Important steps forward in a challenging environment

January 26 2023

Orexo supports the UN's Agenda 2030 with a focus on:

Agenda & presenters Q4 2022 Interim Report

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1

2022 and Q4 Key achievements

2

Business update

- US Pharma
- Digital Therapeutics
- HQ & Pipeline

3

Financial & legal overview

- Financial development
- Outlook
- Legal Update

4

Future value drivers

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2022 & Q4 Key achievements

2022 a challenging year, but good progress in R&D

HQ & Pipeline

- ✓ amorphOX® successfully tested in small and large molecules with consistently good results
- ✓ Strong clinical data for OX640
- ✓ Research partnerships initiated with leading biopharmaceutical companies and a US pharma company
- ✓ Launch of ZUBSOLV® in Europe

OX124 nearly ready for filing, but delayed into early Q1

US Pharma

- ✓ ZUBSOLV® down versus 2021, but with relatively stabilized demand during the year
- ✓ Improved market access in public segment to 48% and maintained 98% access in commercial, in a market with >10 generics on competitors
- ✓ Strong full year EBIT margin (54%) and EBIT (SEK 308m)

Market growth slowed down in H2 and Q4 without “normal” year-end boost

Digital Therapeutics

- ✓ deprexis® included in the Veteran Affairs federal supply
- ✓ Operational implementation at Trinity Health, but with slow start
- ✓ 2,800 patients have received MODIA® from their physician
- ✓ Orexo DTx and services included in two grants (Arizona and Minnesota)

Commercial progress not meeting expectations

Favorable exchange rate supported revenue growth 2022

- ✓ In 2022 net revenues grew 10% versus 2021 due to FX tailwinds
- ✓ EBIT loss reduced, despite high USD exposure in expenses and significant non-recurring expenses in R&D and legal. Improvement mainly due to reduction in DTx expenses.
- ✓ EBITDA positive when excluding non-recurring legal expenses and expenses for clinical trials positive
- ✓ Continued solid cash position, several opportunities for out-licensing in the R&D pipeline and profitability in sight

ZUBSOLV® net revenues ▲

9 %

US Pharma EBIT

308 SEK M

Cash and invested funds

352 SEK M

Business update
US Pharma

Treatment of OUD likely to expand and transform

New legislation enacted by the US Congress December 28th

- Elimination of the DATA 2000/"X" waiver- Effective immediately
- One time, 8-hour education for prescribers of all controlled substances – Implementation timeline unclear

With significant implications on delivery of OUD treatment

- Most physicians in the US likely to be able to prescribe ZUBSOLV®, since most prescribe controlled substances for other indications
- Today's concentration of prescription to DATA 2000 waivered physicians will reduce over time
- Volumes likely to grow as more patients get access to treatment and physicians will have reduced administrative burden

Source: https://www.congress.gov/117/bills/hr2617/BILLS-117hr2617enr.pdf

Transformation of the market will provide new opportunities and challenges

Market will expand and improve access to treatment

- Basically, all primary care physicians will be able to prescribe ZUBSOLV®, will accept insurance and improve access significantly
- Market likely to evolve to a treatment structure similar to other mental health diseases with severe cases being referred to specialists and others managed in primary care

New physicians in the OUD space will need support in delivering treatment

- OUD treatment requires access to counselling and induction of treatment is difficult for most patients
- Orexo field force well positioned to educate and inform new physicians how to induce patients on treatment, maintenance treatment, counselling options and create local networks to specialists
- Synergies with Orexo DTx and pipeline will increase significantly

Market fragmentation will increase and current prescribers likely to lose market share

- New field force strategies needed to ensure cost-efficient approach to an expanded and more fragmented market
- Combining all Orexo resources and knowledge within OUD to provide a more holistic approach to OUD treatment to regional healthcare opens an opportunity for a less field force driven sales model - MATCore™

MATCore™ can fill a void in the market and provide new pathways to OUD treatment providers

