EDISON

# Xbrane Biopharma

Initiation of coverage

## Price-competitive generic and biosimilar therapies

Pharma & biotech

**Xbrane's first sales in 2017 will be of Spherotide: the first generic formulation of the prostate cancer therapy triptorelin (cancer sales about $380m). A SEK7m order is ready for shipment to Iran, once authorised. A Chinese deal worth SEK17m upfront, $8m total, may be signed in Q117. European partnering and launches are possible from 2019 after clinical trials. Xbrane (or a partner) may sell Xlucane, its low-cost biosimilar of Lucentis (2015 sales $3.6bn), in the US after 2021 and from 2022 in Europe.**

| Year end | Revenue (SEKm) | PBT* (SEKm) | EPS* (SEK) | DPS (SEK) | P/E (x) | Yield (%) |
|---|---|---|---|---|---|---|
| 12/15 | 0.4 | (11.0) | (2.5) | 0.0 | N/A | N/A |
| 12/16e | 2.2 | (25.1) | (5.4) | 0.0 | N/A | N/A |
| 12/17e | 24.0 | (15.8) | (3.4) | 0.0 | N/A | N/A |
| 12/18e | 22.1 | (94.4) | (20.4) | 0.0 | N/A | N/A |

Note: *PBT and EPS are normalised, excluding amortisation of acquired intangibles, exceptional items and share-based payments.

## Prostate cancer: First triptorelin generic to market

Triptorelin, sold as various brands including Decapeptyl (Ipsen; 2015 sales: €334m), is used to treat advanced prostate cancer, endometriosis and uterine fibroids. Sales in 2015 for these indications were $380m. Triptorelin is one of a well-known class that suppress GnRH receptors. The leaders are goserelin (Zoladex, AstraZeneca; 2015 sales: $816m) and leuprolide (Lupron, AbbVie; $826m). Initial Spherotide sales are planned in 2017 with a SEK7m order to Iran. An agreed, but not signed, Chinese $8m deal should yield SEK17m cash in Q117 with sales perhaps from 2021/22. EU marketing is expected from 2019 via a partner.

## Lucentis: Limited competition for a share of $3.6bn

Xbrane is developing a biosimilar of Lucentis (ranibizumab, Roche/Novartis; 2015 sales: $3.6bn) to treat wet age-related macular degeneration (wAMD). In 2015, Lucentis sales fell by 15% due to competition with Eylea (Regeneron/Bayer; 2015 sales: $4bn). Xbrane has a patented production method that claims to lower material costs by 85%. The process is being scaled up and needs GMP validation. For the US and EU, Xlucane plans a 400-700 patient clinical trial that might start by late 2017. The US patent on Lucentis expires in 2020 and in 2022 in Europe; Xlucane may be available in the US after 2021 and from 2022 in Europe. Xbrane indicates that Iranian sales are possible from H217. A Lucentis biosimilar was launched in India by Intas in 2015. Formycon (with bioeq GmbH) is in Phase III aiming for H1 2020 data. Pfenex has Phase I/II data on PF582 but no partner.

## Valuation: Attractive markets

The value of the Edison forecast cash flows between 2017 and 2030 is estimated at SEK170m with a continuing NPV at a -1% growth rate of SEK202m. This gives a combined value of SEK372m and equates to SEK78 a share. We assume a partner is prepared to fund half the SEK230m cost of Xlucane trials from 2017, but there is still potential for further dilution. Management anticipates that revenue from deals and sales could meet 2018 cash requirements; a Spherotide EU partnering deal is anticipated similar to the China deal. Delayed or smaller deals could lead to a funding need estimated by Edison at up to SEK100m.

**31 January 2017**

| | |
|---|---|
| **Price** | **SEK38.7** |
| **Market cap** | **SEK184m** |
| | SEK9.14/US$ |
| Cash (SEKm) at 30 September 2016 | 43.9 |
| Shares in issue (October 2016) | 4.76m |
| Free float | 67% |
| Code | XBRANE |
| Primary exchange | NASDAQ First North |
| Secondary exchange | N/A |

### Share price performance


| % | 1m | 3m | 12m |
|---|---|---|---|
| Abs | (4.4) | (2.3) | N/A |
| Rel (local) | (5.2) | (6.3) | N/A |
| 52-week high/low | SEK45.5 | SEK28.9 | |

### Business description

Xbrane Biopharma is a Swedish developer of biosimilars using a patented, more efficient manufacturing system. The lead product is Xlucane, a Lucentis biosimilar. Xbrane's first product will be a triptorelin generic, Spherotide, for prostate cancer. First sales will be to Iran in 2017. European approval is possible in 2019.

### Next events

| | |
|---|---|
| FY16 results | Q117 |

### Analysts


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***Xbrane Biopharma is a research client of Edison Investment Research Limited***

## Investment summary: Competitive generics

Xbrane Biopharma is a Swedish company with two business lines: a range of developing long-acting generic drug formulations and low-cost production of biosimilars. Currently, Xbrane is focusing just on Spherotide (prostate cancer) and Xlucane (AMD). Spherotide is produced by Xbrane's Italian subsidiary. Xbrane plans to run clinical studies from 2017 to enter the European market from 2019. It may have initial Iranian sales in 2017 and Chinese sales from 2021/22. The bigger, but less advanced, product is Xlucane. This requires more clinical development and could reach the US market from 2021 and the European market from 2022. There may be Iranian sales from late 2017/18. Xbrane listed on the Nasdaq Stockholm stock exchange on 3 February 2016 at SEK42.50 per share, raising SEK100m.

### Valuation: SEK372m, or SEK78/share

The overall value comprises the present value of the cash flows after costs and tax between 2017 and 2030 plus a continuing value. The NPV of the cash flows is estimated at SEK169.5m, with a continuing NPV at a minus 1% growth rate of SEK202.5m. This gives a combined value of SEK372.0m. A partner prepared to fund half the SEK230m cost of Xlucane trials from 2017 is assumed, but there is still potential for further dilution. Further deals and clinical data will add value by reducing risk and lowering the dilution potential.

### Financials: Cash for 2017 while deals are done

We forecast Xbrane will start 2017 with about SEK38m cash and a SEK7m Iranian order awaiting shipment. European sales of Spherotide are not expected until 2019. A SEK17m Chinese upfront payment is expected in Q1 on signing a distribution deal. Sales are expected to develop in Iran over 2017 and 2018. The cash outflow in 2017 might be SEK17m on cautious clinical expenditure. Xbrane needs to complete clinical development of the one-month formulation and to develop the higher value three-month Spherotide formulation. Edison expects about SEK21m cash at year end 2017. This implies that Xbrane will need further funding for the estimated SEK230m clinical trial programme required for Xlucane. This funding could come from Xlucane and European Spherotide deals.

### Sensitivities: Opportunity rich but cash poor

Xbrane has a number of short-term sensitivities that will have a high impact on its cash flow and valuation. The Chinese deal, which needs to be signed, yields a SEK17m upfront. This would offset some clinical trial costs and the development of a three-month formulation required for the European market. Once the initial SEK7m Iranian order is fulfilled, sales development will depend on gaining a high market share by aggressive pricing. Validating the one- and three-month formulations to European standards is an essential target for 2017; a European deal may require a validated three-month product. Spherotide competes against Decapeptyl and indirectly against leuprorelin and goserelin. Accordingly, several competitors may compete fiercely.

With Xlucane, Xbrane has the challenge of funding equivalence clinical studies. The obvious route is partnering and Edison has assumed a 50-50 split in the costs. However, a full partnering deal could be concluded, or Xbrane may have to find the cash required itself. The Lucentis market targeted by Xlucane is shrinking and Xlucane might be the third product to market, possibly from 2021 in the US, provided that clinical trials start in 2017. Iranian sales may start from 2018. Roche and Novartis may employ various strategies, including competitive pricing, to prevent Lucentis biosimilars gaining market share. Edison notes that the Xbrane system has never been used for manufacturing at commercial scale, so there may be unexpected technical scale-up challenges and opportunities.

