EDISON

Orexo

FY18 results

The opioid use disorder patient journey

Pharma & biotech

Orexo's FY18 results demonstrated continuing profitability derived from its lead product, Zubsolv, responsible for 21.7% y-o-y net sales growth driven by US Zubsolv Q418 prescription and revenue growth of 22% and 31.8%, respectively. The weakness in partnered products compared to our targets (although FY18 partnered sales were SEK125.4m) and higher Q4 investment (including litigation) reduced FY18 EPS compared to our estimate by SEK1.8. We have tempered our revenue growth expectations for FY19 until the impact of Suboxone film generics is known.

Year end	Revenue (SEKm)	PBT* (SEKm)	EPS* (SEK)	DPS (SEK)	P/E (x)	Yield (%)
12/17	643.7	29.7	0.67	0.0	110.7	N/A
12/18	783.1	92.2	3.99	0.0	18.6	N/A
12/19e	866.7	252.7	7.08	0.0	10.5	N/A
12/20e	844.1	156.6	4.39	0.0	16.9	N/A

Note: *PBT and EPS are as reported.

FY18 financials: Awaiting generic Suboxone impact

FY18 total revenues were SEK783m, with SEK227m for Q418 (FY17: SEK644m; Q417: SEK191m). Zubsolv's Q4 growth countered some of the decline in partnered products. One-off costs including litigation expenses, were higher and lower than we had forecast, respectively. Gross margin was 80% in Q418 and we estimate that this rises to 83% by Q319 following secondary manufacturing improvements. Profit after tax for FY18 rose to SEK138m, with SEK51.6m for Q418, compared to SEK23.2m and SEK26.7m for FY17 and Q417, respectively. Orexo's cash at the end of FY18 was SEK590m.

Impact of the OUD patient journey on Orexo's growth

Following the intense debate in the US and other countries on the increasing number of opioid use disorder (OUD) patients and the resulting deaths due to opioid overdose, we have explored the convoluted OUD patient journey and its commercial relevance to Orexo. We note that the OUD patient journey resembles more a chronic relapsing condition than an acute treatment and cure. This infers longevity to Orexo's franchise. In addition, the comorbidities associated with OUD could bring new opportunities for Orexo's M&A and licensing strategies.

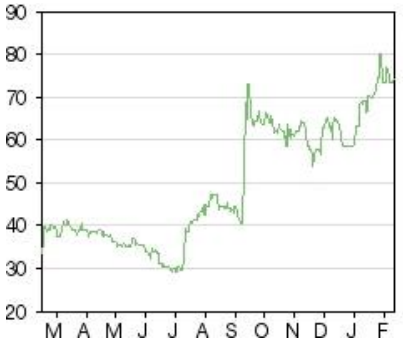
Valuation: Modest increase, many moving parts

The main changes to our valuation have been to reduce administration spend after Q119 because the litigation expense will decline, but keeping total operational expense of c SEK500m in both FY18 and FY19. We have also tempered US Zubsolv revenue growth until the impact of Suboxone generics is known. Our valuation increases modestly from SEK3.4bn or SEK95.8 per share previously, to SEK3.4bn or SEK97.7 per share. We also include lower near-term sales of its minor products and from regaining the EU Zubsolv rights. We have not yet incorporated gross margin improvements as a result of the primary manufacturing improvements noted in Orexo's December 2018 capital markets day, but explore the sensitivity of our valuation to further CoGS efficiencies.

12 February 2019

Price	**SEK74.20**
Market cap	**SEK2,567m**
	$/SEK9.07; €/SEK10.36
Net cash (SEKm) at end Q418	269
Shares in issue	34.6m
Free float	53.8%
Code	ORX
Primary exchange	NASDAQ QMX Stockholm
Secondary exchange	N/A

Share price performance



%	1m	3m	12m
Abs	7.5	15.9	109.9
Rel (local)	2.6	14.4	100.3
52-week high/low	SEK80.0	SEK29.1	

Business description

Orexo is a Swedish speciality pharma company, with expertise in drug delivery/reformulation technologies (in particular, sublingual formulations) and a US commercial infrastructure for its opioid dependence therapy, Zubsolv (being out-licensed to partners ex-US). It also has three other clinical assets including OX124, which has reported positive Phase I results.