Orexo has the knowledge and tools required to improve MAT

- ✓ Comprehensive library of patient education material related to the treatment and disease
- ✓ Counselling support from MODIA™
- ✓ Distribution pathways to provide access to medication
- ✓ Medication
- ✓ Adherence support and monitoring
- ✓ Established networks to leading addiction specialists
- ✓ Hippo compliant data systems to collect and analyze treatment outcome

MATCore™
- One digitized platform to provide access to resources needed in recovery

MATCore™ is based on a collaborative approach with key stakeholders

Program is based on a collaboration with local health care providers

Outreach to patients, non-specialized providers and patient support programs led by Orexo in collaboration with state health services and OUD task force

Orexo initial focus is to work with health care providers to get grants from the opioid settlement funds to support implementation of MATCore™

First grant awarded to Alay Psychiatry in December from the Arizona State Attorney General's office to implement MATCore™

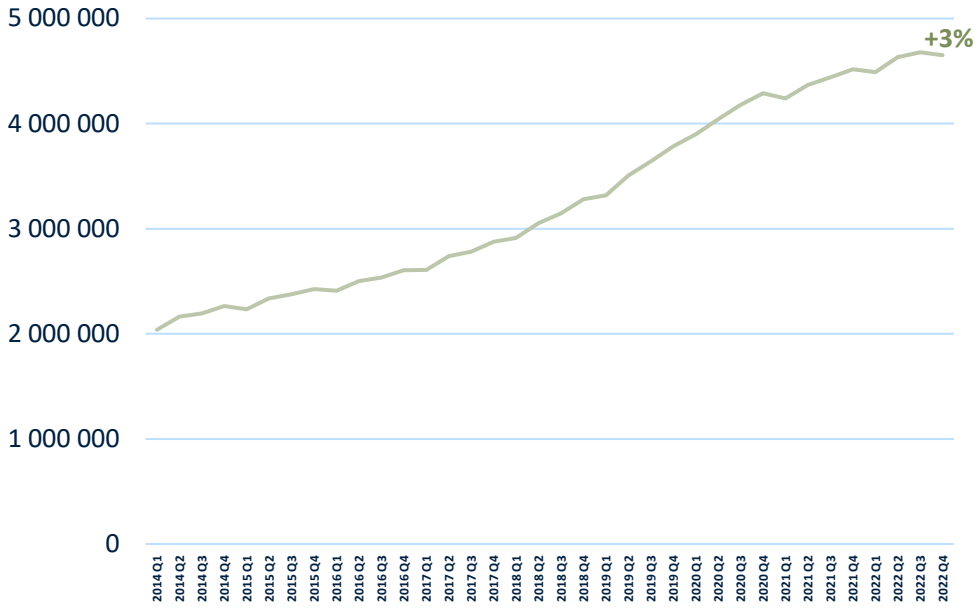
ZUBSOLV® volume slightly down from Q3

- ✓ Mild decline of 2% versus Q3 and 9% versus Q4 2022
  - NY (12%) and Kentucky (18%) Medicaid being prime growth drivers versus Q3 together with some Medicare Part D plans
  - Continued slow decline in UHG and Humana and no market growth had negative impact
- ✓ ZUBSOLV® access of 98% in commercial and 48% in public confirmed January 1
  - Minor changes in smaller commercial plans both positively and negatively

[1] Where ZUBSOLV® is reimbursed and competes on equal terms with both branded products and/or generics

Market growth in Q4 below expectations

3% total market growth Q422 vs Q421[1]



[1] Volume sales, quarterly NTRx

Fentanyl crisis – a new inhibitor for treatment

- Fentanyl addicted patients, more difficult to treat resulting in increased rate of relapse
- Fentanyl causes increased mortality among patients
- Covid-19 effects from less access to treatment, high overdose rate etc
- Few counsellors and access to full MAT treatment

Funding and legislation create new opportunities

- New legislation will enable expanded access to treatment
- **USD 54 billion** in settlements in the “opioid litigation” expected to accelerate access to treatment
- First funds available during Q3 to support specific projects and programs in several states
  - **Orexo involved in first round of grants in Arizona**
  - **Collaboration established in additional states with grant applications pending**

