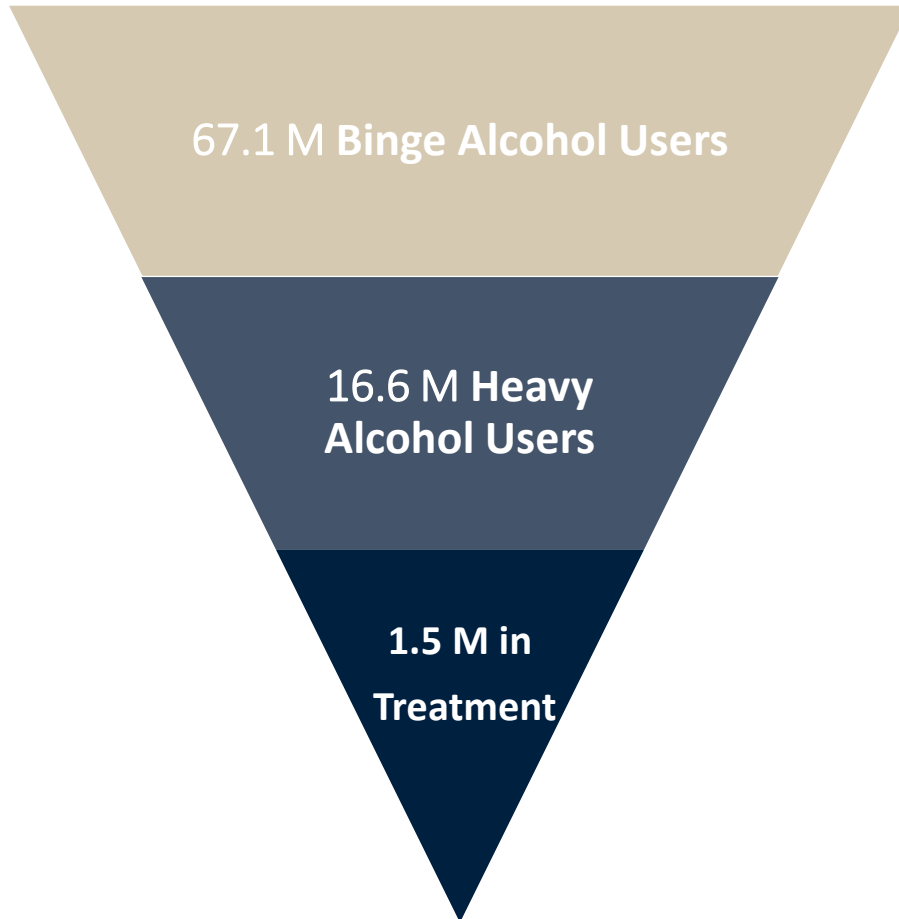
The US potential

120-200

million USD
net sales



16.6 million Americans suffer some problematic drinking and less than 10% are in treatment



- Roughly **95 percent** of Americans struggling with alcoholism do not feel they need treatment for their condition
- In 2014, 431,000 women and 1.1 million men received treatment for an alcohol use disorder
- Lack of treatment is a result of **stigmatization, limited understanding of one's own dependence**, and a lack of effective and private treatment options
- Consequently, there is a significant gap in the market and thus, an opportunity for Orexo

Binge Drinking:

Men: Drinking five or more drinks on the same occasion on at least 1 day in the past 30 days

Women: Drinking four or more drinks on the same occasion on at least 1 day in the past 30 days

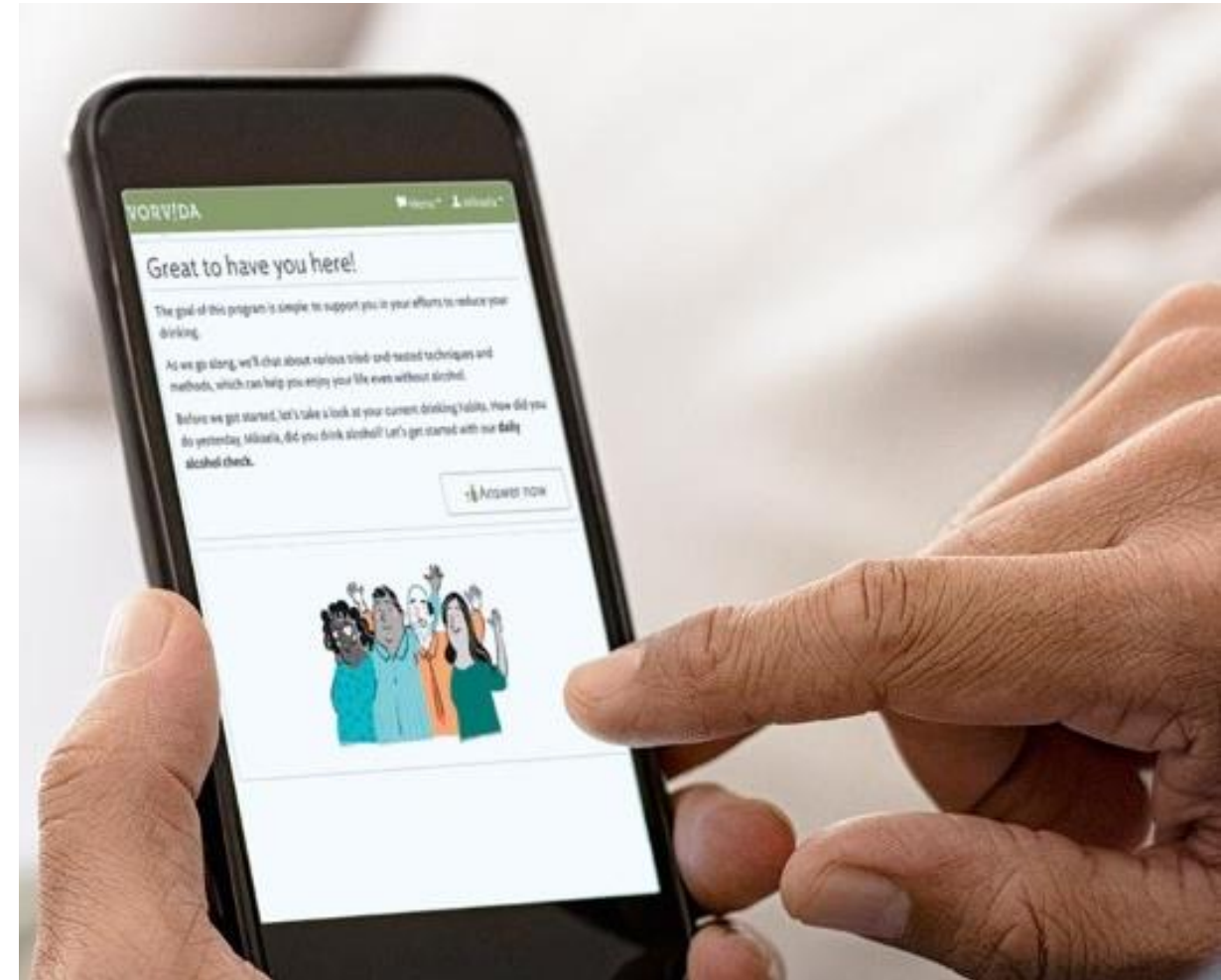
Heavy alcohol use is defined as binge drinking on 5 or more days in the past 30 days

So what is vorvida®?

vorvida® is a digital therapeutic targeted to people with excessive alcohol use who wish to reduce their alcohol consumption

- A 6-month treatment platform anchored in Cognitive Behavioral Therapy (CBT)
- Web-based, self-directed, individualized treatment that can be used with or without the direction or participation of a physician
- vorvida® has been studied in a randomized clinical trial with over 600 adults with problem drinking behavior with results showing significant reduction in alcohol consumption