Next events

Actavis patent infringement trial	End March 2019
Q119 results	2 May 2019
Product in-licensing & M&A announcements	2019

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Edison profile page

Investment summary

Specialists in drug delivery for addiction and pain

Orexo is a Swedish speciality pharmaceutical company founded in 1995 to use its drug delivery technologies to develop and market products to treat addiction and pain. Its products are based on its patented drug delivery technologies and expertise in reformulation (in particular employing sublingual formulations). It has three marketed proprietary drugs. Orexo's lead drug Zubsolv (for opioid dependence) has been sold in the US through its dedicated salesforce since its launch in September 2013. Zubsolv was approved in the EU in Q218 and the ex-US rights are being re-partnered. Abstral (for cancer breakthrough pain) and Edluar (insomnia) are sold by partners worldwide. Orexo also has a pipeline of reformulations of approved compounds, which include OX124, a naloxone rescue medication for opioid overdose that has reported positive Phase I results. Orexo has 89 employees (excluding the c 50-strong US salesforce). US commercial operations are based in New Jersey and its R&D facility is located in Sweden. It adopted the name Orexo in 2003 and was listed on NASDAQ OMX Stockholm in November 2005, raising SEK333m gross (3.7m shares at SEK90). Subsequent equity raises include SEK250m in June 2011 (6.6m shares at SEK38) and SEK346.3m in September 2014 (2.5m shares at SEK139).

Valuation: SEK3.4bn or SEK97.7 per share

We have updated our valuation to include the cash generated in FY18, changes to exchange rates and tempered our FY19 revenue expectations until the impact of Suboxone film generics on US Zubsolv sales is known. Our valuation increases modestly from SEK3.4bn or SEK95.8 per share previously, to SEK3.4bn or SEK97.7 per share based on 7.25% US Zubsolv market share until 2032 (representing 72% of our valuation) and a smaller terminal value (representing 20% of our valuation), which includes Zubsolv sales after 2032, sales of OX124, OX125 and any acquisitions of products to be sold by its US commercial organisation. Orexo's net cash at the end of FY18 represents 8% of our valuation. Royalties on Zubsolv in the EU, Abstral and Edluar are minor components of our valuation compared to Zubsolv in the US. Our model includes the gross margin improvements from the secondary manufacturing of US Zubsolv announced in Q418. We have not yet incorporated gross margin improvements as a result of the primary manufacture improvements noted in the company's December 2018 capital markets day (CMD), but explore the sensitivity of our valuation to continued CoGS efficiencies in this note. We have also excluded any patent litigation settlement with Actavis or milestones as a result of re-partnering Zubsolv ex-US.

Financials: Positive EBITDA expected to continue

Orexo guided to its third year of profitability in FY18 and has met that target. Profit after tax was SEK138m for FY18 and SEK51.6m for Q418. Total revenues were SEK783m in FY18 and SEK227m for Q418. Orexo guided to operational expenses of c SEK500m for FY18 and FY19 vs our FY18 estimate of SEK515m and the SEK516m reported. Gross margin was 80% in Q418 and we estimate that this rises to 83% by Q319 on secondary manufacturing improvements. The key features of 2018 were:

- The key investor concern of 2018 was the initial invalidity of the Zubsolv '330 patent, which expires in 2032. Orexo won its appeal of the case, which was a final judgement.
- Near-term financials have been largely unchanged by Orexo's recent successful patent appeal.
- With Zubsolv US revenues safe from direct generic competition, attention will turn to worldwide growth of the brand in the face of generic Suboxone film in the US, the leveraging of Orexo's US salesforce by M&A, licensing and the development of its R&D pipeline.

Investment proposition

Orexo is an operating speciality pharmaceutical company with positive cash flow and growing franchises. This has the following implications:

- Orexo's positive cash flow should be attractive to investors who want exposure to drug development and commercialisation without the prospect of continual fund-raising or the risk of developing new chemical entities. Orexo's management has committed to maintaining its cash-flow-positive status.
- Orexo's largest product is for opioid dependence, which is a high-profile and growing market, particularly in the US where Orexo sells the product directly.
- The opioid dependency category includes generic formulations of formerly branded products, but not Orexo's Zubsolv. Despite the availability of generics in the category, Orexo has grown its volume market share by negotiating price-volume agreements with public and private payers.
- We believe Orexo has demonstrated the capability to prosper in the complicated US reimbursement space, and grow the Zubsolv brand by volume and value in the face of generic competition.
- Orexo's other products – Abstral and Edluar – are smaller but useful parts for the diversification of its investment case, and Orexo earns royalties on them. Our model includes the expiry of the Abstral IP in the EU in September 2019.
- Orexo's US commercial organisation and network of ex-US licensees provide a compelling conduit for new products in addiction management, pain or the related therapeutic space, whether they are internally developed by Orexo (as in the case of OX124, OX125, OX382 or OX338), or acquired as part of its business development or M&A strategies.

Orexo is targeting the addiction and pain specialists, where new products could leverage its commercial operation.

Patent overhang removed, strategic sensitivities remain

Our model has been updated for the positive events at Orexo in 2018. The potential for generic competition before 2032 in the US has been eliminated with the US District Court issuing a final, non-appealable judgement in January 2019. The costs for Orexo's litigation on the infringement of its IP by Actavis's generic versions of Suboxone and Subutex remain in 2019; although Orexo is not at risk of damages, there is the potential for an upside financial settlement if Orexo also wins this case. This is not currently included in our model. In our most recent note we explored the potential impact on Zubsolv's US market share by the generic Suboxone film launch, which is probably the biggest uncertainty that is outside of Orexo's control in 2019. We have tempered our expectations for Zubsolv's market share in the US to 7.25% from FY19 to reflect the uncertain impact of a number of generic Suboxone film entrants. The key strategic sensitivity in 2019 that is under Orexo's control is the extent of its business development and M&A activities: making the right strategically-aligned product licences and acquisitions at the right price. We have also evaluated the sensitivity of Orexo's valuation to primary manufacture improvements that were highlighted at its recent CMD, but we do not expect to be implemented before 2020.

