Evaluate Vantage

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Alimera clears some of the muddle on Iluvien data

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Keenly awaited 36-month data for Iluvien achieved exactly what Alimera had hoped. In an analysis taking in two separate trials, the drug-eluting eye implant was significantly better than the standard of care in treating diabetic macular oedema.

However, this does not mean there is nothing to worry about: the two phase III trials individually failed to show statistical significance at 36 months, with the effect fading after 33 months because of clinical improvements in the control arm of both trials. Given that the FDA's first-round rejection of the therapy came because of doubts about the validity of 24-month data, this is bound to raise some concern (*Alimera gets unwelcome Christmas message from FDA, December 24, 2010*).

What, me worry?

Still, investors do not seem overly perturbed by the news. Shares in Alimera were down 4% to $9.78 in early trading this morning, 10% off their April 2010 initial public offering price, while shares in Australian partner pSivida, which makes the implantable device, were down 6% to $4.55.

Given that the implant, which secretes the corticosteroid fluocinolone acetonide, is Alimera's only clinical-stage candidate, some nervousness is warranted. The complete response letter inflicted more damage - Alimera lost 9% and pSivida 18% on December 27, the first trading day following the complete response letter.

If there are concerns in Alimera's offices, its executives are not letting on. In a call with investors, chief executive Daniel Myers said the company is planning on submitting its response to the FDA's complete response letter by the end of this quarter. He added that the executive team met recently with FDA staff and were told that regulators were looking only for the 24 month efficacy data.

Lead product

The lead product for both Alimera and pSividia, Iluvien is forecast to sell $409m in 2016, with pSividia forecast to collect $45m in royalties and Alimera $40m from sales outside the US. These forecasts give the implant a net present value of $980m for Alimera and $217m for pSivida, many times both companies' market capitalisations.

In rejecting the therapy in December, the agency raised concerns over the data on Iluvien's efficacy in patients who had not undergone cataract surgery before entering the trial. As a group, these patients showed declining effectiveness between months 6 and 18, and development of cataracts was believed to be a cause – some 80% of that patient group underwent surgery before the end of 36 months.

As the implant's effectiveness for that group had resumed by month 24, the FDA wanted to see if the efficacy could be sustained through 36 months, which it was.

In the pooled analysis at 36 months, 28.7% of Iluvien patients improved their best corrected visual acuity (BCVA) by 15 or more letters from baseline on the early treatment diabetic retinopathy study, compared with 18.9% in the control group, which underwent a sham procedure. In Trial A, the numbers were 28.4% vs 18.9% and in Trial B they were 29% vs 18.9%.

It is an open question whether the FDA now wants to spend time focusing on the separate data from trials A and B, each of which individually missed statistical significance at the 36 month mark. Certainly the pooled data set of 561 patients has greater power to find statistical significance, a point the company will choose to focus on.

Improving care

Given that it was the clinical improvements in the patients in the control arm in the final six months that

resulted in the lack of statistical significance in the individual trials, the regulator could take the position that over time the standard of care is just as effective.

However, the company also is able to show that the Iluvien patients underwent significantly fewer on-protocol procedures - laser photocoagulation therapy – and off-protocol procedures – Lucentis, Avastin, vitrectomy or intravitreal triamcinolone acetonide – than did the control patients. Thus, the company can demonstrate a benefit in fewer interventions and thus fewer clinical risks.

Predicting the FDA's view on any trial data is difficult at best. While Alimera did a little to clear the doubts about Iluvien, it is clear there remains some worry.

Trial ID	NCT00344968