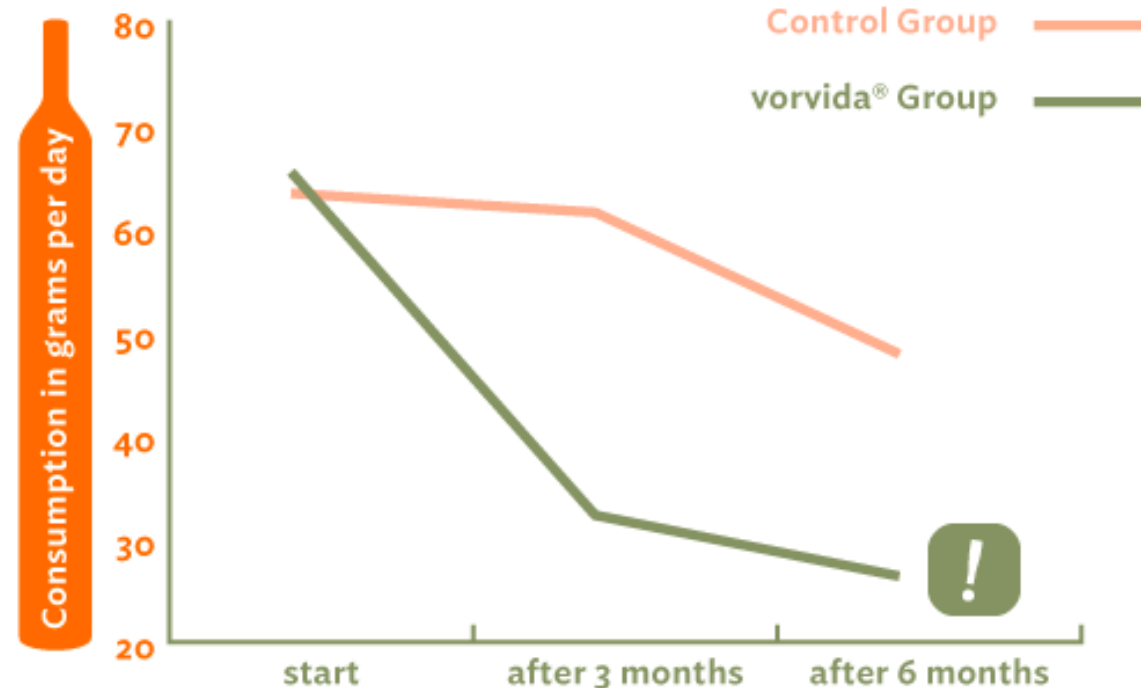
vorvida® is a medical device with its intended use for patient self-management of bothersome or harmful alcohol use patterns or in alcohol dependence as self-diagnosed or diagnosed by a physician



The evidence for vorvida®

- Randomized controlled trial: 608 adults with problematic alcohol consumption randomized to vorvida® or care as usual/waitlist.
 - Mean reduction in alcohol consumption of 104g per week compared to control condition (169g vs 65g after 6 months)
 - **>10 fewer binge drinking days per month** compared to control condition (5.3 vs 16.5 after 6 months)
 - >30% of study participants in the intervention group **reduced their drinking behavior from high to low risk** (vs. 7% in the control group) after 6 months
 - After 6 months: 63% remained in treatment in the vorvida-group and 73% in the waitlist control group.

VORV!DA Significantly Reduces Alcohol Consumption



Notes: * Funded by the German Federal Ministry of Education and Research. Patients were recruited online and offline.

Source: Zill et al. 2019. The effectiveness of an internet intervention aimed at reducing alcohol consumption in adults (vorvida®): Results of a randomized controlled trial. Deutsches Ärzteblatt

Early qualitative market research feedback

PCP

“[The product] looks great – it’s something somebody can do online on a regular basis, in other words not monthly visits which is what I do. That lets them do it privately and shows significant reduction in monthly consumption. All seem like valid endpoints to me.”

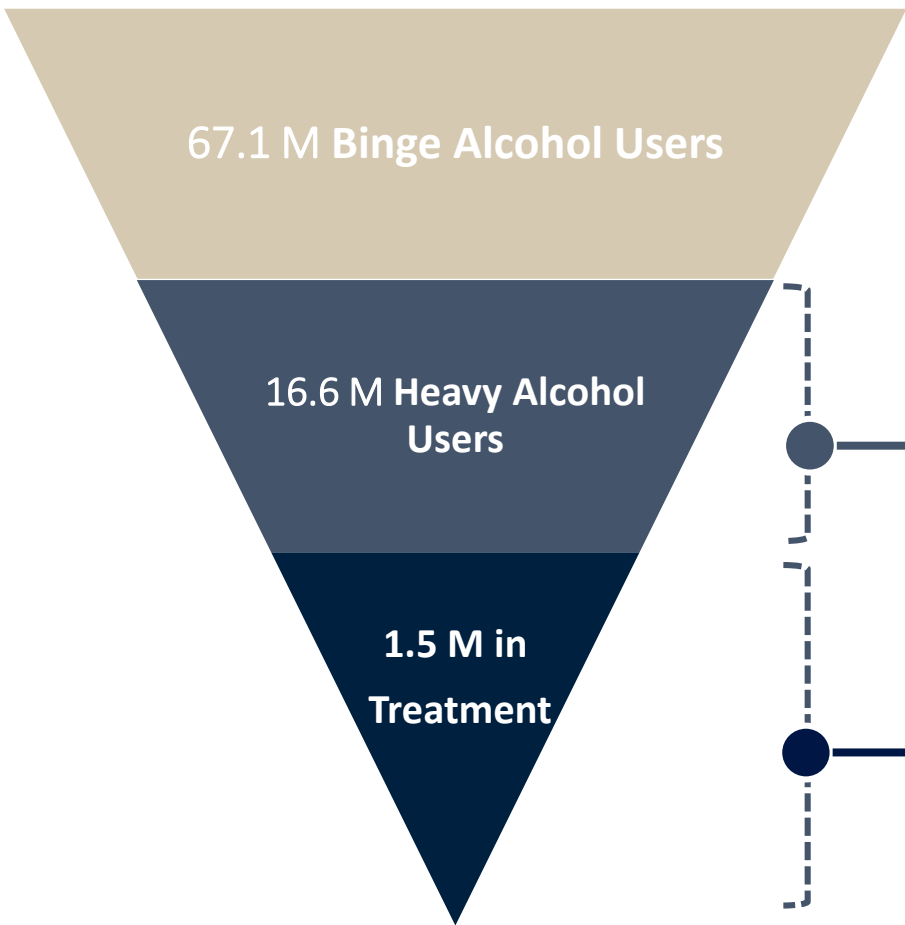
Therapist

“I think it looks great. Cognitive Behavior Therapy is an established theory that you know proven to be effective...And [with a digital therapeutic] there’s no possibility of judgment from a provider.”

Psychiatrist

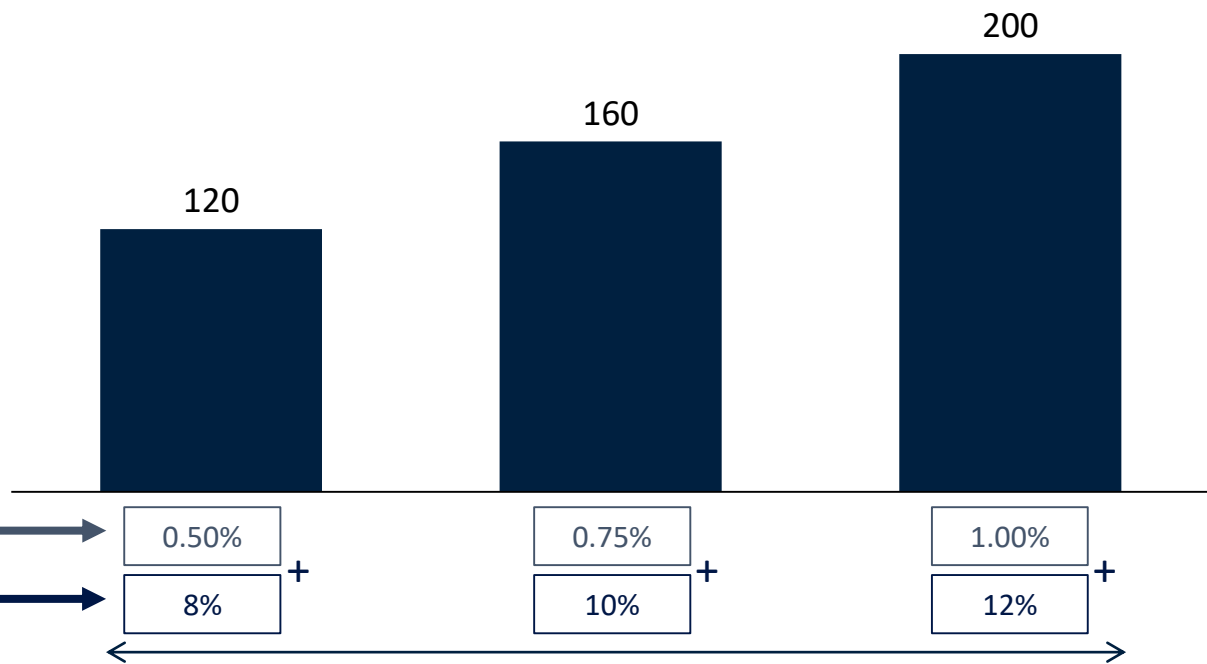
“As long as they are willing to use a smartphone and they are not in denial that they have an alcohol problem, then this will be a great beginning. And if it’s FDA approved, then I’m happy.”