The outlook for Orexo in 2019 and beyond

2018 was a momentous year for Orexo with the lifting of the patent litigation cloud that has hung over the company since 2014. Orexo probably feels comfortable exploring more substantive strategic steps now that the US exclusivity of Zubsolv through to September 2032 has been confirmed. We have summarised our outlook for Orexo in 2019 into organic and inorganic drivers. Looking further out, we expect total revenues to dip in FY20 as the minor products on which Orexo receives royalties lose exclusivity and before Zubsolv in Europe gains traction after its re-launch. We expect revenue re-acceleration from 2021 although even a single licensing or M&A transaction could change these assumptions. The resolution of the litigation with Actavis will eventually remove legal costs from total operational expense, while a settlement with Actavis could help bridge the revenue gap between 2020 and 2021 as the partnered products lose exclusivity.

Organic drivers

We have tempered our expectations for Zubsolv volume growth from 2019 until the effect of multiple Suboxone film generics is determined, although we have assumed stable discounts on the premise that Zubsolv's value proposition – lower active ingredient (CoGS) levels driven by Orexo's higher bioavailability formulation enable it to compete effectively with generics while offering a lower diversion potential – to continue to resonate with payers. We estimate total Zubsolv sales growing by 15% in 2019 to SEK729m; 98.5% of this will be from the US until ex-US Zubsolv is re-partnered and re-launched. We forecast Abstral sales increasing by c 1% in 2019 to SEK120m as it loses exclusivity in the US. Similarly, we forecast modest growth in Edluar royalties in 2019, although, like Abstral, Edluar will decline in 2020. Although Abstral and Edluar are minor royalty contributors to Orexo's total revenues (which we expect to grow 12.5% in 2019 to SEK867m), they do illustrate Orexo's near-term dependency on Zubsolv. While Orexo's continuing stewardship of Zubsolv as the only product showing volume growth in this genericised category should be recognised, and has been accomplished with its own 50-person salesforce, a new product added to Orexo's commercial organisation would provide the advantages of:

- revenue diversification,
- salesforce utilisation leverage, and
- salesforce motivation, since sales representatives like nothing more than to talk to doctors about a new product.

We have also reduced Orexo's net finance costs from 2019 because we expect that with a significant US cost base, most of Orexo's cash will be held in US dollars at a slightly higher interest rate than in our previous model.

CoGS improvements

Orexo recently announced that the CoGS improvements to secondary manufacture (tableting and packaging) are expected to reduce Zubsolv's CoGS by 35% compared to the average level in FY17. These changes were incorporated into our valuation in our last note. In addition, the December 2018 CMD included a discussion of improvements in primary manufacturing (lowering the cost of the active pharmaceutical and excipient ingredients). We do not expect these primary manufacturing improvements to come into effect until Q120, but Exhibit 1 illustrates how minor reductions in manufacturing cost can have a major effect on Orexo's valuation. Every 0.5% reduction in CoGS increases our valuation per share by c SEK1.50. We will incorporate the expected primary manufacturing improvements into our model when Orexo provides more colour on their magnitude.

Exhibit 1: Sensitivity of Orexo's share price (SEK) to 0.5% increments in primary manufacturing CoGS improvements from Q120

	Percentage improvement in primary manufacture cost from Q120										
	0%	-0.5%	-1.0%	-1.5%	-2.0%	-2.5%	-3.0%	-3.5%	-4.0%	-4.5%	-5.0%
Per share valuation	97.73	99.16	100.59	102.02	103.46	104.89	106.32	107.76	109.19	110.62	112.05

Source: Edison Investment Research

Q418 and FY18 financials

FY18 total revenues were SEK783m, which despite growing at c 22% missed our forecast of SEK858.9m due to weakness in the partnered products (Abstral and Edluar). Zubsolv's sales growth in Q4 offset much of the weakness in our ambitious estimates of the partnered products' sales, and combined with the higher investment and one-off litigation expense, resulted in our FY18 EPS estimate being SEK1.8 higher than reported. US Zubsolv revenues continue to increase, illustrating the limited effect so far on Zubsolv's market share of the stuttered generic Suboxone film launch in 2018, which was only on the market for a few weeks, although we are cautious on the effect in FY19. In total, 98% of FY18 Zubsolv revenues derived from the US. Total operational expense guidance was c SEK500m for FY18 (and this has been maintained in FY19). Orexo's reported FY18 operational expense of SEK516m was slightly higher than our estimate, but much of the increase included one-off litigation expenses, which are expected to normalise administrative expenses from Q219. The additional Q4 investment in the pipeline (R&D) and to address the generic film threat (marketing) should be welcomed by investors as defensive. Gross margin was 80% in Q418 and we have estimated that it will rise to 83% by Q319 on the secondary manufacturing improvements announced just prior to Orexo's December CMD. Profit after tax for FY18 was SEK138m, with SEK51.6m for Q418 (vs SEK23.2m for FY17 and SEK26.7m for Q417). Orexo's cash at the end of FY18 was SEK590m, which continues to afford Orexo considerable flexibility in structuring product licensing or M&A transactions.