Business update

Digital Therapeutics (DTx)

Some progress in DTx, but a new approach needed

MODIA® continues according to plan

- Nearly 1000 patients received MODIA® in Q4
- 40 patients are in “billing tests” in three selected states for reimbursement
- Orexo will invoice the clinics when reimbursement is confirmed in Q1
- MODIA® is included in the MATCore™ platform to be implemented in Arizona

Wayside Recovery center awarded a grant to treat 60 patients with deprexis® or vorvida®

- Wayside is a specialized women’s addiction treatment center
- First patients received deprexis® in January

First patients received DTx in Trinity Health, but no material volume

- Continued strong support from management and behavioural health, but patient enrolment in Primary Care not meeting expectations

Implementation in VA is making progress, but associated with administrative hurdles

- Partnership initiated with key stakeholders for implementation in care program for depression
- Distribution and invoicing require unique administrative setup for a digital therapy

Increasing synergies between pharma and DTx
and a need to improve efficiency in DTx

- Removal of DATA 2000 expand the potential prescriber of our OUD tools, increase sales synergies with the pharma pipeline and deprexis® and vorvida®
- MATCore® will provide a platform for healthcare providers to optimize and improve treatment with both medication and counselling, requiring an integrated approach to the customers and key stakeholders across pharma and DTx
- DTx lack of revenue traction short term, warrant an increased focus on sales and reduced overhead expenses

DTx will operationally be integrated into US Pharma starting February 1

- Senior management and some marketing positions are made redundant
- US Pharma sales management will take responsibility for sales of DTx and Pharma products
- Some dedicated DTx roles maintained and new customer focused roles is being added to manage VA and Integrated Health Networks (like Trinity Health)

US Pharma and DTx will continue with separate segment reporting, but DTx increasingly reliant on allocated resources from US Pharma

Business update

HQ & Pipeline

Good progress in pipeline

OX124 – overdose rescue medication based on amorphOX®

- Filing is delayed into early Q1, caused by late response by FDA and some additional analysis required by Orexo
- Ordinary approval timeline of 10 month after filing, but recent approvals in the category has been up to 13 months

OX640 – adrenaline rescue medication based on amorphOX®

- Proceed to prepare large scale commercial manufacturing
- Continued review of development and partnering strategy

AmorphOX®

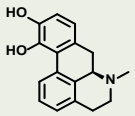
- Successful partnering strategy in biomolecules
- Two leading international biopharmaceutical companies entering feasibility study with Orexo with their proprietary API

Note: product images are prototypes

amorphOX® – A Versatile, World-Class Platform for Intranasal Drug Delivery

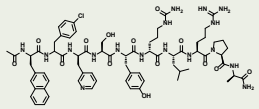
Chemical degradation after accelerated stability studies at 40ºC/75% RH

Apomorphine



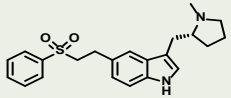
0.3% after 18 months

Cetrorelix



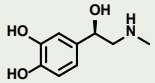
0.4% after 3 months

Eletriptan



0.5% after 3 months

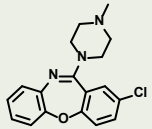
Epinephrine



0.5% after 6 months

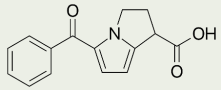
Enzyme

Loxapine



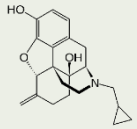
0.3% after 6 months

Ketorolac



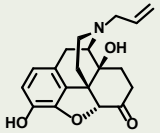
0.8% after 6 months

Nalmefene



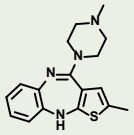
≤0.1% after 15 months

Naloxone



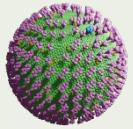
≤0.1% after 12 months

Olanzapine



0.3% after 3 months

Spike protein



SARS-CoV-2 Spike Protein

- ✓ Successfully formulated in the **amorphOX®** platform
- ✓ High production recovery
- ✓ Free-flowing powder
- ✓ Retained activity after formulation and manufacturing
  - Confirmed by binding assay
  - Stability studies ongoing