vorvida[®] net sales potential of USD 120-200 million



vorvida[®] US Net Sales 5 years post launch

Forecast, USD Million given price of USD 600 per treatment¹



vorvida[®] Market Share

- Large unmet need both among treated and untreated Heavy Alcohol Users
- vorvida[®] will be strategically priced to optimize attractiveness of the treatment

¹ USD 600 per treatment used as a conservative price floor

We are expecting clearance from FDA in Q2 and launch in Q3 2020



The Orexo/GAIA partnered therapies – OXD01

- vorvida[®] – digital therapy of alcohol misuse
- **OXD01 – digital therapy of opioid use disorder**

OXD01 at a glance

The unmet need

Access to consistent high-quality counselling is a growing bottleneck in treatment of OUD. Medical assisted treatment should be complemented with psychosocial support

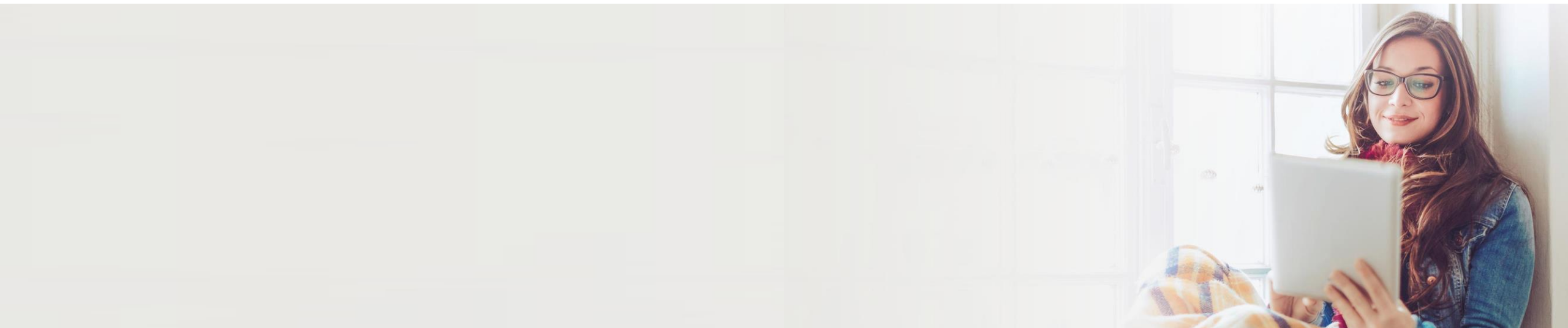
Our aim

Develop the first digital therapy showing significant sustainable positive outcome on patients' treatment of OUD and make it available globally

The US potential

150-225

million USD
net sales



Strong logic for Orexo to invest in OXD01

Compulsory Part of Pharmacological Therapy

- All Buprenorphin/Naloxone (Bup/Nal) come with label instructing it "should be used as part of a complete treatment plan that includes counseling and psychosocial support"
- Limited access to psychosocial support is an issue for many patients and physicians

Well defined market

- Buprenorphine/Naloxone market is well defined and highly concentrated

Opioid Epidemic

- Opioid crisis creates a significant support for new innovative treatment alternatives

Orexo has a strong position

- Orexo is well established in the Bup/Nal market and only company with a field force reaching into the smaller clinics with highly limited access to psychosocial support

Potential spill-over effects

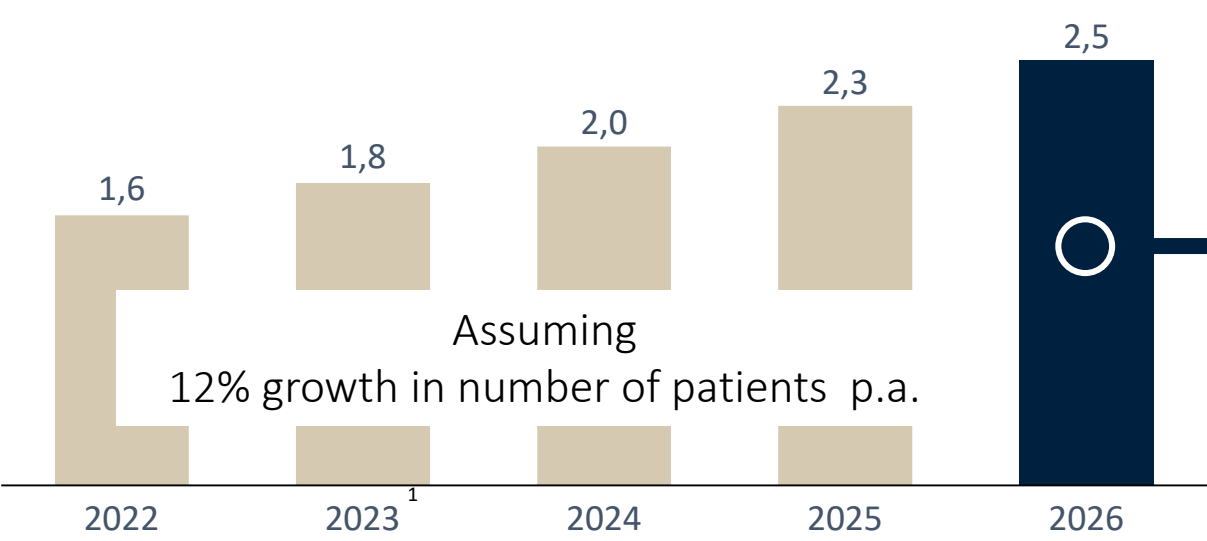
- OXD01 offers significant stand-alone potential, but is likely to have positive spill-over effects on Zubsolv®

**Logic for
investing in
OXD01**

OXD01 has a US sales potential of USD 150-225 million and in addition Orexo has global rights to the product

Buprenorphine MAT Market Development

Forecast, Buprenorphine Treated Population Million

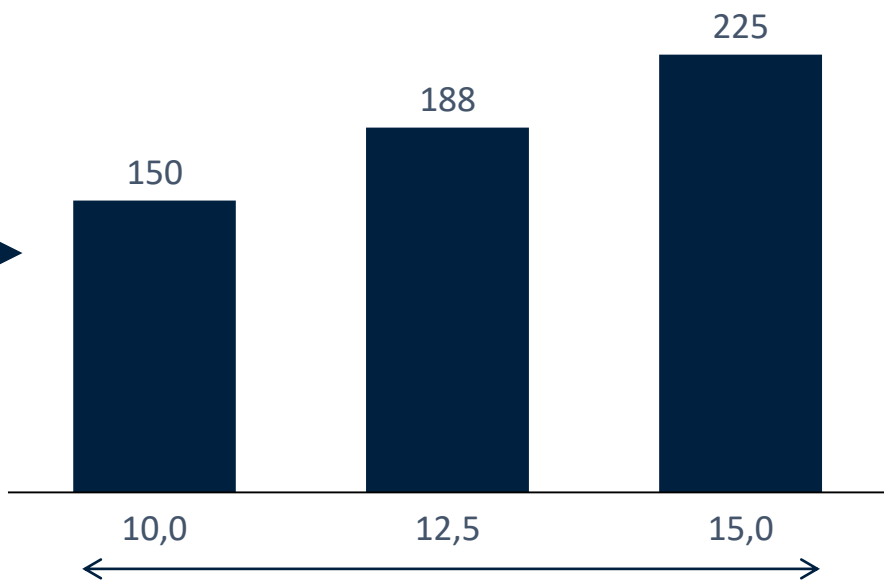


OXD01 Launch

- Continued increase of opioid addicted patients
- OXD01 has further opportunities among patients receiving non-Buprenorphine treatment

OXD01 US Net Sales 5 years post launch

Forecast, USD given price of USD 600 per treatment



OXD01 Market Share

- Stronger product than currently marketed competition
- Existing retail field force with track record to fight for market share in competitive market