## Company description: Generic and biosimilar tracks

Xbrane Biopharma is a Swedish company, founded in 2007, developing long-acting generic drug formulations and injectable biosimilars. The focus on generic molecules means that Xbrane does not have the standard costs and risks of developing novel therapeutic entities. This potentially allows Xbrane to run a broader pipeline in future as it only needs to manufacture the product and run clinical equivalence trials to gain regulatory approval. Currently, Xbrane is focusing on two products Spherotide, a slow-release depot delivery of a generic prostate cancer therapy, and Xlucane, a biosimilar for age-related macular degeneration (AMD). Xbrane listed on the Nasdaq Stockholm exchange on 3 February 2016 at SEK42.50 per share, raising SEK100m.

## Slow-release delivery systems

Xbrane diversified into small molecule delivery systems with the acquisition of Primm Pharma on 30 September 2015. Terms are given in the financial section below. Primm Pharma creates microspheres that are mixtures of biocompatible polymers and small molecule therapeutics.[1] The polymers degrade in the body and release the therapeutic entity at a steady, calibrated rate.

Xbrane, like other companies, uses poly(lactic-co-glycolic acid) (PLGA) as the polymer carrier for triptorelin. PLGA is well understood and approved by regulators. Xbrane's delivery pipeline is shown in Exhibit 1. The lead slow-release delivery project is Spherotide. Exenasphere has completed preclinical testing. The others are in process development.

**Exhibit 1: Small molecule delivery generic portfolio**

| | Process development | GMP Production | Comparative clinical trial | Market registration |
|---|---|---|---|---|
| Spherotide | | 2016 | 2017/2018 | 2019 |
| Exenasphere | 2016/2017 | | | |
| Luprosphere | 2017/2018 | | | |
| Risperisphere | 2017 | | | |
| Octreosphere | 2017/2018 | | | |

| Original drug | Active substance | Indication | Global sales (M USD) | Primary patent expiry |
|---|---|---|---|---|
| Decapeptyl | Triptorelin | Prostate cancer | 500 | Expired |
| Bydureon | Exenatide | Type 2 diabetes | 440 | 2022 (US) |
| Lupron | Leuprolide | Prostate cancer | 1800* | Expired |
| Risperidal Consta | Risperidone | Schizofrenia | 1300 | 2020 (US) |
| Sandostatin LAR | Octreotide | Acromegaly | 1600 | Expired |

Source: Xbrane presentation January 2017

Of the other products, Bydureon (exenatide), a diabetes control agent, is on patent. Leuprolide for prostate cancer already has generic competitors. Risperidone, an antipsychotic, is used to control schizophrenia and bipolar disorder. It came off patent as a molecule in 2003. Risperdal Consta is the only FDA-approved slow-release version of risperidone and is patented until 2020; the first patent (US 5792477) expires in 2017. Sandostatin treats acromegaly: excessive growth due to the pituitary gland producing too much growth hormone; this is often due to a benign tumour.

### GnRH agonists: The world of Spherotide (triptorelin)

Triptorelin is one of a class of gonadotropin releasing hormone (GnRH) agonists. The total market was worth $446m in 2015 (IMS data).[2] This excludes some countries, including Iran. About $388m of these sales are for depot[3] formulations, like Spherotide, with the remaining $58m for single injection

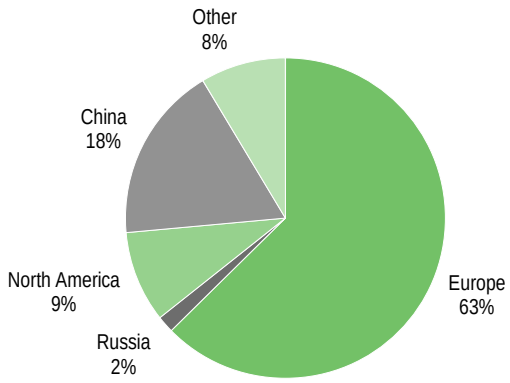
1 The polymer and drug are both polymeric molecules. When these have opposite electrical charges and are mixed, they stick together electrostatically to form water repelling microspheres, a process called coacervation (see example). The microspheres can be coated for improved stability and to form a free flowing powder.

2 IMS data is very reliable in leading major Western markets but can be rather limited in other territories and unavailable in some, like Iran. Xbrane has supplied Edison with IMS on triptorelin only from 2013-15.

3 A depot is when enough drug for a period of days/months is given in one injection and then slowly released. This means that drug has to be encapsulated in some way.

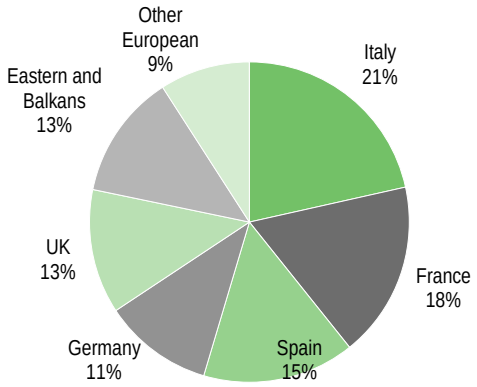
treatments, mainly usually used for fertility treatments. The market was stable over 2013 and 2014, but prices fell about 20% in 2015. World sales by territory are shown in Exhibit 2. The European market is in Exhibit 3; Exhibit 4 gives background.

**Exhibit 2: Depot sales of triptorelin by region**




Source: Edison Investment Research based on IMS data

**Exhibit 3: Triptorelin depot sales by European region**




Source: Edison Investment Research based on IMS data

**Exhibit 4: GnRH background information**

| Aspect | Commentary |
|---|---|
| Indications | GnRH agonists are mainly (at least 75% of sales) used to treat advanced, hormone responsive prostate cancer in men (with localised or distant spread). The incidence of this is strongly age related with men over 65 being at higher risk. Most cases (>90%) of prostate cancer are detected with the cancer contained within the prostate gland so other treatments can be used without effective castration. In women, GnRH agonists treat endometriosis and uterine fibroids. They can also be used to manage precocious puberty. |
| Pharmacology and flare | The pharmacology of these products is well-known. GnRH (also called LNRH) is produced in the brain (in the hypothalamus) and transported in the blood to the pituitary gland where it binds to the gonadotropin-releasing hormone receptor (GnRHR; also known as LHRH). This triggers other hormones that travel in the blood to the gonads to stimulate sex hormones production. Because these agonists at high dose activate all the GnRH receptors, this leads to a flare in sex hormone production. GnRH agonists are also used to trigger ovulation in women undergoing fertility treatments. |
| Long-term therapy | After the initial flare, if the GnRH agonist remains at a constant high level, the pituitary cells become unresponsive. This means that the gonads cease to produce sex hormones. As a steady dose of drug is needed, these drugs are all given by depot delivery to ensure constant delivery over a period of months. Any generic also has to show this constant delivery profile and avoid repeated flares. It is not enough just to use three times more drug in a three-month vs a one-month depot. The characteristics must be adjusted to give a slower rate of release. |
| Dose versions | The standard delivery (dose) periods are one month (3.75mg) and three months (about 11.25mg) but a six-month (22mg) depot of triptorelin is available, largely from Ipsen and Allergan. Pricing varies but a one-month depot costs $90-190. Three-month doses are three times the one-month price. Fertility versions are one-day doses sold in high volumes, priced at about $10 per dose. |

Source: Edison Investment Research based on literature sources

Triptorelin is marketed as Decapeptyl by Ipsen and as Trelstar by Allergan. In 2015, Decapeptyl was Ipsen's second-biggest product with €334m of sales, accounting for 30% of its total revenue. It is therefore likely that Ipsen will try to defend this revenue, at least in core territories. There are two other molecules in this class (see Exhibit 5): Zoladex (goserelin, AstraZeneca) and Lupron (leuprolide, AbbVie). A fourth, related product is a GNRH antagonist, Firmagon (degarelix, Ferring). There are three depot doses of triptorelin sold: one month (3.75mg), three months (11.2mg) and six months (22.5mg). The other two GnRH agonists are similar.