Broad spectrum of API tested to show versatility of the amorphOX® platform and offer potential partnering opportunities for Orexo outside our core business

Financial & legal

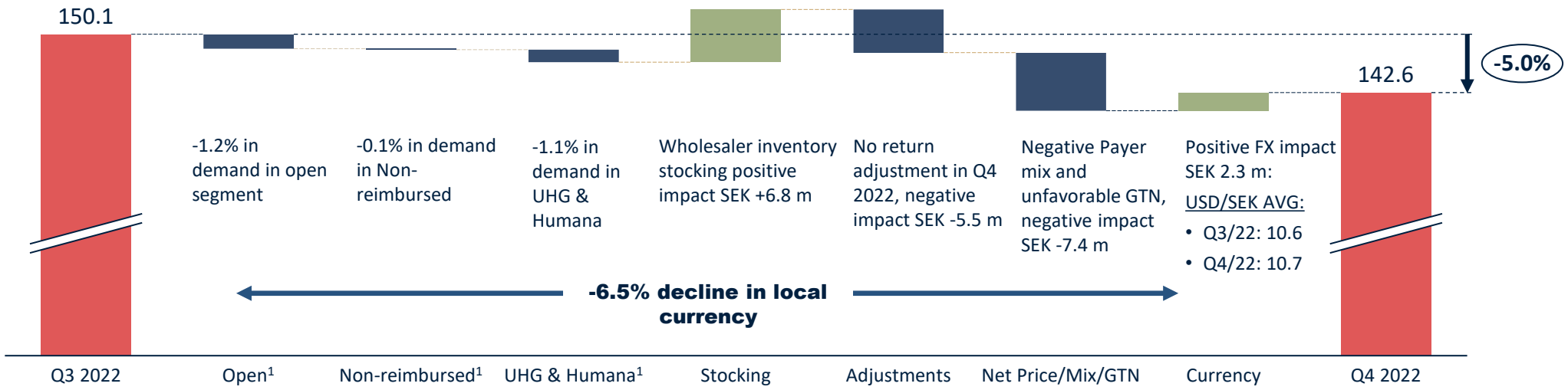
ZUBSOLV® net revenue grew 7% in Q4

Net revenue per segment SEK m	Q4 2022	Q4 2021	Jan – Dec 2022	Jan – Dec 2021
ZUBSOLV® US	142.6	133.6	571.4	522.7
US Pharma – Total	**142.6**	**133.6**	**571.4**	**522.7**
DTx	0.0	0.3	0.4	1.1
DTx – Total	**0.0**	**0.3**	**0.4**	**1.1**
Abstral® royalties	5.5	8.3	30.4	32.1
Edluar® royalties	2.7	1.8	10.4	9.1
ZUBSOLV® – ex US	5.2	—	11.8	—
HQ & Pipeline – Total	**13.4**	**10.1**	**52.6**	**41.2**
TOTAL	**156.1**	**144.0**	**624.3**	**565.0**

Comments Q4

- ✓ ZUBSOLV® Net revenue grew YoY with 7 % primarily due to stronger USD vs SEK US and wholesaler stocking.
- ✓ Partly offset by lower demand and a negative true-up of Gross to Net accruals of SEK 4.1 m.

