Evaluate Vantage

February 11, 2011

# Event – Salix needs Xifaxan IBS win to justify valuation

Within a month the FDA should decide whether to approve a third and crucial indication for Salix Pharmaceuticals' Xifaxan - non-constipation irritable bowel syndrome (non-C IBS). A lot rests on endorsement, which is expected to help push Xifaxan sales into blockbuster territory by 2014.

A green light is widely anticipated, based on strong results from two phase III studies conducted in non-C IBS and two prior approvals for the drug, in traveller's diarrhoea and hepatic encephalopathy. However, measuring improvements in IBS is challenging so there is good reason for some caution. Salix shares almost doubled in value last year to reach record highs of $48, driven by high hopes for Xifaxan - approval is needed to justify this valuation.

| | |
|---|---|
| **Product** | Xifaxan (rifaximin) |
| **Company** | Salix Pharmaceuticals |
| **Market cap** | $2.4bn |
| **Total product NPV** | $2.7bn |
| **Indication-specific NPV** | $1.2bn (46% of total value) |
| **Indication NPV as % of mkt cap** | 51% |
| **Event type** | PDUFA |
| **Indication** | Non-constipation irritable bowel syndrome (non-C IBS) |
| **Date** | March 7, 2011 (estimated) |
| **Trial IDs** | Target-1: NCT00731679 |
| | Target-2: NCT00724126 |

**Flora spread**

Abdominal pain, bloating, and altered bowel function are all common problems for IBS sufferers. It is estimated the condition affects a massive 20% of the US population. However, the range of symptoms and lack of diagnostic tests means the condition is hard to diagnose - it is thought to have various causes at its root. This all makes designing and testing effective treatments challenging, and despite the prevalence of IBS few specific therapeutics have made it to market, other than anti-spasmodics or anti-diarrhoeal agents.

Xifaxan is a broad-spectrum antibiotic - patients can have abnormal growth in their intestinal bacteria, or 'gut flora', hence the rationale for using antibiotics. That said, it is unclear how many IBS cases are caused by the gut bacteria targeted by Xifaxan.

Antibiotics such as neomycin have been used to treat IBS in the past with mixed success, limited by harsh side effects. Otherwise treatment involves sweeping dietary and lifestyle modifications, sometimes coupled with psychological interventions.

**Adequate relief**

Orally-administered Xifaxan was studied in two large pivotal trials – Target 1 and Target 2 – which enrolled 1,260 patients with non-C IBS. With no known biological markers for IBS, patients must be assessed through fairly arbitrary measures, using yes-or-no answer questionnaires to describe how symptoms have improved.

To meet the primary endpoint, patients needed "adequate" relief of symptoms for at least two weeks during a month of treatment. Roughly 40% of Xifaxan patients across the two trials confirmed this improvement, significantly higher than the 32% of patients in the placebo arm.

Meanwhile the secondary endpoints of adequate relief of IBS-related bloating were met, a highly important factor from a patients' perspective. Xifaxan improved bloating in approximately 40% of patients, a significant result against 29% in the placebo group. It also bodes well that the drug significantly met an FDA-requested endpoint of improving abdominal pain and relieving watery stools in patients.

Safety-wise there was little difference in the adverse event profiles of the placebo or treatment arms. Some patients did not respond to the treatment, likely reflecting the fact that these patients' IBS was not bacteria-related.

**Jitters**

Many analysts following Salix have already built in significant sales in IBS. The drug is already on the market for traveller's diarrhoea and the liver condition hepatic encephalopathy (HE).

When it reports quarterly results later this month, Salix is expected to announce Xifaxan sales reached $250m in 2010, with HE accounting for around half of demand. By 2016, consensus is for sales of $1.37bn, and IBS and HE comprise approximately $600m apiece, according to sales by indication data from *EvaluatePharma.*

As such, IBS is a massively important growth driver for the product and Salix itself. Roth Capital Partners, which currently has a $55 price target on the stock, says approval would lift its valuation to $58, whereas rejection would cause it to plummet to $37.

Salix shares are currently trading at $42, dipping in the last month probably on some profit taking after last year's highs but quite possibly on nervousness ahead of this decision. With expectations so high, rejection or even just a delay would be taken badly.

The company signalled its determination to build a strong gastro-intestinal portfolio last week with the licensing of Relistor (*Salix takes Relistor's commercial reins from Pfizer, February 8, 2011*). It needs this IBS approval of Xifaxan for the portfolio to really take off.