## Europe – a three-month market

The European market (excluding single use injections) was worth about $244m in 2015 (IMS). The top five European countries account for about 86% of sales, see Exhibit 3 above. The biggest market is Italy with $54m of sales (apparently due to a high market share according to Xbrane). Xbrane will follow the decentralised procedure with Spherotide, ie country-by-country approvals.

The market by value is dominated by the three-month formulation, which outsells the one-month by 3:1, Exhibit 6. According to IMS data, there were the equivalent of 2.5 million monthly doses sold in 2015, but the actual number of packs was about 1.1 million, comprising 570k one-month, 450k three-month and 80k six-month depot formulations Exhibit 7. However, preferred dose formats vary; Italy, for example, predominantly uses the one-month formulation, whereas Germany prefers three- and six-month formulations. Consequently, Xbrane needs to develop and validate a three-month dose

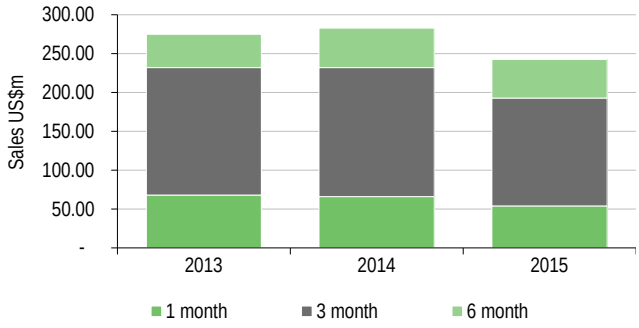
formulation to gain significant sales.[4] In marketing terms, this also means that the number of opportunities per year to switch brands is more limited compared to patients on monthly dosing.

**Exhibit 5: GnRH products – three agonists and an antagonist**

| Product | Commentary |
|---|---|
| Zoladex (goserelin) | Zoladex has been marketed since 1989 and is the GnRH agonist market leader: sales in 2015 were $816m with $200m in Europe; the rest are mostly US. The first generic, Reseligo (sold by Alvogen), was launched in Central and Eastern Europe (excluding Germany and Austria) in May 2016; one- and three-month doses are available. Because no other generic has appeared, AstraZeneca has continued to invest in new production facilities for Zoladex.<br>Zoladex is administered as small white pellets implanted under the skin using a specialist syringe. |
| Lupron (leuprorelin) | Leuprorelin has multiple versions available. Leuprorelin was first approved in 1985 with the first depot FDA-approved in 1989. It was marketed in a joint venture (TAP) between Takeda and Abbott Laboratories. The JV ended in 2008. TAP was integrated into Takeda in 2008. Leuprorelin is now sold as Lupron Depot by AbbVie. Also in the US, leuprorelin is sold as Eligard by Tolmar (US) in various dose strengths. Eligard is distributed in 64 other countries by a variety of partners including Sanofi-Aventis. Takeda sells leuprorelin in the US, Europe, Asia and Japan as Prostap with one- and three-month formulations.<br>In Iran, Leupromer is sold by Varian Pharmed in one-month doses (3.75mg and 7.5mg doses).<br>Leuprorelin is supplied as a syringe containing a powder of microspheres. A separate syringe contains a solution in which to suspend the powder before intramuscular injection (pack leaflet). Systems from different suppliers differ slightly but all are basically the same. |
| Decapeptyl (triptorelin) | Decapeptyl, a depot formulation of triptorelin contained in a D,L-lactide/glycolide copolymer, was developed by Debiopharm and licensed in Europe and other territories where it was launched in 1994. It was approved in the US in June 2000. In 2004 triptorelin was exclusively licensed for the US market to Watson Pharmaceuticals and sold under the Trelstar brand; Watson was acquired by Allergan. A one-month depot generic of triptorelin, Variopeptyl (from Ferring), is sold in Iran by Varian Pharmed. Ferring sells triptorelin as a one-month depot and sells the naked drug for female fertility indications as Gonapeptyl: a low single daily dose; there are multiple generic suppliers of the fertility variation.<br>Decapeptyl is supplied as a powder The polymer particles have to be suspended in the supplied liquid before intramuscular injection. |
| GnRH Antagonists | The alternative to one of the three above GnRH agonists is a GnRH antagonist, that is, a molecule that blocks the receptor. This completely avoids flare. However, GnRH antagonists can have serious side effects; the drug Plenaxis (abarelix) was discontinued after its 2005 launch – it has restricted use in Germany. The only GnRH antagonist authorised for advanced prostate cancer is Firmagon (degarelix, Ferring), approved in the US in 2008 and EU in 2009. It is a depot injection. Other GnRH antagonists are only used in female fertility treatment: Ganirelix and Cetrorelix. |

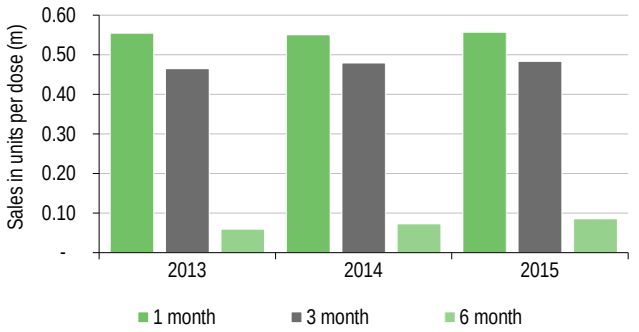
Source: Edison Investment Research, literature sources as cited

**Exhibit 6: European triptorelin sales by pack value**




Source: Edison Investment Research based on IMS data

**Exhibit 7: European triptorelin sales by pack volume**




Source: Edison Investment Research based on IMS data

## US market – too small and costly

The US market is worth $36m, largely the three-month depot formulations. Allergan sells all the product under the Trelstar brand. This makes it uneconomic to run the rigorous trials demanded by the FDA. Canada might be accessible and is worth $6.6m (2015) with falling prices. Edison has not included the US in its market forecasts.

## China – large but inscrutable

The Chinese market, $69m, could be significant for Xbrane; Ipsen sold $57m of the one-month product in 2015 at $195 per dose comprising 290,000 doses; Ferring sold $8m in 2015 a three-month depot product; there were $4m sales of a higher dose formulation. The market is stable with a small price fall in 2015. The high price may reflect the perceived status of Western branded products. Ipsen has stated in corporate presentations that triptorelin has a 50% market share.

[4] Xbrane has stated to Edison that it is not currently developing a six-month dose form. This may change.

Xbrane announced in November that it had signed a non-binding term sheet with a prospective Chinese partner. The $8m deal is expected to complete in Q117 with a down payment of SEK17m, with a further three payments due. Marketing approval is needed from the China Food and Drug Administration (SFDA) and requires prior European authorisation. The willingness of the Chinese partner to buy the rights and fund the Chinese clinical trials indicates an expectation of high returns. Exhibit 8 discusses market expectations. Edison has followed Xbrane in forecasting an 85% share in China, but does not assume volume growth as there is insufficient data to be sure of a growth trend. A 50% probability adjustment is then applied, giving a forecast of SEK100m of Xbrane revenues.

**Exhibit 8: Chinese market assessments**

| Perspective | Market estimates |
|---|---|
| Xbrane | Xbrane anticipates that Spherotide will generate revenues of SEK350m ($38m). This implies that Spherotide, priced at a 50% discount, gains an 85% share of a market predicted by Xbrane to nearly double from about 300,000 doses in 2015 to nearly 600,000 doses by 2030. |
| Edison | We have taken a more cautious approach to forecasting China for the current valuation. Although strong market growth is entirely plausible in the long term, given China's ageing population, the current market fell 5% from 2014 to 2015. So we assume the market is static. Ipsen may also choose to compete on price if significant market growth is seen, although generic penetration rates are 85% in China. Local competitors may enter the market. |

Source: Edison Investment Research

## Other regions – small opportunities add up

There are about $30m of triptorelin sales in Russia and a variety of other countries in Asia, Latin America and Africa. These are all individually small markets using the one-month formulation. IMS tends to underreport these markets. Collectively, these are more likely to take up a lower-priced generic product. Xbrane projects over 80% triptorelin market share with Spherotide.