¹ Clarion Healthcare

The current estimated timeline to market for OXD01



Key take-aways

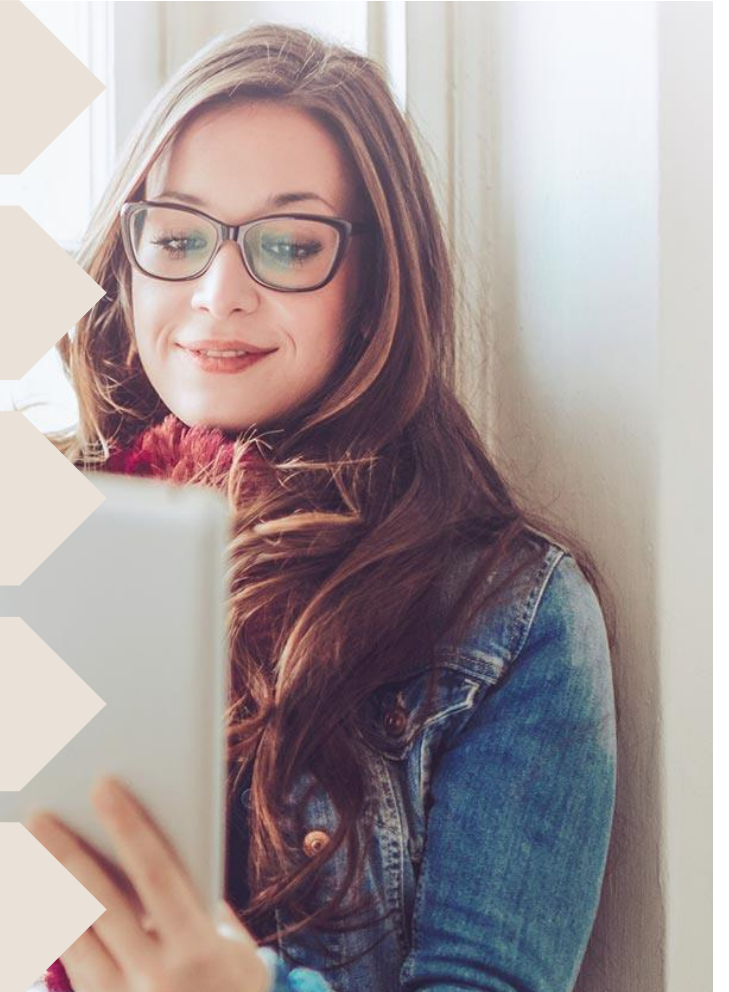
Strong macro tailwinds for digital therapeutics with increasing demand and beneficial legislative initiatives

Orexo has an early mover advantage to help shape the direction of digital therapeutics

Non-traditional payer model approach

vorvida[®] strong US sales potential and estimated to launch in H2 of 2020

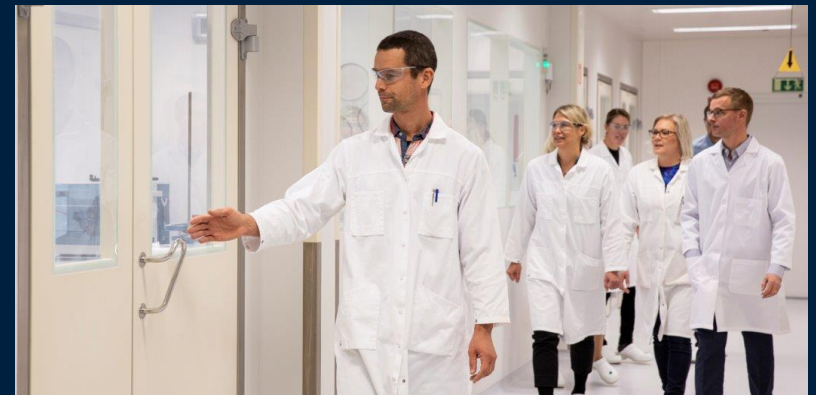
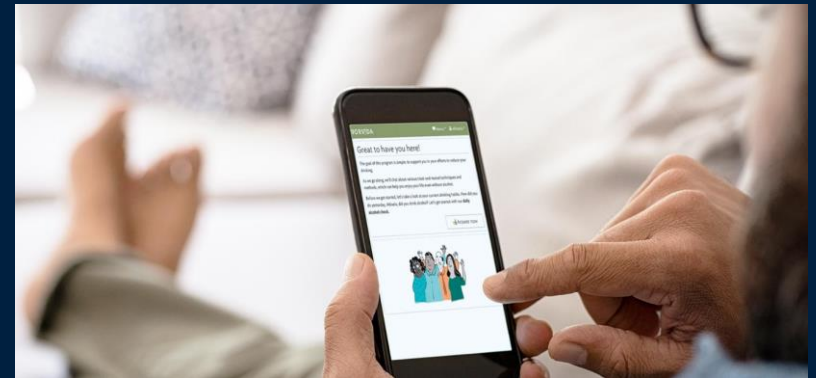
OXD01 is progressing well through development and will be ready for clinical trials early 2021



Part 3 – Digital Therapeutics

GAIA – a global leader in DTx -
Dr. Mario Weiss, CEO and founder of GAIA AG

orexo



GAIA: Inventing Digital Therapy (DTx)

Dr. Mario Weiss, MBA

CEO

Orexo Capital Market Day Stockholm 17/03/2020

GAIA AG

Science | Technology | Therapy

www.gaia-group.com

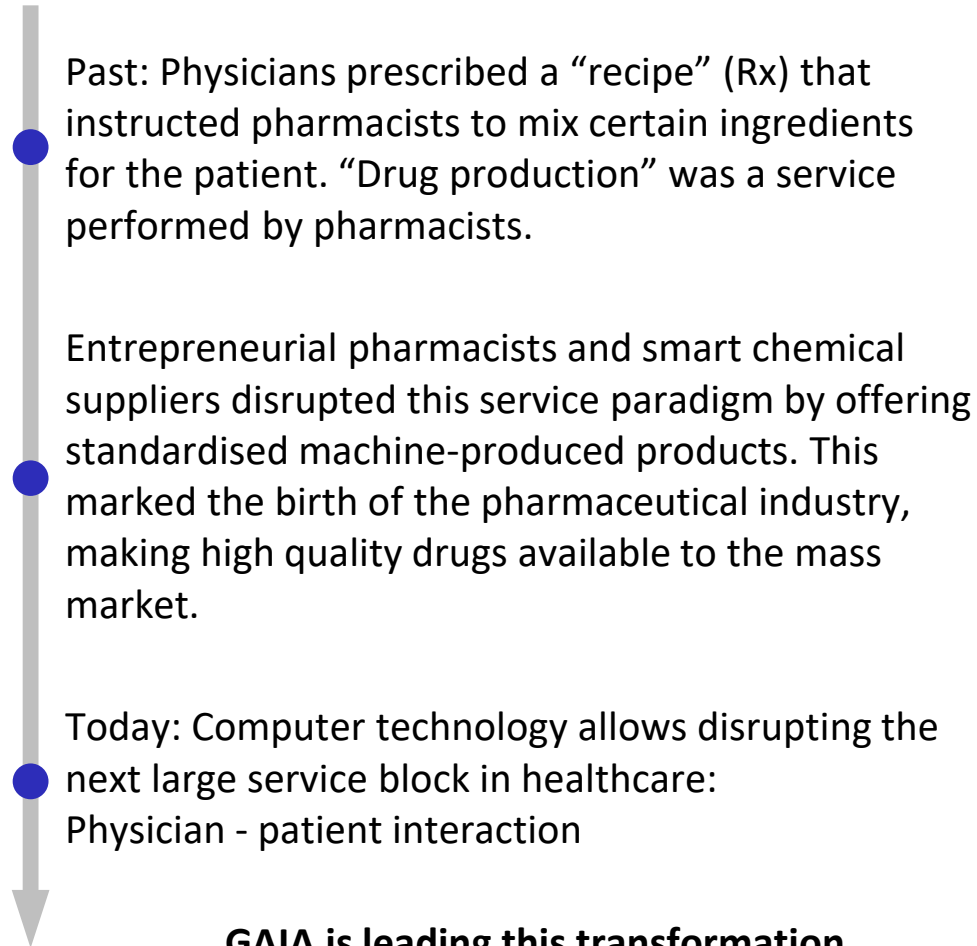
GAIA is leading the next disruption in healthcare: Digital therapy