Effect of generic Suboxone on Zubsolv US market share

A single generic Suboxone film formulation was launched by Dr Reddy's in 2018 and Dr Reddy's have elected not to re-launch the product at-risk because of the continuing litigation. We have changed our US market share estimations for Zubsolv in FY19 to 7.25% from 7.50% to reflect our uncertainty surrounding the effect on Zubsolv of multiple generic Suboxone film launches in FY19. While the initial generic launch had a very minor effect on Zubsolv's market share (-0.15%) multiple launches may have a magnified, although temporary, effect on Zubsolv's US market share. However, the changing reimbursement and product characteristic dynamics for the generic films compared to the branded product (which currently has c 65% market share), could also benefit Zubsolv. This is because payers cover the generic but not the brand and if patients dislike the taste and texture of the generic film formulations, market share could be driven to the alternative covered product, Zubsolv.

2018: A year for records but 2019 could be more profitable

In 2018 Orexo passed a FY18 profitability milestone with an EBITDA of SEK116.6m, having increased by nearly 50% y-o-y. This illustrates the leverage of Orexo's commercial organisation with payers and physicians but also bodes well for its business development and M&A activities since much of the sales of a new product added to the Orexo product portfolio will drop to the EBITDA line with few additional operational costs. Orexo's profitability is driven by increasing Zubsolv sales but is further enhanced by its CoGS and supply chain improvements. The latter resulted in a reduction in wholesaler inventory in Q4. Q418 included Zubsolv's largest ever volume quarter (so far) with 407,000 tablets per week.

Abstral and Edluar experience Q3 pressures

As Orexo have previously reported, Abstral and Edluar sales reported by partners tend to lag Orexo's quarterly reporting by about three months. Abstral sales were slightly down in Q318 to SEK52.4m although for FY18 they increased 4.9% to SEK118.8m from SEK113.2m in FY17. Edluar sales were SEK2.9m for Q318 and SEK6.6m for FY18 compared to SEK3.6m and SEK17.3m, for the comparable periods in 2017. The supply issues affecting Edluar in the US were temporary and have already begun to resolve. We have revised our FY19 expectations for Abstral royalties of SEK120m, but retained our Edluar estimates at SEK18m.

The journey of an opioid use disorder patient

In our previous note, we summarised how patients can become dependent on opioids and that the traditional recreational, intravenous drug abuser of heroin, or gateway drugs that lead to opioid dependency, account for only about a third of opioid use disorder (OUD) patients. The majority of US OUD patients are therefore 'accidentally addicted' after originally being legally prescribed an opioid for pain. These patients eventually use opioids from both legal and illegal sources. Another recent report has outlined the more commercial bottlenecks of the US opioid crisis.[1] For example, in 2011 there were over 200 million opioid prescriptions written for pain management.[2]. Unlike the treatment of OUD (which does restrict the type of practice and the number of opioid-dependent patients under care of more than 4,400 US addiction specialists and 9,600 nurse practitioners), there are few specific requirements or registrations for any of the circa one million US physicians to prescribe opioids.

In this note we review the patient journey starting with a diagnosis of opioid dependency (OUD) and draw conclusions on the commercial implications for Orexo, not just in the growth of Zubsolv, or even the market for its pipeline drugs, but also for Orexo's business development and M&A activity.

Patients seeking treatment

A recent book[3] describes the opioid crisis in the US as the greatest drug epidemic in American history, and lists examples of men and women with supportive families, nice homes and successful careers, all of which were lost. This was as a result of the more than 200 million opioid prescriptions that were written for the treatment of pain as a result of a traumatic or surgical injury. While there are similar stories in other countries, the US consumes more than 80% of the world's opioid painkillers (and 99% of the world's hydrocodone supply), but accounts for less than 4.6% of its population. This is particularly ironic in a country that in 1908 had an opium commissioner and later prohibited the production, importation, transportation and sale of alcohol between 1920 and 1933. These days it is easy to see how a patient with acute traumatic pain after an injury can trust, not just the legal prescription that they are given to do no harm, but also in the brand name recognition of drugs like Tylenol 3, Vicodin, Lortab, Percocet and OxyContin, all of which contain an opiate.

