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EP Vantage Interview - Lundbeck's hands steady on CNS rudder

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Whilst so many of its big pharma competitors have exited or scaled back central nervous system research and development because of high risk and slim rewards, Danish specialty group Lundbeck has remained steadfastly in the field of brain diseases and is betting it will continue to pay off. Despite losing its lone blockbuster, depression pill Cipralex/Lexapro, to patent expiry this year, the company is readying a CNS-focused late-stage pipeline on which it believes it can capitalise because of its specialised knowledge in the field.

Even as AstraZeneca carried out a big cull of its neuroscience R&D staff in Sweden this week, its more southerly neighbour has been avidly pursuing its CNS agenda, with two psychiatric launches and one epilepsy launch and a filing in addiction medicine in the last year. Chief executive Ulf Wiinberg tells *EP Vantage* that the opportunity is still a rich one for drug developers with expertise and the nerve to stay in the field.

“We have had a CNS focus for 50 years, and we believe that with a CNS focus, it’s still very, very difficult but maybe a little less difficult for us,” Mr Wiinberg says. “I have to watch out so I don’t have hubris, but obviously we feel we are having success executing our pipeline right now.”

Execution next

Lundbeck needs to deliver a near-flawless execution of its pipeline. The patent expiry of Cipralex – last year worth $1.59bn in sales and alliance revenue from partners such as Forest Laboratories in the US - has already put a hole in company revenue. The expiry came in February, and in its first quarter 2012 earnings release Lundbeck reported its revenue dropped 8% to DKr3.78bn ($645.5m) over year-earlier figures.

Alzheimer’s treatment Ebixa goes this month, sales of which will drop by $302m by 2018.

The three products it launched in the past year - bipolar disorder treatment Sycrest, epilepsy drug Onfi and Lexapro in Japan, in partnership with Mitsubishi Tanabe Pharma and Mochida Pharmaceutical – will yield just $404m in revenue in 2018, compared with the loss of more than $1bn in Cipralex/Lexapro revenue, according to consensus forecasts at *EvaluatePharma.*

Thus, growth will need to be found from new product introductions or other strategic moves. For now, the executive team has the backing of its investors for a current strategy of repurposing Lexapro and launching smaller products acquired from outside – Sycrest was in-licensed from Merck & Co and Onfi from its acquisition of Ovation Pharmaceuticals – as a bulwark against greater shrinkage until it can derive new sales growth from its pipeline.

“What we said as an overall strategy was that we agreed with our owners that our aim should be long-term growth,” Mr Wiinberg says. “We communicated floor guidance for the period of 2012-2014 where we’ll have a minimum of DKr14bn (in annual sales) and DKr 2bn in (earnings) for that period. The plan is to come back to growth after that period.”

Lundbeck currently has two products filed with regulatory authorities – a long acting injection of Abilify in partnership with Otsuka, targeting schizophrenic patients in the US, and anti-drinking pill Selincro, in the EU. A pill that aims to reduce heavy drinking but not completely stop alcohol consumption, Selincro is forecast only to achieve sales of $69m in 2018, and there is doubt as to whether it will be fully embraced by addiction specialists who prefer talking therapy and total abstinence (*Nalmefene data positive but concerns remain, June 15, 2011*).

The Abilify depot injection is forecast to perform a bit better, bringing in $232m in 2018; an FDA decision is due in September.

Investors have held firm in the face of such a fallow period, reckoned as the biggest patent cliff of 2012 (*As patent storm peaks Lilly and Astra have furthest to fall, February 9, 2012*). In spite of market losses

experienced during the European debt crisis of last summer, shares are still up 29% over the last two years. Its performance has no doubt been helped along by positive news on depression pill Lu AA21004, which inspired a 9% jump in share price on Monday (*Success for depression pill gladdens Lundbeck and Takeda, May 15, 2012*).

Completing the puzzle

It is '21004 that represents the biggest piece of the puzzle for Lundbeck's return to growth, and its potential remains a mystery. With US partner Takeda, the company disclosed no efficacy data other than to state that it had significantly reduced depression symptoms in two US trials and one European trials – indeed, a full data set will not be disclosed until 2013. A filing in Europe is anticipated in the third quarter of 2012 and the fourth in the US.

It will be a challenging market – such flagship brands as Prozac and Zoloft have been off patent for years, and best seller Cymbalta loses market exclusivity next year. As such, there seems to be a low likelihood that '21004 would routinely be prescribed as a first-line drug.

A better side effect profile is hoped will be its selling point – fewer instances of sedative, insomnia or sexual side effects - as well as efficacy in the elderly and no cardiac signals.

Jefferies analysts raised this issue earlier this year, questioning whether it could achieve blockbuster sales numbers – current consensus forecast puts worldwide sales at $573m in 2018. "If '21004 can be differentiated in head-to-head Phase III trials, most likely on the basis of tolerability, then the competitive environment could make it easier to position the drug to clinicians, albeit not 1st line given payor pressure," they wrote. One of the three trials did include a Cymbalta reference arm.

This is an issue Mr Wiinberg acknowledges: "I don't think '21004 is going to be used in every depressed patient. Depending on the patient, clearly if you have a have patient coming in with mild to moderate symptoms they are likely to get a generic SSRI, most likely Cipralex.

"But you also have many patients who are not successfully treated. If you have failed on an SSRI, does it make sense to give a patient another SSRI after that?"

Fuller disclosure of the data will no doubt help define the potential of '21004. Physicians and payers alike, not to mention investors and analysts, will be anxious to compare it to marketed products to determine its clinical value more exactly. Stellar performance by the pill would be a good sign that Lundbeck can at last see the light at the end of the tunnel.