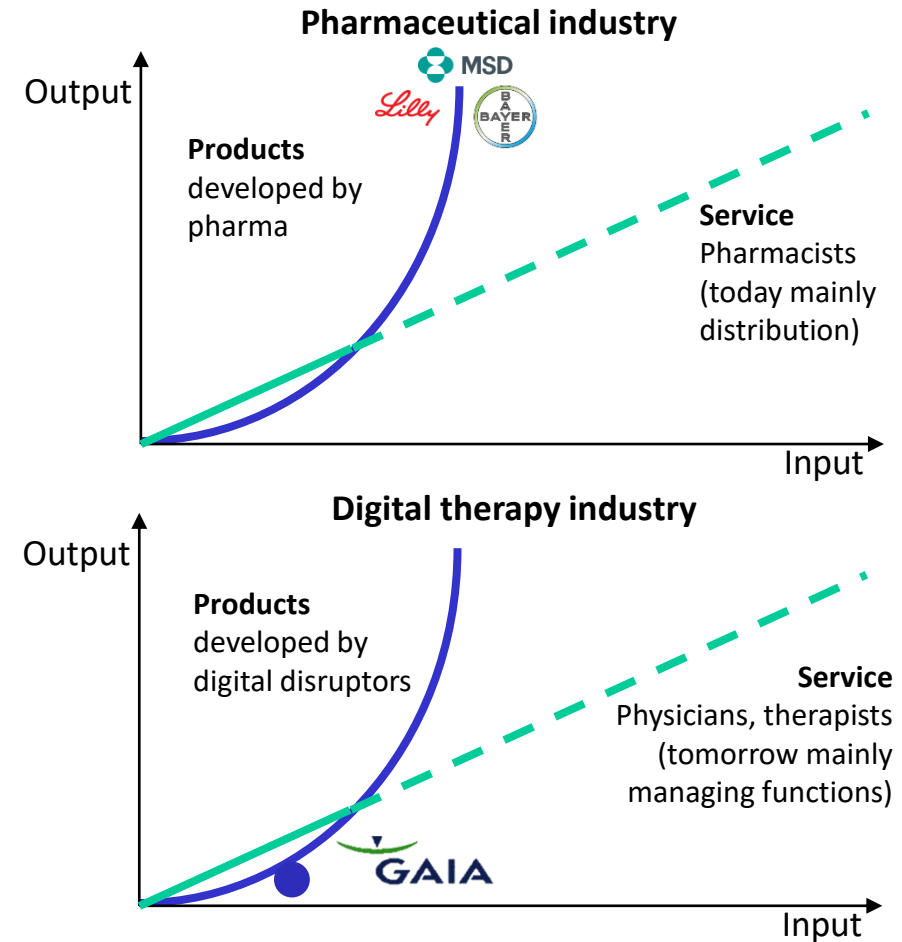
- ▶ GAIA's digital therapeutics (DTx) are **as effective as drugs and medical devices**, demonstrated in both numerous RCT's with over 9,000 patients in various healthcare settings and real-world experiences in the US, Latin America, Europe and Asia
- ▶ First DTx launch 2001
- ▶ Strong R&D: Broad product pipeline in the fields of behavioural health, immunology, oncology, SUD and pain
- ▶ 150+ experts in life science, psychology, management, software (incl. UI/UX), and regulatory affairs
- ▶ Located in Hamburg, Germany, with R&D activities in the USA and in the EU



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.



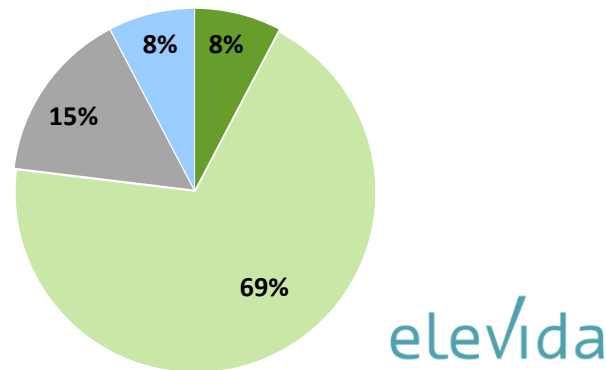
GAIA is leading this transformation



*But: Can consultation with software be **as satisfying** for the patients as a personal consultation? Feedback examples of GAIA products:*

Psychotherapeutic consultation


- ▶ “How would you assess the quality of GAIA’s software *elevida*® compared to ‘real therapy’ (by a human psychotherapist)?”¹



- | | |
|---------------------|--------------------|
| ■ Definitely better | ■ Rather worse |
| ■ Rather better | ■ Definitely worse |
| ■ Just as well | ■ Cannot evaluate |

Orthopaedic consultation

- ▶ “How would you rate GAIA’s software *Dr. Beck*® compared to a real physician?”²

- ▶ 84% patients say Dr. Beck® provides at least as much support as their respective physician
- ▶ 2/3 of patients who suffer from back pain state that Dr. Beck® helped them in overcoming the pain
- ▶ Patients describe Dr. Beck® as helpful, informative, and likeable 

▶ **GAIA is able to develop software that the majority of patients like / accept as much as a personal interaction with their physician and psychotherapist**

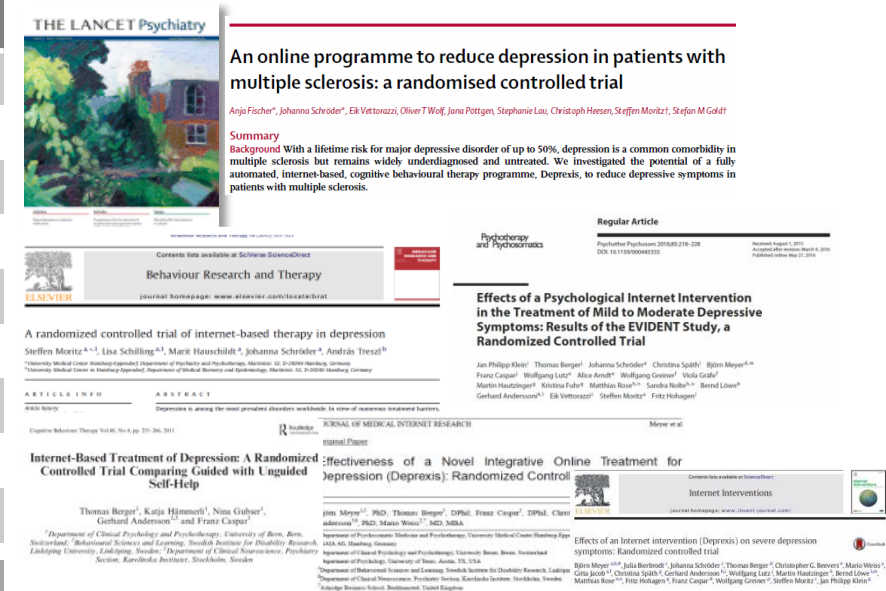
¹Poettgen J et al. Abstract 135. Presented at: The European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) Congress; Oct. 7-10, 2015; Barcelona.

²Internal Aribus company valuation., Richard-Merten-Grant for quality management in healthcare.

But: Is software consultation **as effective** as personal consultation with a physician or psychotherapist?

Example: Effectiveness of GAIA's therapy software deprexis® (depression treatment)

RCT	# of Patients	Effectiveness (Cohen's d)
Meyer (2009)	396	Medium 0.639
Berger (2011)	76	Large (0.853)
Moritz (2012)	210	Medium (0.433)
Schröder (2014)	78	Small (0.220)
Fischer (2015)	90	Medium (0.425)
Meyer (2015)	163	Medium (0.570)
Klein (2016)	1,013	Medium (0.386)
Beevers (2016)	376	Large (0.816)
	2,402	Medium (0.544)
Personal psychotherapy consultation (CBT)		Medium (0.50 ¹)

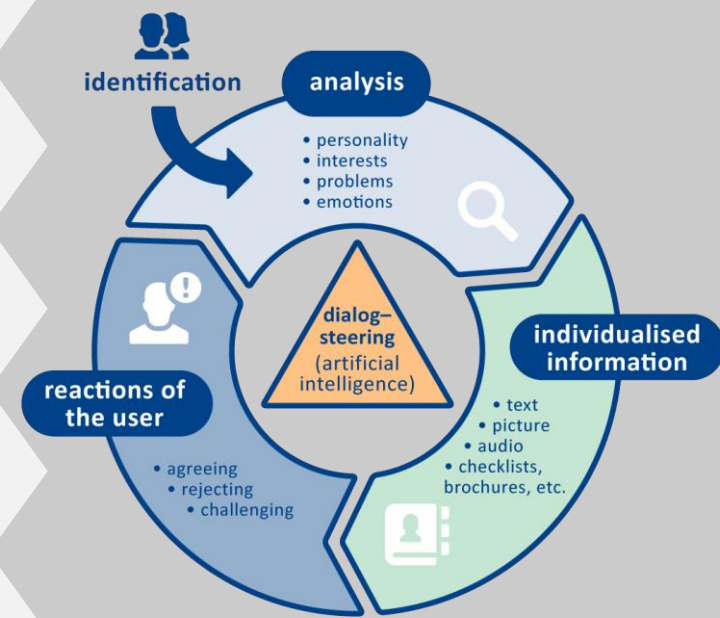


- ▶ **GAIA's software has the same effectiveness as personal consultations - even in the most sensitive doctor patient interaction (psychotherapy). This has been proven in numerous published RCTs**
- ▶ **Availability:** 24/7 on mobile devices = unmet high demand for helpful consultations can be met
- ▶ **Scalability:** Hardly any production and distribution costs on global scale


¹Barth, J., Munder, T., Gerger, H., Nüesch, E., Trelle, S., Znoj, H., ... & Cuijpers, P. (2013). Comparative efficacy of seven psychotherapeutic interventions for patients with depression: a network meta-analysis. PLoS Med, 10(5), e1001454.