The historical origins of the US opioid crisis have a number of roots that include the recognition in the 1970s of the significant utility of opioids in the developing field of palliative care for end-of-life cancer patients (where addiction was never an issue). By extension, opioid treatment was thought to also provide pain relief in non-cancer patients. An irony of the US opioid crisis is that rigorous scientific long-term studies that would have highlighted the dangers of addiction were not done after the 1970s and by the time the epidemic was largely recognised, it was the real world data on

1 www.economist.com/books-and-arts/2018/12/15/americas-opioid-tragedy

2 www.apa.org/about/gr/science/spin/2013/05/prescription-drug-abuse.pdf

3 *American Overdose, the opioid tragedy in three acts*. Chris McGreal, 2018, Faber & Faber

deaths due to overdose, rather than controlled clinical trials, that was compelling. A recent GlobalData webinar on OUD noted that 40% of opioid-related deaths in the US involve a prescription opioid. While a few specialty pharmaceutical companies that developed and marketed opioids have some blame to shoulder in this respect (OxyContin sales doubled to $2bn in three years to 2003), so do direct-to-the-consumer TV advertising and the academic literature, which at the time played down the potential addictive potential of opioids with the now-discredited theory of pseudo-addiction.

Much has been speculated on pre-identifying the segment of between 5–12% of patients prescribed opioids who will become addicted, although the genetic psychological and environmental bases of opioid addiction while contributory have not been quantified. Familial predispositions to alcoholism, gambling and opioid dependency are well-known, as is the type of personality that seeks thrills and an adrenalin rush. Linked to this are functional MRI studies that can identify activity in the reward centres of the brain in opioid-dependent patients, but whatever the aetiology of a particular patient's addiction, the first step in becoming a patient seeking medication-assisted treatment (MAT) is the recognition that the patient has a problem. This not a given, hence the 49,000 deaths due to opioid overdose estimated by the CDC in 2017, which rose from 5,500 in 2001. Although there were an estimated four million treatment-eligible OUD patients in the US in 2017, this number probably belies the dynamic journey OUD patients make after reaching the point where they seek treatment for the first time. Their lives probably become punctuated by periods of recovery with the help of family support, willpower and MAT, and relapse and renewed addiction, either of which can last for many years. Much like cancer patients, OUD patients can be in remission for the rest of their lives, or relapse and ultimately overdose. While the absolute numbers of patients is commercially attractive to any company with a viable franchise in this area, like Orexo, the dynamic and chronic nature of these patients (implying a lifetime of treatment) also suggests a long-term demand for safe and effective MAT.

In a similar way to some forms of multiple sclerosis (MS), opioid addiction can be seen as a relapsing-remitting chronic disease with all the commercial implications that implies. Like MS, OUD patients could be considered a heterogeneous patient group with some patients benefiting from different doses and frequencies of MAT depending on the stage of their treatment, their relapse rate and previous opioid exposure.

Exhibit 2: The range of Zubsolv doses available in the US

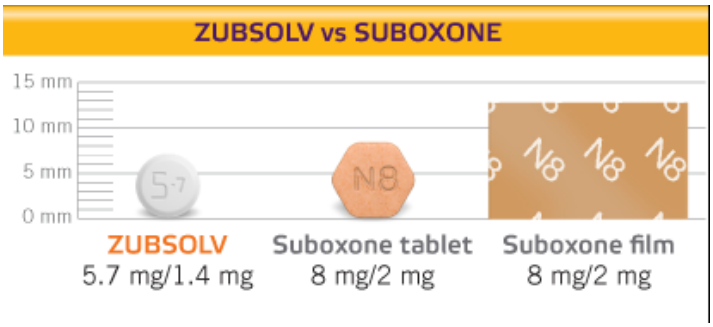
Source: Orexo

Zubsolv is available in a number of strengths (see Exhibit 2) through which a patient can hopefully cycle in their treatment journey from their initial diagnosis and any subsequent relapses. The range of Zubsolv dosage forms has three other advantages. Firstly, the higher doses, which were not the launch doses when Zubsolv was first approved, now allow better treatment with patients with experience of the more powerful synthetic opioids like fentanyl. Secondly, the drug delivery technology in Zubsolv allows for lower equivalent doses of buprenorphine and naloxone compared

to other products (see Exhibit 3). Lastly, Suboxone tablets and films have only two and four dose variants, respectively, with Zubsolv having more flexible dosing potential.

Payers, regulators including the DEA and physicians almost certainly prefer these lower equivalent doses that are brought about by the higher bioavailability of the Zubsolv formulation, and the range of doses allows greater flexibility in bringing a patient down to lower doses over their treatment journey. The lower equivalent dose of Zubsolv also contributes to its reduced CoGS compared to other film and tablet formulations and, as active ingredients are the most expensive part of the formulation, partly explains Orexo's ability to compete with generic formulations of buprenorphine and naloxone.