US Pharma net revenue Q422 vs Q322



[1]Estimated change in demand by segment, based on Net Sales development during the quarter , IQVIA demand data, institutional sales and claims data from insurance companies

Negative FX impact of SEK 6.8 m on EBIT

Income statement SEK m	Q4 2022	Q4 2021	Jan – Dec 2022	Jan – Dec 2021
Net revenues	156.1	144.0	624.3	565.0
Cost of goods sold (COGS)	-25.9	-20.3	-102.6	-78.9
Gross Profit	**130.2**	**123.7**	**521.7**	**486.1**
Operating Costs	**-201.3**	**-187.8**	**-705.6**	**-700.2**
EBIT	**-71.1**	**-64.1**	**-183.9**	**-214.1**
Net financial items	-24.4	-2.1	13.5	-8.4
EBT	**-95.5**	**-66.2**	**-170.4**	**-222.5**
Tax	3.7	0.3	-7.2	-1.0
Net profit/loss	**-91.8**	**-66.0**	**-177.6**	**-223.5**
EBITDA	**-53.1**	**-48.5**	**-115.2**	**-161.0**

Comments Q4

ZUBSOLV® COGS higher due to a negative FX impact and negative production variances.

OPEX higher due to

- Higher expenses for IP litigation and higher costs for MODIA® study.
- Negative impact from stronger USD
- Partly offset by significantly lower selling expenses in DTx

ZUBSOLV® US EBIT contribution of SEK 77 m (72)

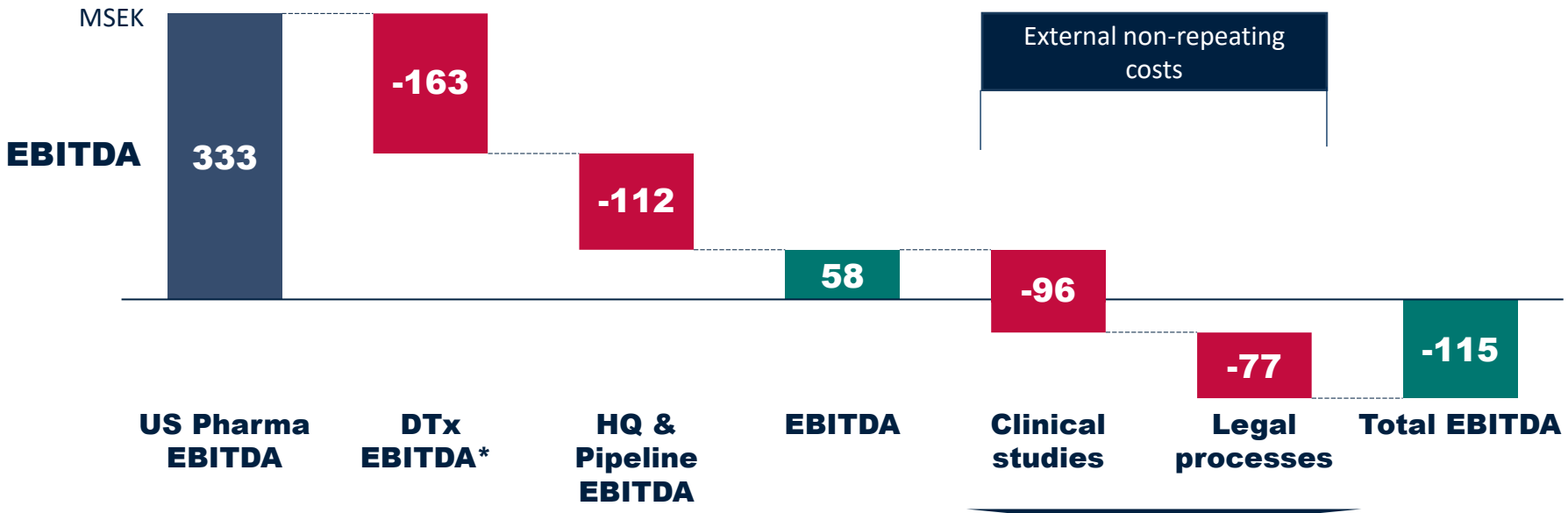
- EBIT Margin for the quarter 54% (54%) and 54% (53%) for the full year.

EBITDA of SEK -53 m (-49)

NET FINANCIAL ITEMS of SEK -24.4 m (-2.1)

- Negative unrealized exchange rate impact of SEK -18.2 m (4.0) derived from the parent company's foreign currency bank accounts mainly in USD, which depreciated from 11.2 in September to 10.4 in December
- Higher interest rate, which had a negative impact on costs for corporate bonds of SEK 7.8 m (5.5).
- Partly offset by interest income of SEK 2.2 m (-) from short-term cash investments.