*The tech backbone: GAIA's Artificial Intelligence (AI) software **broca**® simulates interaction between the patient and an empathetic physician/ therapist – highly individualized, fully automated and scalable.*

- ▶ **100% mobile and cloud-based:** for 24/7 usage on any mobile device (PC, tablet, smartphone)
- ▶ **Complex cognitive-functional interventions** to modulate brain functions and thought processes
- ▶ **Individualised:** Tailored provision of information and exercises based on continuous identification of the patient's needs and emotional situation
- ▶ **In-depth collection** of individual **patient data** to trigger further research and patient interaction
- ▶ **Input from wearables** used to drive further content and user interaction

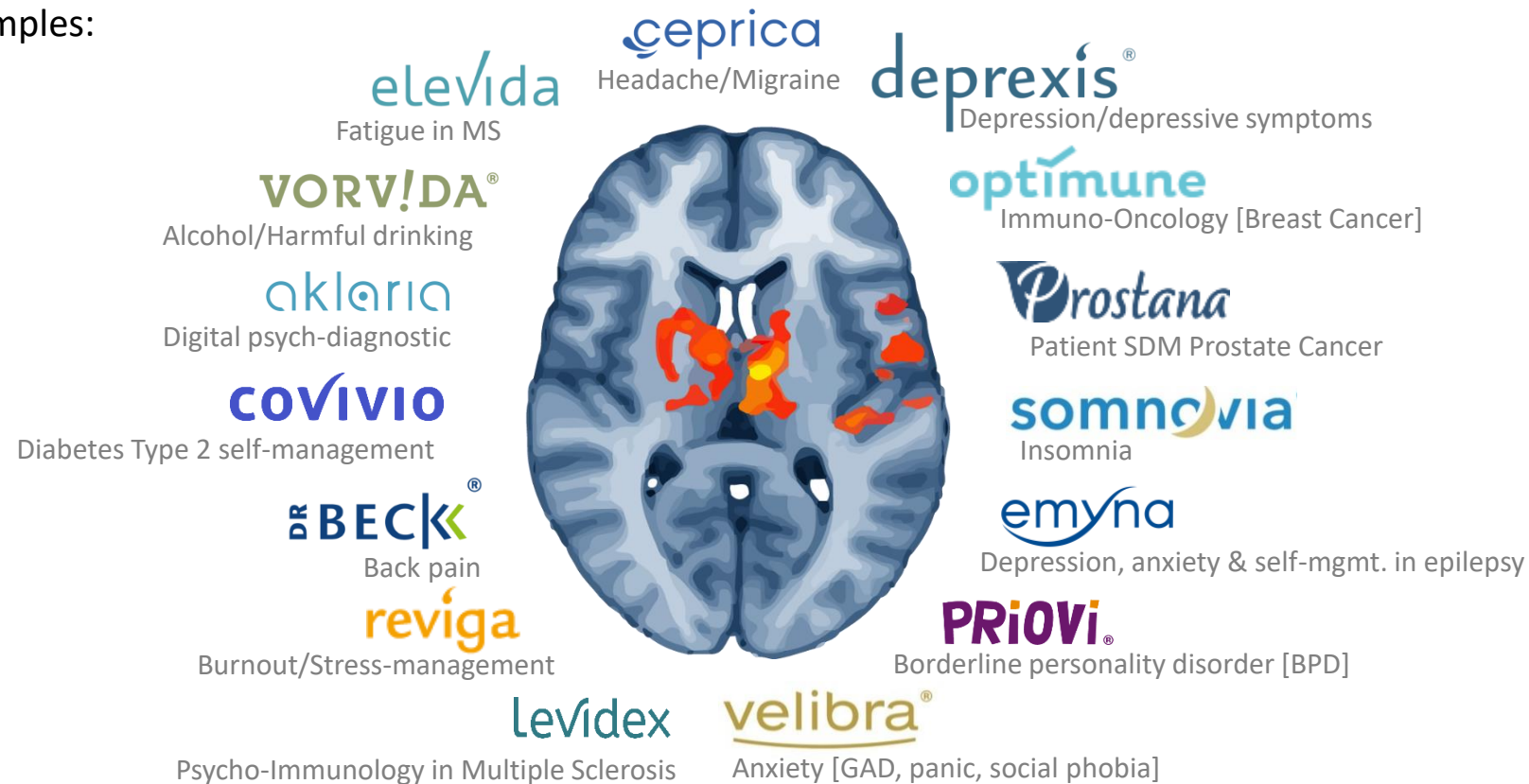


HIPAA / GDPR / MDR 2020

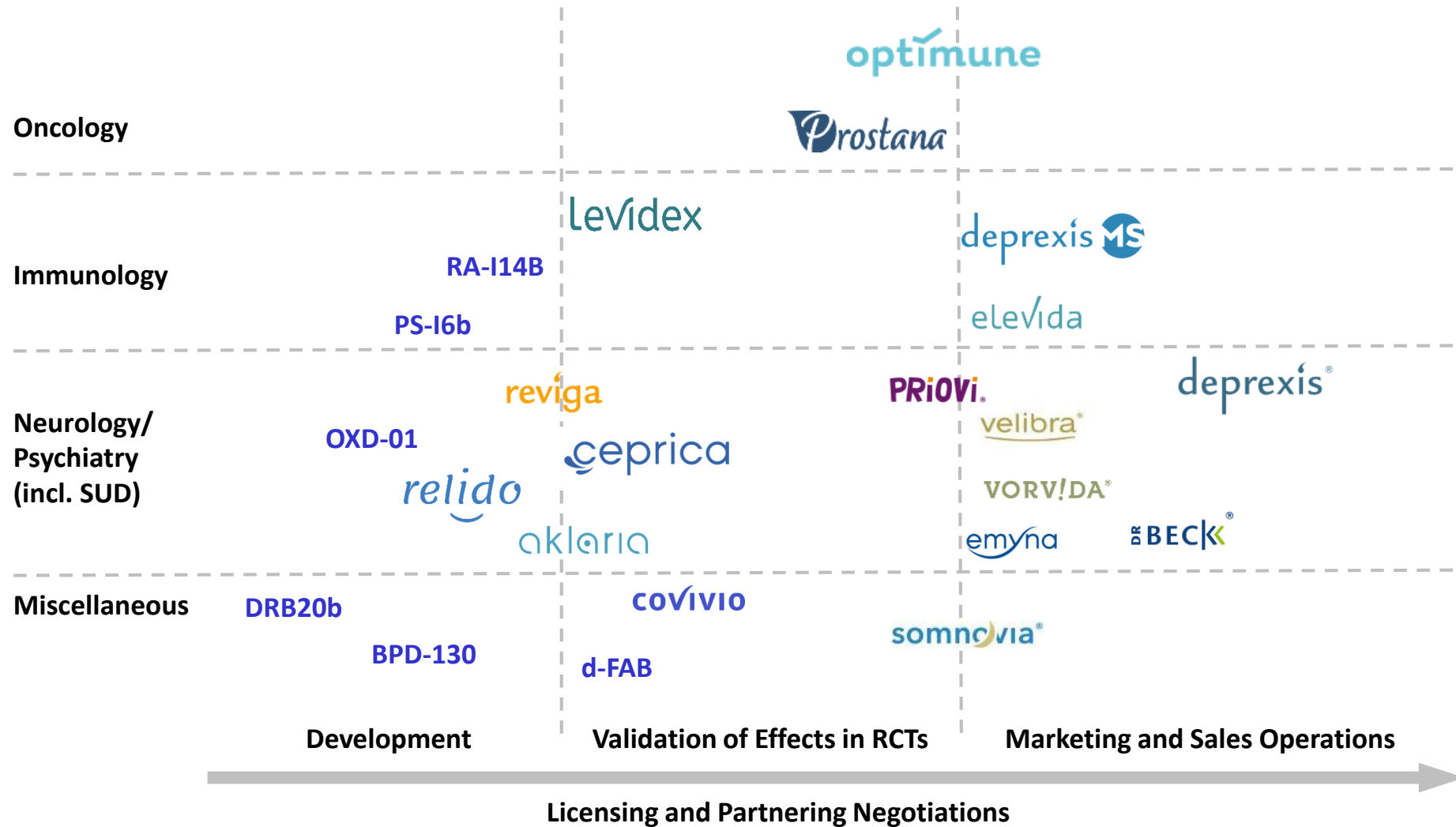
Technologically supported by the Airbus Group 

*Our development pipeline focuses on large dynamic markets:
Neurology/Psychiatry (incl. SUD), Immunology, Oncology and Pain*

Examples:



Our development projects are in different stages



GAIA is cooperating with leading scientific institutions in the development and evaluation of our DTx.