Exhibit 3: The dose advantage of Zubsolv



Source: Orexo

How the patient journey influences Orexo's pipeline

The continued success of Zubsolv in the US allows Orexo to survey the requirements and unmet needs of OUD patients via their physicians and payers through their interactions with its commercial operation. The most visible and tangible of these developments are the most advanced new products in Orexo's pipeline: OX124 and OX125. The products are spray formulations of either naloxone or nalmefene, respectively, designed to offer improvements to the existing products for opioid overdose reversal (Narcan and Nyxoid are the naloxone spray formulations in the US and Europe, respectively). Opioid overdose patients are typically unresponsive to external stimuli, can suffer respiratory depression and die as a result of exposure to too high, or too potent a dose of opioids. These existing products were developed in a time before the most potent synthetic opioids became available and recent reports have suggested that about 34% of opioid overdose patients in the US require more than one dose of Narcan to recover. This is because the most potent opioids such as fentanyl have higher receptor occupancy rates and longer half-lives than less potent opioids like heroin. Of the 47,600 deaths due to opioid overdose in the US in 2017, 60% were due to synthetic opioids. Because Narcan and Nyxoid are typically administered in the community, either by family members or by emergency medical response staff, these responders may not have more than one reversal dose available.

OX124 and OX125 are nasal sprays that are being developed to address this deficiency of the existing products to treat opioid overdose by using Orexo's formulation technologies. Positive Phase I results on OX124 were reported in January, demonstrating all formulations to be well tolerated and all showed higher plasma concentrations of naloxone, sustained duration of elevated plasma concentrations and equivalent or faster time to onset of activity compared to Narcan. The same patented formulation technology in OX124 can be used for a different active ingredient in OX125, and both products are expected to be filed with the FDA in 2021 and 2022, respectively. These are relatively short development timelines but play to Orexo's historical strengths of developing enhanced formulations of known active ingredients. OX124 and OX125 are expected to be approved, while Zubsolv has many years as a branded and promoted product. These products will be promoted by Orexo's existing salesforce, which calls on addiction specialists. There are two

advantages to this complementary pipeline expansion as pharmaceutical sales representatives are motivated by talking to physicians about new products, but also Orexo's existing commercial organisation will be leveraged by the addition of OX124 and OX125, with the new products requiring minimal additional investment in order to start generating sales.

A recent FDA announcement suggested that the Agency was exploring labelling and legal changes to allow naloxone sprays to be sold in the US without a prescription. If OX124 and OX125 have better efficacy and or safety profiles than Narcan, this could not only increase their commercial value, but also open up another sales channel for Orexo's commercial organisation (see the next section below). Competition between over the counter naloxone sprays for opioid overdose could have an impact on pricing, although the higher volumes are likely to offset this pressure on revenues, which in any event are not currently in our model.

Further back in Orexo's pipeline is OX338, a preclinical sublingual tablet formulation of the non-steroidal anti-inflammatory drug (NASID) ketorolac. Orexo's bioavailability-enhancing formulation may result in pain relief with morphine-like efficacy without exposing the patient to the risk of opioid addiction. Also in preclinical development is OX382, which is a swallowable buprenorphine formulation that protects the drug from the first-pass metabolism that has confined all current treatments for OUD to either oral sublingual or depot subcutaneous formulations. All four of Orexo's pipeline products could be promoted through its existing commercial organisation to its existing target group of physicians, enabling significant salesforce leverage and providing a number of commercial touchpoints with those physicians who treat OUD patients. In addition, as an alternative to short-term pain relief after, for example dental extraction, OX338 could also be co-promoted by a partner to a different set of clinicians than addiction specialists.

The patient journey and Orexo's M&A strategy

In Orexo's recent capital markets day presentation, the perfect M&A partner was described now that the uncertainty surrounding Zubsolv's exclusivity until 2032 has been removed. No transaction has yet been announced and while business development is almost certainly ongoing, it is also likely that the perfect partner may not currently exist at the price at which Orexo is willing to transact. Orexo's internal pipeline described above gives the company ample complementary products with which to leverage the salesforce and expand the franchise in the physicians who treat OUD patients. In addition, the OUD patient journey may suggest different avenues for the expansion of Orexo's commercial franchise by targeting different physician specialties who treat current or former OUD patients, but with different products to those that treat OUD.

Depression and anxiety are the two most common co-morbid psychiatric conditions observed in patients receiving MAT for OUD. There are many studies that have associated patients with major depressive disorder, generalised anxiety syndrome or panic disorder with higher rates of prescription opioid use, than those without those diagnoses. It is however important to note that the association between OUD and psychiatric indications has not been determined to be causal in that either OUD results in depression or anxiety, or vice versa. An association, if not a correlation, is however logical since most OUD patients will be anxious about their next opioid dose, whether it is needed to subdue post-surgical pain or to reduce the symptoms associated with OUD. Whatever the direction of the association, it is clear that the many OUD patient journeys, as well as being punctuated by relapse and remission in opioid use, will either be preceded or followed by the treatment of a psychiatric disorder.

