Evaluate Vantage

October 10, 2011

Event - Alimera and pSivida hope Iluvien will be second time lucky

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Alimera Sciences' and pSivida's Iluvien diabetic retinopathy therapy is due for a decision from the FDA by November 12, and the emerging question is whether its mixed performance in improving eyesight will prompt a more restrictive label than the company is seeking.

The drug eluting implant has performed best in patients with chronic diabetic macular oedema (DME), whilst in the broader DME population it failed to show statistical significance in improving visual acuity following 36 months of treatment (*Alimera clears some of the muddle on Iluvien data, February 4, 2011*). Even with the statistical questions, the regulators could very well see clinical advantage to a treatment that lasts up to 36 months without additional intervention; yet they may want to focus on subgroups with the best risk-benefit profile.

Product	**Iluvien**	
Company	**Alimera Sciences**	**Psivida**
Market cap	**$245m**	**$98m**
Product NPV	**$1.06bn**	**$251m**
% of market cap	**432%**	**255%**
Event type	**PDUFA date**	
Indication	**Diabetic macular oedema**	
Date	**November 12, 2011**	

Leaky eyes

In diabetics hyperglycaemia damages the small blood vessels in the eyes, they can become leaky after periods of poor glycaemic control. The fluid leaked can cause the macula to swell, blurring vision. In severe cases, surgeons must be called in to drain the fluid.

The only FDA-approved therapy for the condition is laser coagulation surgery, although intravitreal injections of steroids such as triamcinolone acetonide are sometimes used off label. European authorities have also approved Roche's Lucentis in the indication, which is undoubtedly being used off-label in the US, along with the related antibody Avastin.

Iluvien is a tiny implant that slowly emits the corticosteroid fluocinolone acetonide, which has been used to combat inflammatory skin conditions. Based on long-release drug technology developed by Alimera's Australian partner pSivida, Iluvien is implanted in the eye via an injection at a doctor's office.

Second time around

Its first hearing with the regulator did not go well. The FDA sent a complete response letter based on its failure to achieve statistically significant improvements in visual acuity at 24 months, when compared with laser coagulation therapy, as well as deficiencies at third-party manufacturing plants (*Alimera gets unwelcome Christmas message from FDA, December 24, 2010*). The manufacturing issues have been resolved, but it is the 36-month data sought by the agency that has raised bigger questions.

In a study population of more than 900 patients, Iluvien achieved statistically significant improvements at month 30 and 33, but fell short after 36 months. Presenting to a Rodman & Renshaw investment conference in

September, chief executive Dan Myers said that was a consequence of the drug completely eluting from the implant – in all their analyses of the study data Iluvien's performance has tended to peak at 30 months, Mr Myers said.

It is in the population of persistent DME patients, those with three or more years of the condition before entering the trial, where it has performed best, with statistically significant improvements in visual acuity established and maintained through 36 months.

With such an analysis in the regulatory submission, the FDA staff could choose to focus on the chronic DME population. In speaking to the conference, Mr Myers prepared investors' for the possible disappointment of a narrow label by saying those patients are the ones most likely to be treated with Iluvien, as ophthalmologists have told the company they are more likely to treat less serious cases with the laser procedure.

Transformative

Approval on a generous label would be a transformative moment for Alimera. Iluvien is its one product, and its net present value is estimated at $1.06bn, more than four times the company's market capitalisation, according to *EvaluatePharma's NPV Analyzer*. Whilst the Georgia group is preparing for a launch there would likely be a flurry of partnering interest for such a niche product with an FDA stamp of approval (*Most valuable unpartnered pipeline assets - what's hot and what's not, August 25, 2011*).

Likewise for pSivida, approval triggers a $25m milestone and makes it eligible for a 20% profit share on sales, which are forecast at $417m in 2016.

Should Alimera decide to keep the US rights, an FDA approval would provide some security for partners interested in European rights; the company is anticipating first regulatory approvals in the EU in the first quarter of 2012.

Whilst there is good reason to believe the FDA will approve it on the second try, a second complete response letter would be a major blow to Alimera. It had $44m in cash, and regulatory approval in addition will release $11m of a $17m term loan it has secured. Should more trials be necessary, the company would likely need to raise more cash or surrender some US rights to a larger partner.

With ever increasing numbers of diabetics in the US, the need for better DME treatments is clear, a trend that may play to Alimera's favour as regulators look to the clinical need. It is unfortunate for the company, however, that it was unable to establish more clearly that Iluvien is better than laser therapy, which makes the decision less clear-cut.