Selection of R&D cooperation projects:

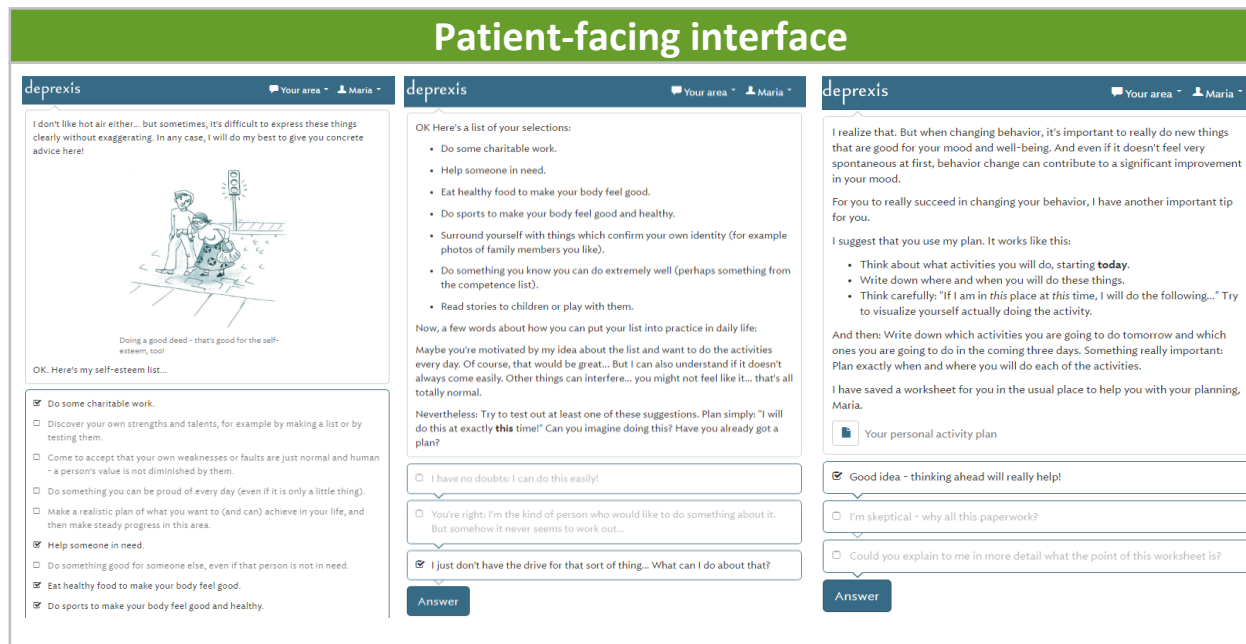
- ▶ HORIZON 2020: EU grant that is evaluating the possibilities to combine GAIA software with “wearable sensors”
- ▶ IDEMS (US patient MS society co-financed): Evaluating the effects of deprexisMS® in the US and Europe
- ▶ REACT: Evaluating the immunomodulation effect of optimune® on breast cancer patients
- ▶ Healthy Metropolis: Evaluating the impact of various GAIA software products in routine care Supported by the German Ministry of Health

Case study: **deprexis**[®] - fully automated psychotherapy (I)

Overview

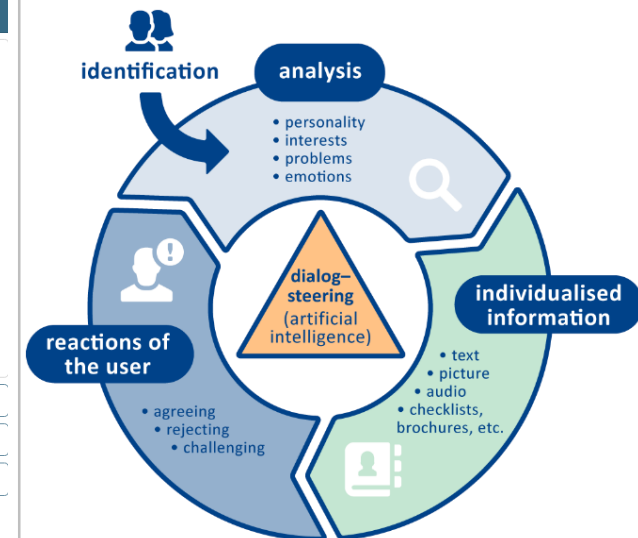
- ▶ Deprexis is a software that successfully simulates top of class psychotherapy against depression
- ▶ Tailors interaction according to individual patients and therapy needs
- ▶ "Deep data" of every patient globally are anonymously captured and analysed (psych profile, behavioural change, treatment effectiveness etc.)

Patient-facing interface



The interface consists of three panels, each with a header bar containing the 'deprexis' logo, a 'Your area' dropdown, and a user profile icon labeled 'Maria'.

- Panel 1 (Left):** Features a cartoon illustration of a person standing on a path. Text includes: "I don't like hot air either... but sometimes, it's difficult to express these things clearly without exaggerating. In any case, I will do my best to give you concrete advice here!" and "Doing a good deed - that's good for the self-esteem, too!". Below is a section titled "OK. Here's my self-esteem list..." with a list of activities and checkboxes.
- Panel 2 (Middle):** Starts with "OK Here's a list of your selections:" followed by a bulleted list of activities. It then says "Now, a few words about how you can put your list into practice in daily life:" and provides motivational text. At the bottom, there are input fields for user responses and an "Answer" button.
- Panel 3 (Right):** Begins with "I realize that. But when changing behavior, it's important to really do new things that are good for your mood and well-being. And even if it doesn't feel very spontaneous at first, behavior change can contribute to a significant improvement in your mood." It includes a section "I suggest that you use my plan. It works like this:" with a bulleted list of steps, followed by text about writing down activities and a section "I have saved a worksheet for you in the usual place to help you with your planning, Maria." with checkboxes and an "Answer" button.



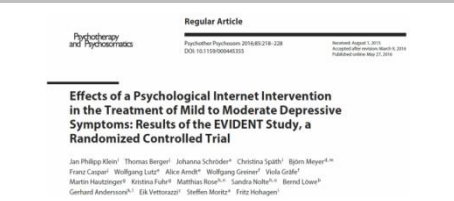
Case study: **deprexis**[®] - fully automated psychotherapy (II)

Current development status

- ▶ Deprexis proved its effectiveness and safety in 14 trials with over 7,000 patients
- ▶ 9 validated languages, ready to market globally with current focus on the US and Japan*

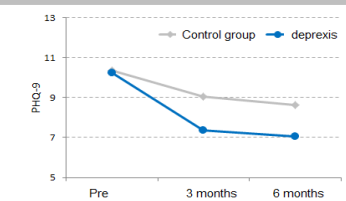
The EVIDENT trial (sample 1013 patients)

Psychotherapy and Psychosomatics



- ▶ The largest multicentre trial of its kind to date, confirmed efficacy of deprexis
- ▶ Significant effects on depression severity, both self-report and rater-based, stable intervention effects over time

Depression Score (PHQ-9)



Further potential deprexis indications

deprexisMS in multiple sclerosis (MS)