Orexo core FY EBITDA positive excluding external non-repeating costs



	Completed
• MODIA® phase III	Q2, 2023
• OX640 phase I	Q4, 2022
• OX124 HF studies	Q4, 2022
• Sun Litigation	Q1, 2023 (District Court)
• Subpoena	TBD

* DTx EBITDA including internal allocations from US Pharma

Sufficient cash position to continue R&D investments and defend IP rights

Cash Flow SEK m	Q4 2022	Q4 2021	Jan – Dec 2022	Jan – Dec 2021
Cash flow from operating activities	-48.9	-80.6	-156.6	-229.0
Investment activities	66.2	-2.9	-234.7	-52.9
Financing activities	-5.8	-5.5	-21.4	250.6
Cash flow (excl. exchange rate differences)	11.5	-89.0	-412.8	-31.2
Add back short-term investments	219.6	—	219.6	
Liquid funds	**351.9**	**504.1**	**351.9**	**504.1**
Net cash position including short-term investments	-142.9	11.7	-142.9	11.7

Comments Q4

- ✓ Liquid funds (SEK 352 m) decreased with SEK 92 m from Q3 (SEK 444 m)
  - ✓ SEK 49 m negative contribution from operating activities mainly due to negative operating earnings partly offset by positive changes in working capital
  - ✓ Gross investments in fixed assets for the development organization of SEK 12 m and amortization debt of SEK 6 m
  - ✓ The remaining change explained by negative currency effect on cash assets in USD as well as on short-term investments.
- ✓ Out of the total liquid funds, invested surplus cash in certificates of deposits and in US treasuries, i.e. short-term investments, amounted to SEK 220 end of Q4.

Financial outlook

Based on exchange rates in December 2022

Metric	Outlook 2023	Reaffirmed/revised
Key market development	The buprenorphine/naloxone market will grow 4-7 percent, based on current growth trajectory. The new legislation, effective January 1, 2023, will have a positive effect over time, but due to uncertainty related to timeline of the implementation its impact on market growth in 2023 is excluded.	N.A.
Group revenues	Group revenues will increase, with ZUBSOLV® US revenues being in line with 2022	N.A.
Group OPEX	OPEX H1 2023, slightly higher than H2 2022 (SEK 385 m), but H2 2023 will decline versus the same comparison period	N.A.
Group EBITDA	EBITDA in balance in H2	N.A.

Q4 legal update

ZUBSOLV® patent dispute vs Sun Pharmaceuticals

✓ In Q4 2022 the work continued to prepare for the trial that will start on January 30, 2023, in the US District Court for the District of New Jersey.

Overall strong IP rights for ZUBSOLV®:

- In total 10 patents listed in the Orange Book
- Patent expiring dates Dec 2027 – Sep 2032
- Previously successfully managed to defend ZUBSOLV® IP rights in the US appeal court

30 month stay expires in February, but no generic expected prior to final court decision

