Evaluate Vantage

August 29, 2014

Upcoming events: FDA panels take on liraglutide and Natpara

Joanne Fagg

Welcome to your weekly digest of approaching regulatory and clinical readouts. FDA panels are coming up on September 11 and 12 to discuss liraglutide for obesity and Natpara for hypoparathyroidism respectively.

Gaining first-pass approval for obesity has proved notoriously difficult, but Novo Nordisk will be eager to win over the regulators with its injectable treatment, which is already marketed as Victoza for type 2 diabetes. Meanwhile, NPS Pharmaceuticals will be hoping that its orphan drug can make up for the revenue shortfalls of Gattex, so far its only marketed product.

In four phase III trials liraglutide, a GLP-1 agonist, produced placebo-adjusted weight loss of 3.9-6.5%. Vivus's Qsymia and Arena Pharmaceuticals' Belviq – oral drugs – were approved on the strength of efficacies of around 8.5% and 3.4% respectively *(Novo's obesity strategy will turn on safety, May 24, 2013)*.

Novo filed a 3mg dose for the obesity indication – much higher than the 0.9mg, 1.2mg and 1.8mg approved for diabetes.

While the efficacy looks approvable the FDA will have tough questions on safety, most likely over cardiovascular safety, cancer risks and pancreatitis – a known risk for the GLP-1 class. The FDA decision on liraglutide is expected in the fourth quarter.

For the obesity indication consensus forecasts from *EvaluatePharma* give 2020 sales of $867m, 19% of the drug's total forecast revenue that year. Liraglutide is expected to lead the obesity market by 2020, followed by Qsymia and Belviq with $687m and $403m respectively.

The two oral drugs were approved in 2012 and underwent significant FDA scrutiny. Both initially had high sales expectations, but prescriptions have been modest and forecasts have tumbled; 2018 forecasts for Qsymia were $1.4bn back in September 2012, for instance.

Both drugs also come with CNS-related warnings such as depression and suicidal behaviour, which at present do not feature on Victoza's label. And while oral dosing is seen to have a convenience advantage, it also has a greater opportunity for abuse, where an injectable has lower potential.

NPS Pharmaceuticals: Natpara

The Natpara panel was originally expected in July but the US regulator shifted the date to September with little explanation. The PDUFA date is October 24. The project, a recombinant human parathyroid hormone, has orphan designation for hypoparathyroidism in the US and Europe.

The condition, in which the body produces insufficient levels of parathyroid hormone, is managed by oral calcium and vitamin D supplementation to raise calcium levels in the blood and reduce symptom severity. However, these current treatments can lead to organ calcification and kidney failure.

In a phase III registration study called Replace, 53% of patients treated with subcutaneous Natpara decreased their doses of calcium and vitamin D supplements – the primary endpoint – by 50% or more, with only 2% of the placebo recipients doing so (p=<0.001).

Also, those treated with Natpara had improved bone remodelling, which patients on supplements did not show. Leerink analysts assume an 80% probability of approval given the project's efficacy and safety profile. However, its impact on quality of life is likely to drive the regulator's decision.

Worth it?

Consensus forecasts from *EvaluatePharma* give Natpara $552m in sales by 2020, which would make it NPS's second-biggest growth driver behind the short bowel syndrome treatment Gattex.

Sales of Gattex are forecast to reach $636m by 2020, but have so far been lacklustre, and the company

trimmed $10m off its 2014 guidance to $100-110m.

Last year Takeda handed the ex-US rights back to NPS for both Gattex and Natpara. The latter had been marketed in the EU as Preotact/Preos for osteoporosis until being withdrawn owing to manufacturing problems *(Takeda's NPS move does not alter US attraction or risk, March 20, 2013).*

In the US Natpara received a complete response letter in osteoporosis over the risk of hypercalcaemia, something the company has said would not be an issue in hypoparathyroidism. Meanwhile rumours of a takeover by Shire earlier this year caused shares to rally over 18%, but no deal materialised, and Shire is now being bought by AbbVie.

The biggest question remaining is whether NPS can convince payers and regulators that a higher-priced injectable treatment as an alternative to oral supplements is really worth it.

Study	**Trial ID**
Replace	NCT00732615

To contact the writer of this story email Joanne Fagg in London at joannef@epvantage.com or follow @JoEPVantage on Twitter