A deal for Israel was signed in December 2016 with BioAvenir. Xbrane estimates a sales potential of SEK5m per year. Xbrane and BioAvenir will share the profits. Xbrane will receive a licence fee of SEK1m divided in upfront and milestone payments prior to launch in 2020.

## Iran and the Middle East – eastern promise

The other market being addressed by Xbrane is the Middle East. There is limited data on the markets in the small countries; most are minute. The major market identified by Xbrane is Iran, Exhibit 9, where triptorelin is sold by Ipsen as Diphereline (Ipsen in a 2011 presentation claimed a 65% market share in Iran) and by Varian as Variopeptyl (from Ferring). Xbrane has received a SEK7m initial order of the one-month triptorelin formulation from its partner, Pooyesh Darou. Pooyesh Darou will sell using the brand name Microrelin. To avoid high import tariffs, the drug-loaded microspheres will be manufactured in Italy and dispensed into vials in Iran. This will be supplied once Primm Pharma has received Italian GMP quality approval.

**Exhibit 9: Iranian market assessments**

| Perspective | Discussion |
|---|---|
| Pooyesh Darou | Ipsen stated (2011) that triptorelin accounted for 65% of the total Iranian GnRH market. Xbrane's partner estimates the market is worth $30m but this cannot be verified by Edison. The Xbrane distributor intends to capture 90% of the triptorelin market by 2020 as the Iranian healthcare system requires the lowest priced product to be used. Pooyesh Darou claims to have done this with high-value biosimilars. Xbrane has stated a target of SEK80m of sales in the Middle East by 2020. |
| Edison | We have followed the Xbrane estimates but been more cautious. Based on a population of men aged over 65 of two million, we would expect at most 2,000 cases of advanced prostate cancer per year (Li et al. 2012). These may then have a long survival so prevalence is possibly tenfold higher. This depends on adequate medical coverage for diagnosis and treatment. An Iran database survey (Pakzad et al. 2016) found 2,678 new cases a year of prostate cancer; there was no staging information. |

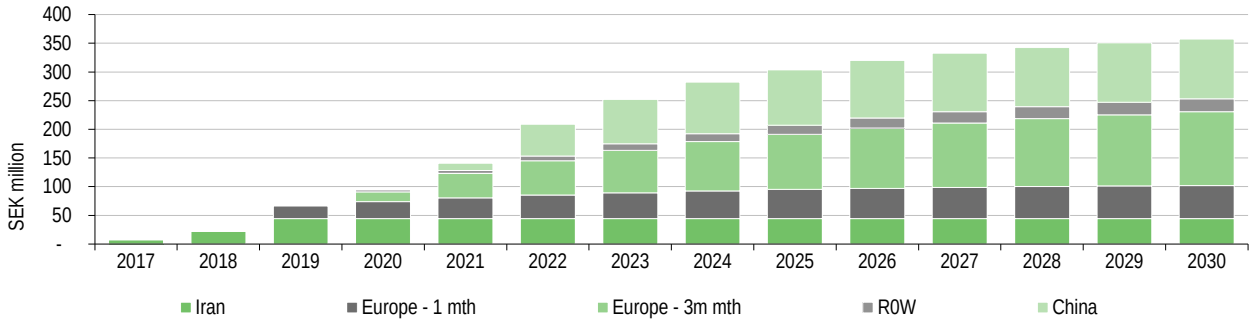
Source: Edison Investment Research

For forecasting, Edison has used the distributor market estimate of $30m and followed Xbrane in assuming that Spherotide gains 90% share by 2020. This gives an Edison estimate of SEK44m in Xbrane revenues from 2020. We assume a 50% gross margin and apply a 50% probability given the various uncertainties and lack of firm data.

## Projecting the Spherotide market

In the IPO prospectus, Xbrane stated its goal of Spherotide revenues of over SEK200m by 2020. The more conservative Edison market projection (not risk-adjusted) is shown in Exhibit 10. To avoid too many assumptions, we have assumed that the overall market share of triptorelin is stable with Spherotide taking share only from other triptorelin brands. Before probability adjustment, this gives an Xbrane revenue forecast of SEK357m by 2030, about $39m. The unadjusted Spherotide gross margin would be SEK243m, about $27m. After adjustment, this is SEK114m.

**Exhibit 10: Xbrane non-risk adjusted Spherotide revenue forecast**




Source: Edison Investment Research. Note that the in-market sales by partners would be twice these values.

The core of the forecast is Iran, with SEK44m peak sales per year at a 50% margin. The actual sales growth in Iran is particularly important over the 2017-20 period for cash management. The one-month formulation could be sold in Europe from 2019 if approved. This is a low-margin product.[5] Volume is also relatively low outside China and Iran. However, it is reasonable to assume that CoG will fall as volumes increase; Edison assumes an annual 5% decrease from 2020.

Chinese sales are estimated to start in 2021/22. Because the current Chinese price is $195 for one month, even after dropping prices by 50% then giving a 50% distributor margin there is still a significant gross margin; Edison estimates maybe 60%. However, competition could erode this.

The core market is the European three-month dose. CoG is marginally higher than the one-month dose, but the market price is three times higher, so a gross margin of over 70% is possible. Edison has seen no data on the three-month formulation and EU launch is unlikely before 2020. One or more European marketing partners is assumed to be required. While these could be agreed at any time, Edison assumes a deal for SEK80m with SEK20m upfront and SEK60m on approval of the key three-month formulation. As deal structure is uncertain, a 60% probability is applied to the one-month and 45% to the three-month formulation milestones. The deal value could be much higher.

## Biosimilars: Seeking lucrative niches

Many biological drugs are complex proteins like antibodies that must be manufactured in expensive mammalian cell culture systems; an example is Humira (adalimumab) with sales of $14bn in 2015. Large, well-resourced companies target these. By contrast, the Xbrane bacterial fermentation system is designed to make smaller, less complex biological drugs such as antibody fragments, peptides (small proteins or sections of larger proteins) or simple enzymes. Bacterial systems are much simpler and cheaper to run, where they can be used. Lucentis, of which Xlucane is a proposed biosimilar, is a

[5] Xbrane aims to halve the current price, typically $90; this gives a wholesale price of $45/dose. Distributors will take 40-50%, leaving perhaps $23/dose for Xbrane. CoG has not been published by Xbrane but is assumed by Edison to be $15-20 (based on Iran bulk estimates plus filling costs and packaging).

smaller monoclonal antibody fragment. As such, it can be made in the Xbrane system, similar to the Lucentis system. Exhibit 11 shows the current Xbrane biosimilar pipeline with two other products:

Cimzia (certolizumab) is a pegylated antibody fragment with an improved half-life. It binds TNF and is used to treat inflammatory diseases like Crohn's disease and moderate rheumatoid arthritis. It is sold by UCB.

Oncaspar (pegaspargase) is used to treat acute lymphoblastic leukaemia alongside chemotherapy. It is sold by Shire. It is a bacterial enzyme: L-asparagine amidohydrolase. This is then covalently conjugated to monomethoxy-polyethylene glycol (mPEG) to improve its half-life when injected. The treatment of ALL is potentially being changed by the development of CAR T-cell therapies.