The outcome of the trial is expected during the summer of 2023

Subpoena with regards to ZUBSOLV®

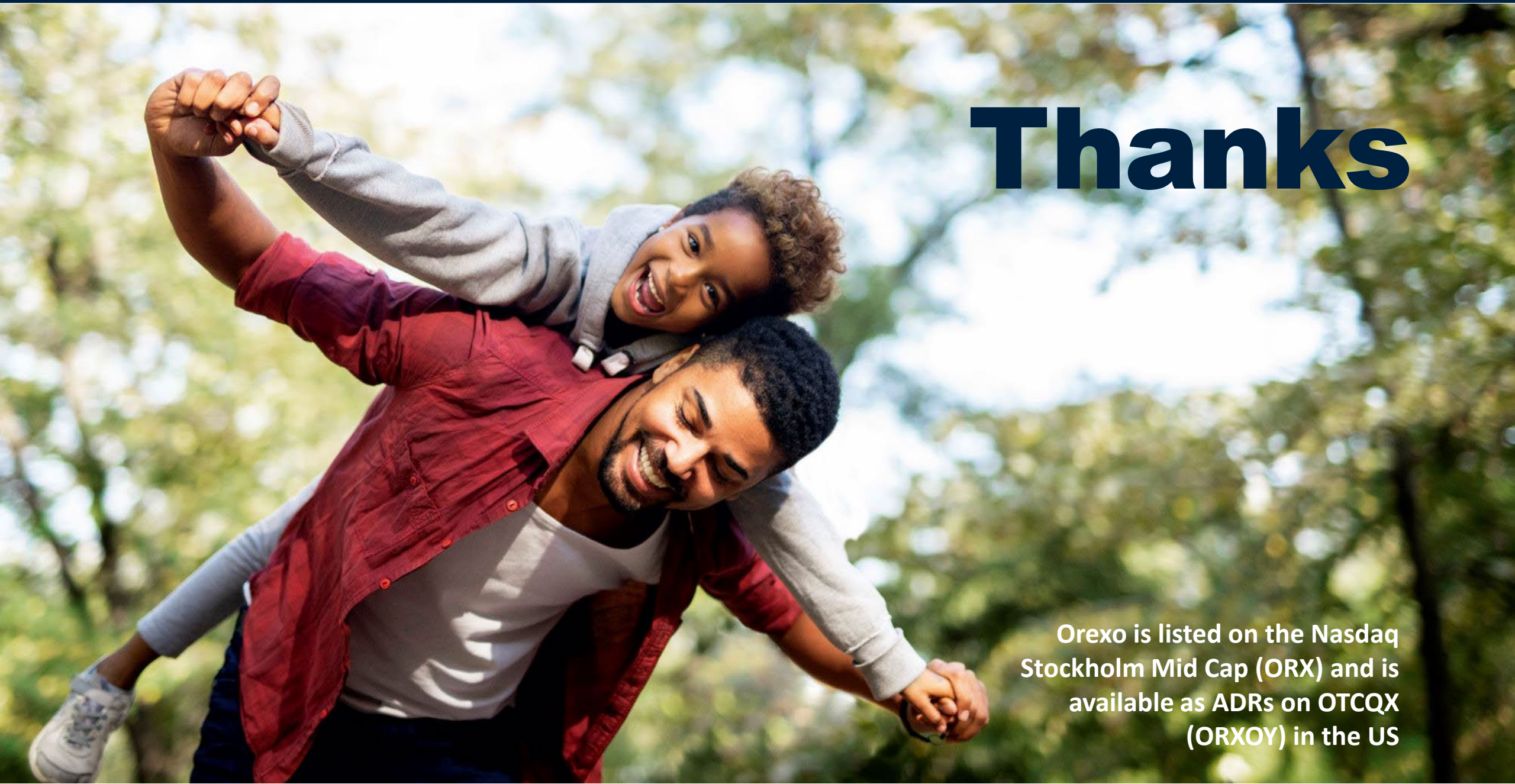
✓ No material activities in Q4 and YTD 2023

Future value drivers

Why Orexo?

- ✓ **Corporate profitability** in sight[1]
  - Main external cost drivers will diminish during H2 2023
  - No new activity driving external expenses to be initiated without certainty of associated revenues
  - Significant focus on cost efficiency
- ✓ **R&D pipeline** is expected to result in revenue generating partnerships during 2023
  - OX124 filing with the FDA in early Q1 2023
  - OX640 and amorphOX® partnering discussions on-going
- ✓ **DTx revenues** expected to build from Q1 2023 and beyond
  - Reimbursement model confirmed
- ✓ **ZUBSOLV® sales** stabilized and opportunities to grow
  - Settlements providing USD 54 billions announced
  - New legislation open up for all physician's to prescribe ZUBSOLV®

[1] Assuming no unexpected events outside the control of Orexo



Thanks

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