The correlation, even without causation, between OUD and psychiatric disorders could in our opinion bring Orexo a larger number of licensing and M&A options than their existing OUD specialist franchise focus. Orexo's salesforce could be leveraged by visiting psychiatrists and addiction specialists in the same hospital, practice or close geographic location if they also had a relevant product to detail.

Valuation: SEK3.4bn or SEK97.7 per share

The most recent updates to our valuation derive from the changes we incorporated after the Q418 results. Although the Q4 selling and administration costs increased above our forecasts, these have not been maintained beyond Q119 since the bulk of the litigation expenses are expected to come to an end then, and the extra marketing spend to address the re-launch of generic Suboxone films is not currently required until the number and impact of the generic Suboxone launches is known. On that note, we have tempered our US market share expectations on Zubsolv from 7.50% to 7.25% until we can fully assess the effect of the generic Suboxone film launches. The normalisation of administrative spend after Q119 as a result of lower patent litigation activity was a positive driver that offset the maintenance of a higher R&D spend in FY19 and FY20 as the pipeline moves into more advanced (clinical) stages. We regard the one-off patent litigation expense, and then the continuing higher R&D and administrative spends (which contributed to a 31% lower net income than we had estimated) as investments in the company and expect them to be welcomed by investors.

Our DCF valuation of Orexo largely hinges on the commercial prospects for Zubsolv in the US, and hence our interrogation of the OUD patient journey earlier in this note. The successful commercialisation and patent defence of Zubsolv in the US to date now brings the question of what is next for Orexo. Although we have hypothesised the compatibility of anti-psychotics and antidepressants with US Orexo's commercial operations, neither its pipeline, nor the result of M&A or product in-licensing are included in the horizon period in our model but are represented as a modest future revenue component of the terminal value that also includes some branded (or authorised generic) Zubsolv revenues after loss of exclusivity. We have also not included any value for a settlement or damages payable to Orexo from the patent infringement case against Actavis before or after March 2019, although we have included the costs of the litigation until Q219. We consider some advantage is likely for Orexo as Actavis did not appeal the validity of Orexo's '996 patent.

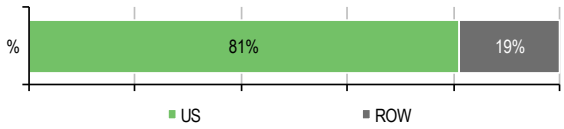
We have updated our valuation to include the cash generated in Q418, the changes to exchange rates and our estimation of the exhaustion of Orexo's tax-losses in 2025. Our valuation changes modestly from SEK3.4bn or SEK95.8 per share previously to SEK3.4bn or SEK97.7 per share based on tempered US Zubsolv market share growth until 2032 (representing 72% of our valuation) and a smaller terminal value (representing 20% of our valuation) that includes Zubsolv sales after 2032, sales of OX124, OX125 and any acquisitions of products to be sold by its US commercial organisation. Orexo's net cash at the end of FY18 represents 8% of our valuation. Royalties on Zubsolv in the EU, Abstral and Edluar are minor components of our valuation in comparison to Zubsolv in the US. Based on Abstral's Q418 weakness, we have also reduced our growth in FY19 to 1%. A new but minor change to our model for FY19 is to reduce the net interest payable from SEK48.4m to SEK12.5m from 2019 to reflect our expectations that most of Orexo's cash balances will be denominated in US dollars.

We have previously included the gross margin improvements to US Zubsolv announced at the Q418 results that will show a 35% improvement over the average CoGS in FY17, from H219 onwards, but we have not yet incorporated gross margin improvements as a result of the primary manufacture improvements noted in Orexo's December 2018 capital markets day. These have been explored in the sensitivity of Orexo's per share valuation to continued CoGS efficiencies in Exhibit 1 (above).