**Exhibit 11: Xbrane biosimilar pipeline**

| | Process development | GMP Production | Phase I/II | Phase III | Original drug | Active substance | Indication | Global sales (M USD) | Primary patent expiry |
|---|---|---|---|---|---|---|---|---|---|
| Xlucane | 2016 | 2016/2017 | n/a | 2018/2019 | Lucentis | Ranibizumab | Age related macula degeneration | 3600 | 2020 (US) |
| Xcimzane | 2017 | | | | Cimzia | Certolizumab pegol | Rheumatoid arthritis | 950 | 2022 |
| Xoncane | 2017 | | | | Oncaspar | Pegaspargase | Acute lymphocytic leukemia | 200 | 2017 |

Source: Xbrane presentation January 2017

## High-efficiency manufacturing of small proteins

Xbrane owns IP pertaining to a protein expression system in *E. coli*. Xbrane's system, named Lemo21, has been published (Wagner et al. 2008). It is detailed in Exhibit 12. The core patent is titled "Expression system for proteins" (WO2009106635). The patent has been granted in the US (US8138324B2) and Europe (EP2268818B1); protection in both regions extends to February 2029.

**Exhibit 12: Lemo21 background**

| Aspect | Comment |
|---|---|
| Technology | Lemo21 consists of an *E. coli* bacterial strain tunable for membrane protein overexpression. This works by adding in calibrated amounts of a sugar, rhamnose or arabinose, to alter the expression level of the T7 RNA polymerase. This enables the synthesis rate to be optimised for the fermenter conditions so the overall yield can be higher. |
| Advantage | Xbrane states that this results in an eightfold higher yield compared with the conventional, non-tunable T7 system for *E. coli*. Xbrane has used this system to undertake contract development so has experience from 10 client projects. |
| Research use sales | Lemo21 is sold as a research product through New England Bio Labs. It has been licensed to Oxford Nanopore (a DNA sequencing company) for commercial use. This produces a small annual revenue stream. |
| Other cost factors | Bulk production costs are only one element of the overall cost; purification, packaging and quality control are also factors and in effect largely fixed costs. Lower raw material production costs are more likely to be important once the product gains significant market share. |

Source: Edison Investment Research, Xbrane presentations and patents

Xbrane has used this system to develop tailor-made expression systems for specific proteins and enzymes for clients in the biopharma sector achieving up to 85% lower production costs compared to standard T7 systems. This could give a cost advantage in a competitive market for products made in bacterial systems such as Lucentis, Cimzia, Oncaspar and others.

Xbrane runs a 20l pilot-scale facility and does not have its own GMP production facility for Xlucane. Commercial manufacturing will be outsourced to a CMO with capacity to produce at a larger scale. The plan is to scale up production for the clinical trials required for registration in the US and EU.

# Xlucane: A dent in the $3.6bn Lucentis market

Xlucane is Xbrane's proposed biosimilar of Lucentis. Lucentis is used to treat wet AMD (wAMD), Exhibit 13 and competes with Eylea (aflibercept Regeneron) and off-label Avastin (Bevacizumab, Roche) (Exhibit 14)

**Exhibit 13: Basics of wet AMD and Lucentis**

| | |
|---|---|
| Wet AMD | Wet age-related macular degeneration AMD is caused by the abnormal growth of blood vessels beneath the retina, which may leak fluid and blood and cause swelling. It is associated with age and prevalence in 2015 was 1.5 million patients in the US (DataMonitor). |
| Lucentis | Lucentis (ranibizumab, Roche/Novartis) is an antibody fragment of 48.4 kDa with a binding region similar to Avastin (bevacizumab, Roche, Avastin is much larger as a whole antibody). Lucentis is a vascular endothelial growth factor (VEGF) inhibitor that prevents endothelial cells from forming blood vessels. Lucentis was first approved in the US in 2006 for the treatment of wAMD. It has subsequently been approved for macular oedema following retinal vein occlusion (RVO), diabetic macular oedema (DMO), non-proliferative diabetic retinopathy and proliferative diabetic retinopathy. |

Source: Edison Investment Research

**Exhibit 14: Anti-VEGF products for wAMD**

| Product | Price/injection (US$) | Quantity (mg) per injection | Dosage | Price/two-year treatment (US$) |
|---|---|---|---|---|
| Lucentis (US) | 2,000 | 0.5 | Once per month | 48,000 |
| Eylea | 1,850 | 2 | Once per month (first 3 months); once every other month | 24,050 |
| Off-label Avastin | 50 | 1.25 | Once per month | 1,200 |

Source: Edison Investment Research. Note: Eylea dosing intervals may be more frequent in reality.

There are three potential biosimilar competitors alongside Xlucane, Exhibit 15. A proposed biosimilar Lucentis, Razumab, is already marketed in India by Intas. It is unclear whether Razumab will pass the FDA and EMA biosimilarity standards so it is not included in our forecasts. Two other projects are visible. The major threat seems to be from Formycon, which is the most advanced and in a Phase III study. The other, from Pfenex, is on hold while a fresh partner is sought after the withdrawal of Pfizer.

**Exhibit 15: Competition**

| Company | Product | Status | Comments |
|---|---|---|---|
| Intas | Razumab | Market (India) | Not clear if it is a biosimilar by US and EU standards. Launched in India in June 2015 at 25% discount vs Lucentis. Was withdrawn from market due to safety issues and then re-launched to specialist centres. |
| Formycon | FYB201 | Phase III | Phase III trial started in February 2016 in partnership with Santo Holdings. Deal involves single-digit upfront payment (€m) plus milestones in the three-digit €m range. N=650 patients; the primary endpoint is change in retinal thickness; and the completion date is March 2020. |
| Pfenex | PF582 | Phase I/II study completed. No timeline for Phase III given | In February 2015, Pfenex signed a deal with Hospira (later acquired by Pfizer) for $51m upfront + $291m milestones and tiered double-digit royalties on net sales. In August 2016 Pfenex regained rights from Pfizer following a strategic review of its biosimilar pipeline. There are no meaningful differences in intraocular pressure, visual acuity, or central retinal thickness between PF582 and Lucentis |

Source: Edison Investment Research

## Development of Xlucane

As Xlucane is in early development, there are very limited preclinical and no clinical data. Xbrane plans to register and market Xlucane in Iran in 2017 through a partnership with Helvetic Biopharma, which involves a small PK/PD clinical trial, manufacturing, registration and launch of the product during H217. The deal involves an exclusive distribution agreement in which the company gets development, regulatory and sales milestones plus royalties on net sales. According to Helvetic Biopharma, 70,000 people suffer from wAMD in Iran.

A biosimilar product typically needs to be tested in clinical trials, a PK/PD Phase I study and potentially a Phase III trial. The Phase I with the analytical data package shows similarity and the Phase III confirms that the biosimilar has the same therapeutic action at the expected dose levels. As the dose is known, there is no need for a Phase II dose ranging trial. The Phase I and Phase III elements can be combined in a two-stage trial.

Xbrane will send a full biosimilarity package to the EMA and FDA during Q117. This will enable Xbrane to meet with the agencies to seek advice on the design of a Phase I/III trial. However, the agencies will need to see the comprehensive GMP analytical package before approving use in clinical trials.

The proposed Phase III primary endpoint will be either the change of retinal thickness after one month or visual acuity (ETDRS letters). In the current Formycon Phase III trial being run in Europe and the US, the primary endpoint is retinal thickness at one month, with visual acuity at six months as a secondary endpoint. This trial involves 650 patients and will take at least three years to run. In our

view, the FDA will require a visual acuity test and a trial design similar to the Formycon study is used in our forecast. Clinical costs could be between SEK200m and SEK250m plus manufacturing costs of about SEK16m: Edison uses a figure of SEK230m in the valuation model. The cost is high because it includes the cost of Lucentis at market prices plus all the ancillary clinical costs.

We assume that Xbrane gains a partner able to fund between 50% and 100% of the clinical trial costs. We have not assumed any milestones or upfronts on this deal but does assume a 50% chance of finding such a partner. Xbrane is then assumed to receive a 15% royalty.