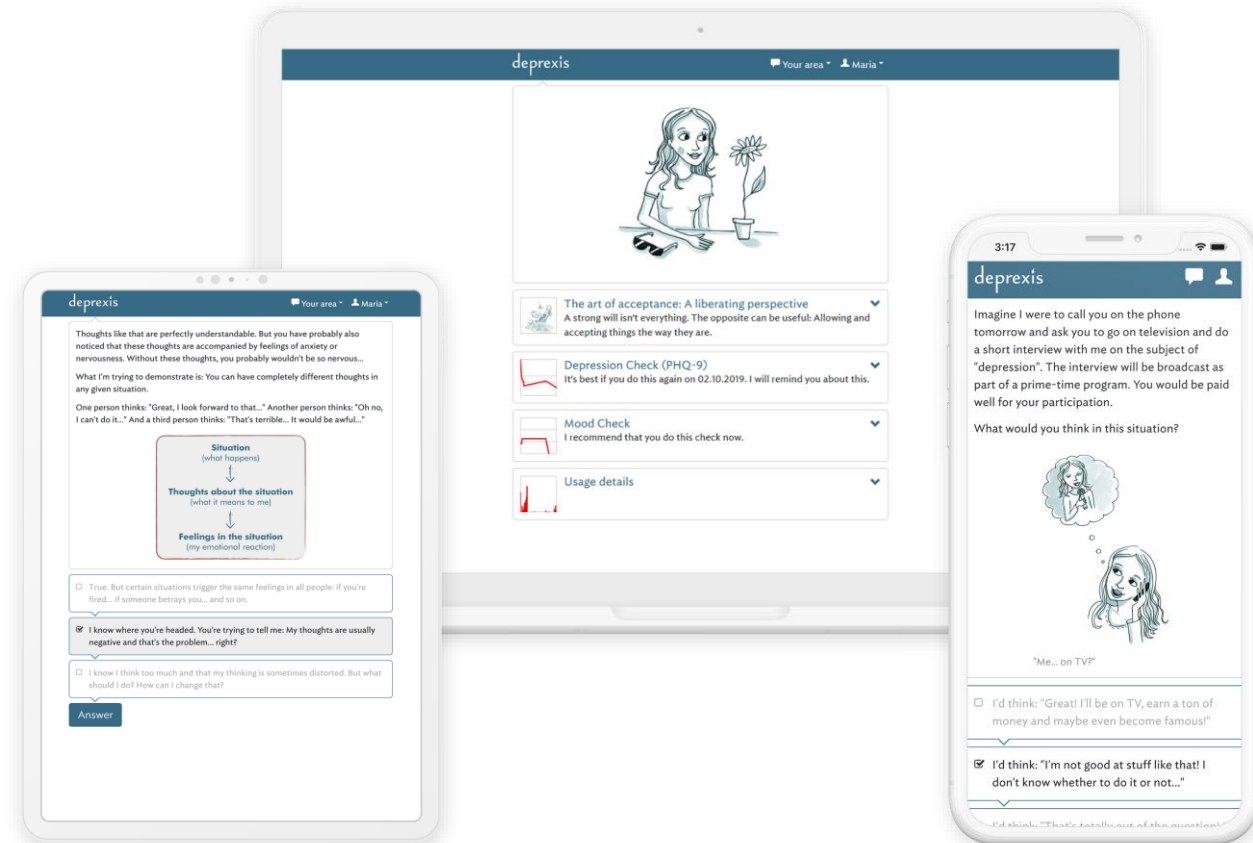
- ▶ Treating depressive symptoms/depression in multiple sclerosis patients is a clinical challenge (40% of MS Patients suffer from depression)
- ▶ Digital therapeutics like deprexisMS offer a solution as SSRIs are not favoured by neurologists and psychotherapy is not liked by patients

deprexis epilepsy

- ▶ Treating depressive symptoms / depression in epilepsy patients is clinically important. Side effect free interventions are in high demand
- ▶ deprexisEpilepsia offers an RCT proven therapeutic option

*licensed to Servier in selected countries in EU, LATAM and Asia

Hello, I am deprexis.



www.deprexis.com

*Thank you very much
for your attention!*

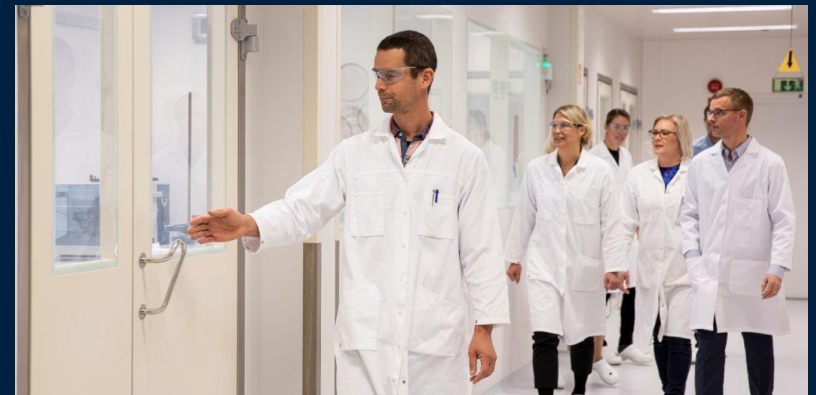
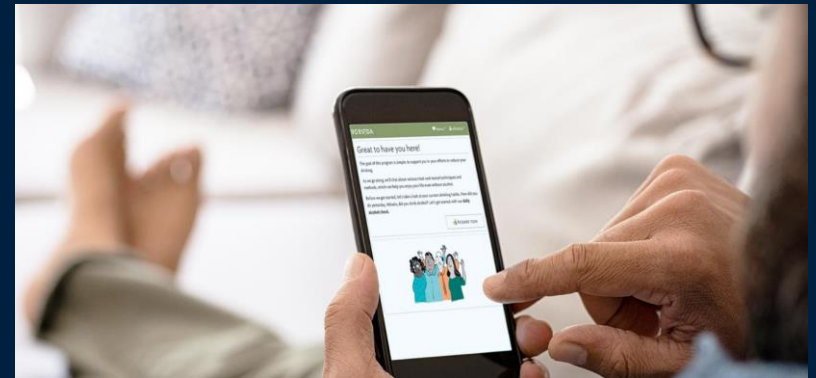


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Part 4 – Outlook

Nikolaj Sørensen, CEO and President

orexo

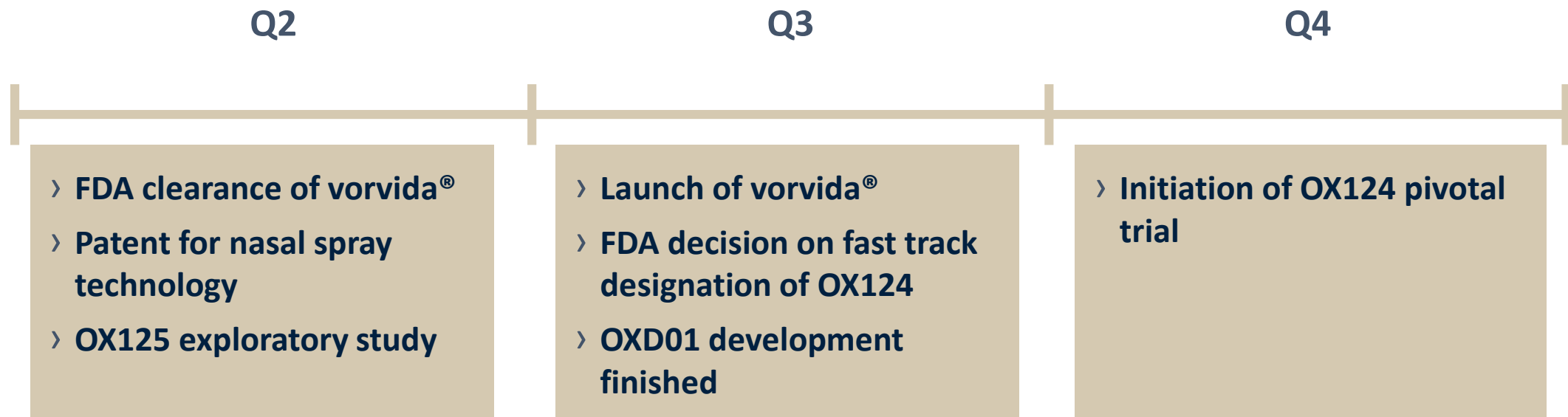


Financial outlook 2020

- › The buprenorphine/naloxone market will continue to show a double-digit growth
- › Net sales of Zubsolv® in the US are expected to be in line with 2019. The open formulary businesses will grow, while the previously highly rebated exclusive segments and cash will decrease
- › EBIT margin from Zubsolv® US will be in the range of 45-50 percent
- › vorvida® will be launched in the US H2 2020
- › Due to increased R&D investments, OPEX will reach a level of SEK 550-600 million
- › Due to a decrease in the Abstral® royalty of approximately SEK 85 million, as an effect of expiration of IP protection in the US and the EU, and increased investments in R&D, EBITDA will decrease

The outlook is based on exchange rates in December 2019

2020 a year with a steady news flow expected



Strong value drivers for long-term growth

Investment thesis

1. Addressing large markets with significant patient needs

Focusing on becoming a leader within the large and growing space of addiction, alongside addressing the opioid epidemic, one of the largest health crises ever in America and a growing global concern

2. Strong financial position and profitability

Fueled by the sales of the lead product Zubsolv® which will continue to be an important cash and profitability contributor

3. Leverage the US commercial platform

Strategic focus on product portfolio expansion, through M&A and business development, to leverage the US commercial infrastructure

4. Expanding pipeline

Continues to build on the strong track record of developing products with worldwide approval by expanding the pipeline with multiple assets based on innovative drug delivery technologies and digital therapeutics addressing unmet medical need in addiction

5. Entering DTx, the new megatrend in life science

Digital therapeutics (DTx) will become an integral part of the healthcare landscape and addiction is one of the therapeutic areas where it is most needed

Thank You!

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