Exhibit 4: Financial summary

SEKm	2016	2017	2018	2019e	2020e
Year end 31 December	IFRS	IFRS	IFRS	IFRS	IFRS
INCOME STATEMENT					
Revenue	705.9	643.7	783.1	866.7	844.1
Cost of Sales	(149.6)	(164.4)	(171.8)	(114.9)	(136.4)
Gross Profit	556.3	479.3	611.3	751.8	712.3
Reported operating profit	51.7	57.4	95.8	265.2	176.2
Net Interest	(16.1)	(27.7)	(3.6)	(12.5)	(19.6)
Profit before tax (reported)	35.6	29.7	92.2	252.7	156.6
Reported tax	(6.5)	(6.5)	45.7	(7.6)	(4.7)
Profit after tax (reported)	29.0	23.2	137.9	245.1	151.9
Minority interests	0.0	0.0	7.0	0.0	0.0
Net income (reported)	29.0	23.2	144.9	245.1	151.9
Basic average number of shares outstanding (m)	35.0	35.0	34.6	34.6	34.6
EPS - basic reported (SEK)	0.84	0.67	3.99	7.08	4.39
EPS - normalised fully diluted (SEK)	0.84	0.67	3.93	6.98	4.32
BALANCE SHEET					
Fixed assets	185.1	176.5	227.1	219.9	213.3
Intangible assets	138.2	121.0	103.9	93.9	84.9
Tangible assets	22.1	20.1	20.0	22.7	25.0
Investments & other	24.8	35.4	103.2	103.2	103.2
Current assets	833.7	827.4	1,059.5	1,311.9	1,470.5
Stocks	344.2	250.2	173.6	150.0	159.2
Debtors	178.5	249.3	296.1	321.9	282.7
Cash & cash equivalents	282.4	327.9	589.8	840.0	1,028.6
Other	28.6	0.0	0.0	0.0	0.0
Current liabilities	(309.5)	(349.9)	(483.4)	(483.4)	(483.4)
Creditors	0.0	0.0	0.0	0.0	0.0
Short-term borrowings	0.0	0.0	0.0	0.0	0.0
Other	(309.5)	(349.9)	(483.4)	(483.4)	(483.4)
Long-term liabilities	(399.0)	(324.9)	(327.1)	(327.1)	(327.1)
Long-term borrowings	(397.8)	(319.1)	(320.6)	(320.6)	(320.6)
Other long-term liabilities	(1.3)	(5.8)	(6.5)	(6.5)	(6.5)
Net assets	310.3	329.1	476.1	721.2	873.1
Shareholders' equity	310.3	329.1	479.6	724.7	876.6
CASH FLOW					
Operating cash flow before WC and Tax	67.5	108.1	70.6	257.2	163.3
Working capital	88.7	0.0	116.7	(2.2)	29.9
Exceptional & other	(20.8)	(37.2)	(14.3)	(12.5)	(19.6)
Tax	(7.5)	0.0	(18.1)	(7.6)	(4.7)
Net operating cash flow	156.2	146.6	187.3	255.0	193.3
Capex	0.5	(1.6)	(6.8)	(4.8)	(4.7)
Acquisitions/disposals	5.0	0.0	0.0	0.0	0.0
Equity financing	2.2	0.1	0.0	0.0	0.0
Other	0.0	0.0	0.4	0.0	0.0
Net cash flow	163.9	145.1	261.9	250.3	188.6
Opening net debt (cash)	296.3	115.4	(8.8)	(269.2)	(519.4)
Other	17.0	(20.9)	18.9	0.0	0.0
Closing net debt (cash)	115.4	(8.8)	(269.2)	(519.4)	(708.0)

Source: Orexo accounts, Edison Investment Research

Contact details	Revenue by geography
Virdings allé 32 A SE - 753 50 Uppsala Sweden +46 (0)18 780 88 00 www.orexo.com	

Management team

CEO: Nikolaj Sørensen

Mr Sørensen has been CEO since 2013, having joined Orexo in October 2011 as chief commercial officer. He has international commercial experience of the pharmaceuticals industry from roles at Pfizer and the Boston Consulting Group. He was a board member of the Swedish Pharmaceutical Industry Association (LIF) until 2012, and holds an MSc in business and economics.

CFO: Joseph DeFeo

Mr DeFeo is located in the US and has previously been the head of finance and head of operations in Orexo's US subsidiary. Prior to joining Orexo he worked in several senior finance positions; among other roles, he established the US operations of a large Italian pharmaceutical company, was the head of International Treasury and also led the finance teams for the US commercial operations of two major pharmaceutical companies.

President of Orexo US: Robert DeLuca

Mr DeLuca has been president of US operations since 2013. He has extensive experience in establishing commercial operations in the US, with a background in market access, marketing and sales. He was most recently chief commercial officer at Archimedes Pharmaceutical and previously held positions at Sanofi-Aventis, Schering-Plough, Berlex and Pharmacia.

Chairman: Martin Nicklasson

Dr Nicklasson has been chairman since 2012. He is also chairman of Farma Holding, a board member of Pozen, Oasmia, Biocrine and Denator, and a member of the Royal Academy of Engineering Sciences (IVA). His previous roles include CEO at Swedish Orphan Biovitrum, senior management roles at Astra/AstraZeneca with responsibilities for global drug development and marketing and business development, and CEO at AstraZeneca Sweden. He was also CEO at Astra Hässle and responsible for R&D within KABI. He holds MSc Pharm and PhD degrees and is associate professor at the Faculty of Pharmacy, Uppsala University.

Principal shareholders	(%)
Novo As	27.9
HealthCap Venture Capital	11.5
Arbejdmarkedets Tillaegspension (ATP)	5.9
HealthInvest Partners AB	4.8
Walldov, Anders	4.3
Försäkringsaktiebolaget Avanza Pension	3.4
Lancelot Asset management	1.6
Nordnet Pensionsförsäkring	1.4

Companies named in this report

Actavis Generics (acquired by Teva Pharmaceutical Industries Ltd), Dr Reddy's Laboratories

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