## Xlucane market forecast

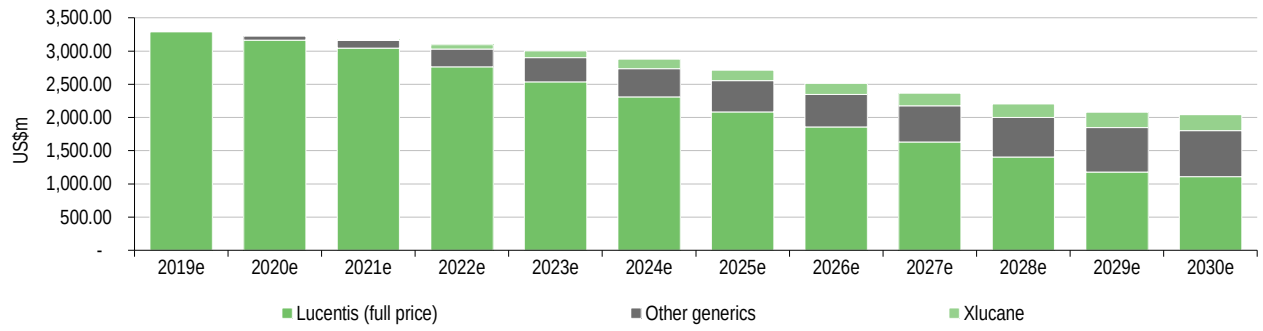
Sales of Lucentis were $3.6bn in 2015, down 15% vs 2014 as competitor Eylea (aflibercept, Regeneron/Bayer) gained market share due to its clinical profile, longer dosing interval and lower overall cost. Eylea had 2015 sales of $4bn, up 45% vs 2014.

The Lucentis market is split between the US, with about 930,000 doses used at $2,000 per dose (monthly), and other territories, largely Europe, selling 2,441,000 doses at $1,000 per dose. Accordingly, the two are roughly equal in value but the US offers better margins.

There is currently no Lucentis biosimilar in the US or EU as the composition of matter patents do not expire until 2020 and 2022, respectively. On expiry in the US, Formycon should be in a strong position to launch its product first. Edison assumes a decline in the Lucentis market with share taken by Eylea in wAMD; off-label Avastin is the current low-cost option, but is not easy to use in practice. Market launch in the US at the time of Lucentis patent expiry in 2020 seems difficult, hence we believe Xlucane will be third to market in the US as its competitors are ahead in development. Launch in 2022 in the EU could be possible if clinical trials begin in 2017 and complete successfully by late 2020. In Europe, we expect either one or two other competitors to launch alongside Xlucane.

We forecast the Lucentis market to decline to $3.3bn by 2019. By 2030, Edison forecasts that Lucentis retains a 41% volume share at full price with biosimilars taking 70% by volume of the European market and 51% of the US market at 55% discounts. The biosimilar share of this market is estimated by Edison to be worth about $930m. If Xlucane is third in the market in the US, it may capture a 20% biosimilar share. In the EU, the market share could be higher at 30% if launched at the same time as competitors. This indicates peak partner sales of $242m, Exhibit 16.

**Exhibit 16: Lucentis market and Xlucane sales development**




Source: Edison Investment Research

The strategy that Roche and Novartis adopt is an additional factor that may hamper market penetration of biosimilars. They may decide to lower the price to keep it closer to the biosimilar or even match it. This will help to retain market share and defend its price.

Xbrane's Iranian partner intends to start selling Xlucane in H217. As Lucentis is not currently sold in Iran, the market is new and the market dynamics are unknown. Edison has assumed, on a nominal basis, that Iran equates to 5% of the projected European sales value (based on population size and the relative proportion of people aged over 65). A 50% probability adjustment is then applied reflecting the significant uncertainties and lack of data.

# Sensitivities

Xbrane has a number of short-term sensitivities that will have a high impact on its cash flow and valuation. The Chinese deal, which needs to be signed, yields a SEK17m upfront. This would offset some clinical trial costs and the development of a three-month formulation required for the European market. Once the initial SEK7m Iranian order is fulfilled, Iranian sales development will depend on gaining a high market share against an established competitor by aggressive pricing. Validating the one- and three-month formulations to European standards is an essential target for 2017. More deals could be concluded, adding value. Spherotide competes against Decapeptyl and indirectly against leuprorelin and goserelin. Accordingly, several competitors may compete fiercely.

With Xlucane, Xbrane has the challenge of funding considerable clinical studies. The obvious route is partnering and Edison has assumed a 50-50 split in the costs; however, a full partnering deal could be concluded. If not, Xbrane may have to find the cash required. The Lucentis market targeted by Xlucane is shrinking and Xlucane might be the third product to market, possibly from 2021 in the US, provided that clinical trials start in 2017. Roche and Novartis may employ various strategies, including competitive pricing to prevent Lucentis biosimilars gaining market share. Edison notes that the Xbrane system has never used been for manufacturing at scale so there may be both unexpected technical challenges and opportunities.

# Valuation

## Spherotide

Edison has applied probability adjustments to Spherotide, as in Exhibit 17.

**Exhibit 17: Spherotide value before costs and tax**

| Territory | Sales (SEKm) in 2030 before risk adjustment | NPV (unadjusted) SEKm | Probability | NPV adjusted SEKm | Notes |
|---|---|---|---|---|---|
| NPV 1 month (Europe +RoW ex Iran) | 80 | 71 | 60% | 42 | Some data so treated as Phase III at a 60% probability. The margin depends on lower CoG gains |
| NPV 3 month (Europe) | 129 | 210 | 45% | 94 | High Phase II probability of 45%. It is not regarded as Phase III is because there is no data. |
| Iran | 44 | 141 | 50% | 70 | A difficult market to externally forecast so a 50% probability adjustment has been made |
| China | 104 | 182 | 40% | 73 | A very significant opportunity but the uncertain timeframe means treated as a Phase II at 45% |
| Totals | 357 | 604 | | 280 | |
| Clinical | Cost of SEK60m | (47) | | (47) | Edison assumption of costs |
| Milestones | US$8m for China, SEK1m for Israel SEK80m Europe | 98 | 60%/45% | 67 | One-month milestone at 60% probability. Three-month milestone (Europe) has a 45% probability |
| Total NPV | | 668 | 0 | 300 | |

Source: Edison Investment Research

The net present value calculated is the annual gross margin for Xbrane before other costs and tax. Unadjusted peak sales are shown. Probabilities are conservative since Edison has seen very little technical information on the products and no clinical development has been run to date. Xbrane is confident of achieving up to SEK80m in revenues from Spherotide in Iran and the Middle East by 2020. Edison is more cautious about this, but has nonetheless projected SEK44m revenues before

risk adjustment. Xbrane has been successful in agreeing terms for a major Chinese deal, which would partially offset the likely clinical trial costs of SEK60m for Spherotide in 2017. A European deal of at least the same size as China is assumed, but focused on the three-month formulation needed for the European market.

## Xlucane

The net present values of the Xlucane royalty streams from 2017 to 2030 are shown in Exhibit 18. These are before any clinical trial costs and other administration. Royalties in 2030, before probability adjustment, are estimated at SEK343m. These, in effect, have no costs attached other than tax.

**Exhibit 18: Xlucane value before costs and tax**

| Territory | Sales ($m) in 2030 before adjustment | NPV (unadjusted) SEKm | Probability | NPV adjusted SEKm | Notes |
|---|---|---|---|---|---|
| Europe | 167 | 393 | 55% | 216 | Because Europe has approved a large number biosimilars, a 55% probability of success is used. |
| US | 75 | 210 | 45% | 95 | The US regulatory pathway is much less used and the market for biosimilars is also more uncertain. As a result, Edison has used a 45% probability adjustment. |
| Iran (nominal) | 8 | 20 | 50% | 10 | Nominal based on 5% of European sales. |
| Production costs | | (11) | | (11) | |
| Clinical costs less partner share | SEK230m before partnering | (153) | 50% | (82) | Assumes partner pays 50% of the costs. |
| Total NPV | | 459 | | 227 | |

Source: Edison Investment Research

## Overall valuation

The overall value comprises the present value of the cash flows after costs and tax between 2017 and 2030, Exhibit 19. Xbrane could be a highly profitable business because all marketing costs are delegated to partners, leaving only manufacturing, core regulatory and quality assurance functions within the business. Edison has therefore assumed a 30% cost level (after cost of goods) which is typical of pharmaceutical companies. A simple adjustment for working capital changes has been made after the detailed forecast to 2018. This assumes some low-level research costs on other projects.

