Evaluate Vantage

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Dosing the jewel in VEGF Trap-Eye's crown

Reducing the number of times ocular disease patients need injections in their eyes can only be a good thing. Promising results today for Regeneron Pharmaceuticals and Bayer's VEGF Trap-Eye (aflibercept) show the partners are one step closer to providing that option; Regeneron shares jumped 15% to $28.39 at the start of trading.

The wet age-related macular degeneration (wet AMD) therapy with blockbuster potential has reported topline pivotal data showing it to be at least as effective as Roche and Novartis' Lucentis (ranibizumab), the current market leader selling $2.4bn last year and dosed once-monthly. VEGF Trap-Eye, however, requires dosing only once every two months (*Event - Regeneron hoping to show clear advantages for VEGF Trap-Eye, August 18, 2010*). The companies will file for approval in the US and Europe in the first half of next year.

Leading cause of blindness

The risk of developing AMD, as the name suggests, increases with age, although lifestyle, diet and genetic factors can affect onset. It is a disease of the macula, a tiny central region of the retina, which leaves central vision detrimentally affected. The centre of one's visual field can be blurred and eventually become blank.

Wet AMD accounts for 10-15% of AMD cases, and occurs when cells in the macula malfunction. The body's natural response is to grow new blood vessels, a process known as neovascularisation. This, however, leaves damaging scarring which can permanently affect central vision and is a leading cause of blindness in the elderly. As such, treatment with drugs such as Lucentis or Novartis' Visudyne needs to be administered quickly to minimise damage.

Similar efficacy, similar safety

VEGF Trap-Eye, a human fusion protein constructed from VEGF receptor components, specifically targets vascular endothelial growth factor (VEGF), a common cancer target involved in the formation of new blood vessels. Indeed, a higher-dose version being tested by Regeneron and Sanofi-Aventis in colon, lung and prostate cancer will report data in 2011.

Results from two phase III trials compared efficacy with Lucentis. View 1 randomised 1,217 patients in North America, conducted by Regeneron; View 2 randomised 1,240 patients in Europe, Asia Pacific, Japan, and Latin America, managed by Bayer.

The drug met primary endpoints of demonstrating non-inferiority to Lucentis in both trials, measured as the percentage of patients losing fewer than 15 letters in a visual eye chart test after week 52. In the top cohort, testing a 2 mg dose of VEGF Trap-Eye every two months, this was 95.1% in View 1 and 95.6% in View 2, compared with 94.4% of patients in both trials for 0.5 mg Lucentis once-monthly.

With regulatory submissions in the first half of 2011, under a 10-month standard review, approval is unlikely before early 2012. Current consensus sees $913m in global sales by 2016, although the positive data means those forecasts should break the billion-dollar barrier.

With similar efficacy, and indeed safety profile, to Lucentis – adverse events, such as eye pain and retinal haemorrhage, were evenly balanced across all study arms – Regeneron reckons convenient dosing that also reduces the need for patient monitoring presents a best-in-class therapy.

Cancer drug Avastin, essentially a high-dose version of Lucentis, is currently being administered off-label for AMD, which Cowen & Co analysts estimate captures 60-65% of the US AMD market. Whilst Medicare pays about $1,600 per dose for Lucentis, it pays only $40 for Avastin. As such, the pricing of VEGF Trap-Eye will be key and likely to be influenced to some extent by the outcome of the head-to-head CATT trial of Lucentis and Avastin, due to report in early 2011 (*Head-to-head trials could threaten Lucentis franchise, May 27, 2010*).

Dosage will win out

In a conference call today Regeneron insisted time and again that patients, physicians, caregivers have told the company that the reliable visual gains, convenient dosing, and reduced need for regular monitoring are the key tipping points.

Robert Terifay, commercial senior vice president said: “More and more, convenience is chosen over efficacy.”

Not willing to be drawn on pricing or potential market share versus Lucentis and Avastin, he did remark that, on the basis of VEGF Trap-Eye’s unique construction and regimen, a national coverage reimbursement decision would unlikely be made as a comparison with its antibody-based rivals.

VEGF Trap-Eye is also being studied for macular oedema, representing 40%, or $365m of the total global sales estimate in 2016, and retinal vein occlusion representing roughly 14%, or $128m, of the total forecast. Respectively, data will be presented before year end, and early next year.

Of course the data also means more great news for Bayer, which after paying a very reasonable upfront - $75m - for its ex-US rights to VEGF Trap-Eye, now has more phase III glory to add to recent Rocket data for Xarelto.

Full AMD results will be presented at an ocular disease conference in February, and even more distinct advantages may become clearer, as well as important clarity on safety; Roche and Novartis will likely jump on any safety signals linked to VEGF Trap-Eye.

For now though Regeneron and its investors seem confident that VEGF Trap-Eye represents a unique opportunity to treat AMD at least as well as existing therapy, but with a significantly reduced burden on both patients and the ocular care infrastructure.