**Exhibit 19: Xbrane indicative value**

| Item | Notes | Subtotal NPV (SEKm) | Total NPV (SEKm) |
|---|---|---|---|
| Spherotide gross margin | | 280 | |
| Spherotide clinical costs | | (47.13) | |
| Milestones | | 67 | 300.0 |
| Xlucane royalties | | 321 | |
| Xlucane clinical | | (93) | 227.4 |
| Total net income | | | 527.4 |
| Core cash costs | | | (247.3) |
| Tax | Rate 22% | | (59.3) |
| Net working capital and non-cash adjustments | | | (51.3) |
| NPV | Discount rate 12.5% | | 169.5 |
| Continuing value | Growth rate -1% | | 202.5 |
| Current value | | | 372.0 |
| Shares in issue | million | | 4.76 |
| Per share | SEK | | 78.21 |

Source: Edison Investment Research

This period allows sufficient time for market development and ends with the expiry of the core manufacturing patent for Xlucane. Because these are generic products, there seems no reason to assume a drastic fall in market shares after 2030, and therefore a continuing value is applied. However, they will generally decline as treatments change so a -1% growth rate is applied. The significant continuing value element implicitly assumes a return on invested R&D from other pipeline products, but this cannot be quantified at this time.

The overall value net of tax and adjustments for working capital is SEK372m. This equates to about SEK78 per share. However, as discussed in the financials section, Xbrane has to meet significant short-term clinical trial costs to launch products on the timescales envisaged above. Xbrane either needs to sign partnering deals or raise further funds. There is therefore a significant potential for further dilution. If the trials are delayed or extended, the value will be lower than currently estimated.

However, Edison also notes that it has used conservative probability assumptions on generic products entering well-defined, established markets. Hence, value will develop rapidly if probabilities rise and as further deals are signed. As a scenario, a risk-free valuation would currently be about SEK200 per share, but this depends on all timelines being met and all products performing at least as well as forecast in the market and meeting the required technical and clinical standards.

# Financials

Xbrane listed on the Nasdaq First North exchange in Stockholm in February 2016. Xbrane issued 2.33m shares at SEK0.224 par value at a price of SEK42.50. This raised SEK100m gross, SEK90m after expenses, and increased the shares in issue from 2.23m to 4.59m shares. The proceeds were partly used to repay a 2015 loan of SEK10m from the main shareholder.

## Income statement

Revenues for 2016 to 30 September comprise SEK2m in upfront fees paid to secure the rights to Spherotide in Iran. Xbrane has stated that a SEK7m order has been received and will be shipped in early 2017 once the Primm subsidiary has achieved Good Manufacturing Practice (GMP) standards. In addition, Xbrane had received SEK149k in Italian tax credits to 30 Sept 2016. A deal for Israeli distribution was signed in December and may have given a SEK0.25m payment.

Overall, Edison expects a reported loss of about SEK31m in 2016 with a slightly lower loss in 2017 due to the expected SEK17m upfront payment on the Chinese distribution deal and limited expenditure of up to SEK26m on clinical trials. Iranian sales of only SEK7m are assumed with a 50% gross margin. Note that although Edison includes deal estimates in valuation forecasts, it only includes signed deal values in financial and cash flow forecasts.

It is assumed that the sales will increase in 2018 to at least SEK11m but, at the moment, no milestones are forecast. It is assumed that at least half of the Xlucane clinical trial costs are offset by a partnering deal.

## Cash flow

Cash use for the first nine months of 2016 was SEK27.2m in operations and a further SEK12.6m in investments, of which SEK8.6m was in capital expenditure. This investment has largely been in the Swedish operation (SEK6.9m). R&D valued at SEK3.4m seems to have been capitalised as an intangible asset held in the Italian subsidiary. This made the overall outflow SEK41.2m. The IPO yielded SEK81.1m after expenses and loan repayments; cash on 30 September was SEK43.9m.

Edison forecasts an operational cash use of about SEK33m for 2016 plus SEK12m of investment. This would leave year end cash at about SEK38m. This does not appear to be sufficient to fund the required clinical expenditure over 2018. Xbrane management expects to do major new partnering deals on Spherotide and Xlucane. However, as these deals are as yet undisclosed and unsigned, Edison has included an illustrative long-term debt of SEK100m in 2018 as is its normal practice.

## Balance sheet and corporate structure

The group consists of the parent Swedish company and an acquired Italian subsidiary; see below. The balance sheet shows a large intangible asset of SEK59.4m, mostly comprising goodwill from the Primm Pharma acquisition but also including capitalised R&D in Primm. The goodwill is being amortised over 10 years by the group but is contained in the Primm subsidiary balance sheet at cost.

On 31 December 2015, the Xbrane parent company reported the Primm Pharma shareholding value at SEK62.8m. During 2016, the parent made a cash investment in Primm Pharma of SEK20.3m taking the book value to SEK83.1m. We estimate that Primm Pharma held SEK1.4m in cash on 30 September so this may have been an accounting adjustment. The value of fixed assets in Primm is estimated at SEK9.9m at the end of 2015, rising to SEK10.9m on 30 September. Investment in 2016 to September appears to have been SEK1.7m; depreciation was SEK0.7m.

The total value of consolidated fixed assets on 30 September was SEK17.2m. During 2016, capital investment of SEK6.3m was made in the Swedish company, largely laboratory equipment. Depreciation was SEK0.8m.

Xbrane has low short-term liabilities of SEK8.1m. Creditors amounted to SEK3.3m. Other short-term liabilities include a liability acquired with Primm of SEK1.8m and deferred revenue of SEK2.6m. There is a long-term liability in Primm Pharma of SEK4.4m (SEK5.5m in 2015) plus provisions of SEK0.6m. The long-term liability contains SEK2.7m due to Primm CEO Paolo Sarmiento.

On 30 September, Xbrane had SEK43.9m of cash in the consolidated accounts.

## Acquisition and consolidation of Primm Pharma

The Italian company Primm Pharma was created by Primm Srl, a biotech services company founded in Milan in 1990, trading as Primm Biotech. In 2014, Primm Srl is stated to have had a turnover of €3.8m. Primm Srl developed a generic microsphere technology. This technology was used to found Primm Pharma and a small production site outside Naples was established.

On 30 September 2015, Xbrane acquired Primm Pharma Srl from four private shareholders for a deferred consideration of SEK56,203,200. The value of fixed assets and capitalised investments at the date of acquisition on 30 September 2015 was SEK15.3m. At the time of acquisition, there were three employees at Prim Pharma, of which one was the CEO, Paolo Sarmiento. On 30 September 2016, there were four employees at the Naples plant.

The consideration for Primm Pharma, SEK56.2m, is a contingent convertible bond being redeemed in stages as detailed below (Exhibit 20). The conversion price is SEK42.5 per share. If fully converted, the number of shares in issue will increase by 1,322,428. This is equal to a further dilution of 22%. The first of these milestones was reached in September 2016. The convertible liability is treated as equity.

**Exhibit 20: Primm Pharma acquisition terms**

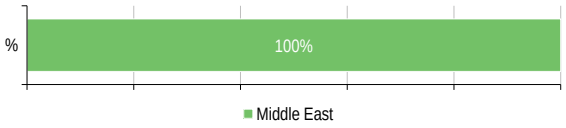
| Date | Milestone | Value | Note |
|---|---|---|---|
| July 2016 | An application to the Italian medicines agency for GMP approval of the facility – completed. | 10%, SEK5.62m | Milestone achieved in September 2016 and 132,243 shares issued in Q416. |
| Expected Q117 | GMP approval of the Naples production facility by the Italian Medicines Agency. | 20%, SEK11.2m | This was scheduled for December 2016. Expected Q117. |
| July 2017 | Sales initiated in Iran. | 20%, SEK11.2m | A SEK7m order has been received and is expected to be shipped in H117. |
| March 2018 | Sales equivalent of 200 000 doses of Spherotide realised. | 25%, SEK14.1m | In Edison's view, this target is now potentially achievable by the end of 2018. |
| July 2018 | Positive bioequivalence study for the approval of Spherotide EU completed. | 15%, SEK8.4m | This is assumed by Edison to be a three-month dose as the most common form. |
| March 2020 | One million doses of Spherotide sold. | 10%, SEK5.6m | This might equate to cumulative in-market sales of SEK200m. |

Source: Edison Investment Research based upon Xbrane Prospectus page 39

**Exhibit 21: Financial summary**

| SEK000s | 2014 | 2015 | 2016e | 2017e | 2018e |
|---|---|---|---|---|---|
| Year end 31 December | GAAP | GAAP | GAAP | GAAP | GAAP |
| PROFIT & LOSS | | | | | |
| Revenue | 190 | 393 | 2,208 | 24,000 | 22,050 |
| Cost of Sales | 0 | (257) | (750) | (3,500) | (11,025) |
| Gross Profit | 190 | 136 | 1,458 | 20,500 | 11,025 |
| EBITDA | (3,831) | (10,660) | (22,931) | (13,640) | (92,220) |
| Operating Profit (before GW and except.) | (3,889) | (10,710) | (24,907) | (15,616) | (94,197) |
| Intangible Amortisation | 0 | (1,391) | (6,222) | (6,222) | (6,222) |
| Other | 0 | 0 | 0 | 0 | 0 |
| Operating Profit | (3,889) | (12,101) | (31,130) | (21,839) | (100,419) |
| Net Interest | 2 | (294) | (174) | (208) | (238) |
| Exceptionals | 0 | 0 | 0 | 0 | 0 |
| Profit Before Tax (norm) | (3,887) | (11,004) | (25,081) | (15,824) | (94,435) |
| Profit Before Tax (FRS 3) | (3,887) | (12,395) | (31,303) | (22,047) | (100,657) |
| Tax | 1,315 | 550 | 199 | 199 | 199 |
| Profit After Tax (norm) | (2,572) | (10,453) | (24,882) | (15,626) | (94,236) |
| Profit After Tax (FRS 3) | (2,572) | (11,845) | (31,105) | (21,848) | (100,458) |
| Average Number of Shares Outstanding (m) | 4.1 | 4.1 | 4.6 | 4.6 | 4.6 |
| EPS - normalised (SEK) | (0.6) | (2.5) | (5.4) | (3.4) | (20.4) |
| EPS - normalised fully diluted (SEK) | (0.6) | (2.5) | (5.4) | (3.4) | (20.4) |
| EPS - FRS 3 (SEK) | (0.6) | (2.9) | (6.7) | (4.7) | (21.7) |
| Dividend per share (SEK) | 0 | 0 | 0 | 0 | 0 |
| BALANCE SHEET | | | | | |
| Fixed Assets | 133 | 67,897 | 72,313 | 69,591 | 66,868 |
| Intangible Assets | | 57,873 | 54,988 | 52,266 | 49,544 |
| Tangible Assets | 133 | 10,024 | 16,690 | 16,690 | 16,690 |
| Investments | 0 | 0 | 635 | 635 | 635 |
| Current Assets | 6,556 | 7,433 | 48,044 | 30,668 | 35,932 |
| Stocks | 0 | 161 | 2,869 | 2,869 | 2,869 |
| Debtors | 355 | 4,585 | 7,118 | 7,114 | 10,877 |
| Cash | 6,201 | 2,688 | 38,057 | 20,685 | 22,186 |
| Other current assets | 0 | 0 | 0 | 0 | 0 |
| Current Liabilities | (391) | (23,405) | (8,105) | (9,854) | (12,854) |
| Creditors | (391) | (13,405) | (8,105) | (9,854) | (12,854) |
| Short term borrowings | 0 | (10,000) | 0 | 0 | 0 |
| Long Term Liabilities | 0 | (4,064) | (4,437) | (4,437) | (104,437) |
| Long term borrowings | 0 | 0 | 0 | 0 | (100,000) |
| Other long term liabilities | 0 | (4,064) | (4,437) | (4,437) | (4,437) |
| Net Assets | 6,298 | 47,862 | 107,815 | 85,967 | (14,491) |
| CASH FLOW | | | | | |
| Operating Cash Flow | (3,985) | (12,643) | (32,713) | (11,489) | (92,586) |
| Net Interest | 2 | (294) | (174) | (208) | (238) |
| Tax | 1,315 | 550 | (199) | (199) | (199) |
| Capex | (187) | (1,127) | (12,614) | (5,476) | (5,476) |
| Acquisitions/disposals | 0 | 0 | 0 | 0 | 0 |
| Financing | 180 | 0 | 90,696 | 0 | 0 |
| Dividends | 0 | 0 | 0 | 0 | 0 |
| Net Cash Flow | (2,676) | (13,513) | 44,996 | (17,372) | (98,498) |
| Opening net debt/(cash) | (8,877) | (6,201) | 7,312 | (38,057) | (20,685) |
| HP finance leases initiated | 0 | 0 | 0 | 0 | 0 |
| Other | 0 | 0 | 373 | 0 | 0 |
| Closing net debt/(cash) | (6,201) | 7,312 | (38,057) | (20,685) | 77,814 |

Source: Edison Investment Research, Xbrane Biopharma accounts

| Contact details | Revenue by geography |
|---|---|
| Xbrane Biopharma<br>Banvaktsvägen 22<br>171 48 Solna<br>Sweden<br>info@xbrane.com<br>http://xbrane.com |  |

## Management team

| Chairman: Professor Saeid Esmaeilzadeh | CEO: Martin Åmark |
|---|---|
| Saeid is a serial entrepreneur having established and managed a range of research-intensive companies in various industries. In 2002 he became the youngest associate professor in Sweden. Saeid is an experienced board member and since 2010 has been the CEO of Serendipity Innovations. Saeid has a PhD in materials chemistry from Stockholm University. | Martin Åmark holds an MSc in industrial engineering and management from Linköping Institute of Technology and an MBA from INSEAD. He has eight years of experience from Bain & Co as a management consultant. At Bain, Martin worked mainly with M&A, strategy and organisation with Nordic clients across multiple industries, including life sciences and pharmaceuticals. |
| **Head of controlled release generics: Dr Paolo Sarmientos** | **COO and head of biosimilars: Siavash Bashiri** |
| Paolo Sarmientos has a PhD in bio-organic chemistry from the University of Naples. He has more than 25 years of experience in biopharmaceuticals with Pfizer, Genetica and Menarini. For the last 15 years Paolo has served as CEO of Primm and successfully built up a service business as well as pioneering production of biopharmaceuticals with slow-release microsphere formulations. | Siavash Bashiri holds an MSc in molecular biotechnology from Uppsala University. His latest position was with Agilent Technologies where he was the head of sales in EMEA for one of Agilent Technologies' products within the Genomics department. He also has great experience in the commercialisation of biotech start-ups. |

| Principal shareholders | (%) |
|---|---|
| Serendipity Ixora AB | 26.41 |
| Försäkringsaktiebolaget Avanza pension | 4.76 |
| Nordnet Pensionsförsäkring A | 3.84 |
| Jan-Willem De Gier | 2.57 |
| Christer Skogum | 2.42 |
| Martin Åmark (CEO) | 2.39 |
| Siavash Bashiri (COO) | 1.88 |

## Companies named in this report

Ipsen, Shire, Allergan, Roche, Formycon, AstraZeneca, Takeda, AbbVie, New England Biolabs, Regeneron



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