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Outlook heads to regulators with eye-friendly Avastin

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But questions remain about both the Norse Two trial and the commercial opportunity.

Roche's cancer drug Avastin is already used off-label in wet age-related macular degeneration, and has shown comparable efficacy to the group's similarly acting eye drug, Lucentis. Outlook Therapeutics, a former biosimilars company, now hopes to make the use of Avastin's active ingredient official in AMD.

The company is heading to the FDA after reporting positive results from the Norse Two trial of ONS-5010, a version of bevacizumab formulated for ophthalmic use. ONS-5010 outperformed Lucentis in the study, but there are reasons to be cautious: for one, the comparator arm used a less frequent than recommended Lucentis dosing regimen, which might have flattered the Outlook project. There is also the question of why doctors would choose ONS-5010 over off-label Avastin, which costs around $50 per dose.

Cost effective?

During a call to discuss the data yesterday, Outlook's chief executive, Russell Trenary, said the rubber stamp from the FDA would be enough to convince physicians who are currently reluctant to prescribe off-label Avastin.

"If you survey doctors and ask them, why do you not [prescribe] off-label Avastin? A lot of them will say: I want to take the best care of my patients that I possibly can and I rely on FDA-approved products to do that."

He concluded: "It's a big deal to bring an FDA approved product to this space."

Still, Lucentis only accounts for around 12% of the US anti-VEGF market in wet AMD, Outlook estimates, and it is obvious why: the drug costs nearly $2,000 per dose, according to *Evaluate Pharma*.

The biggest chunk of the market is off-label Avastin, with 50% of sales, so this is what Outlook would need to aim at. And presumably, in order to compete, ONS-5010's price tag would have to come close to that of off-label Avastin.

Outlook execs did not give specific details of ONS-5010's expected price, other than to say that the drug would be "cost effective".

Approval beckons?

Outlook's job for now is to get ONS-5010 approved, and the Norse Two data might have smoothed the path ahead. The 228-patient study found that the proportion of patients gaining 15 or more letters in best-corrected visual acuity (BCVA) at 11 months, the primary endpoint, was 41% with ONS-5010 versus 23% with Lucentis. The difference was statistically significant with a p value of 0.0052.

ONS-5010-treated patients also gained a mean of 11.2 letters versus 5.8 letters with Lucentis, a secondary endpoint.

However, when asked, Outlook declined to give details of the baseline visual acuity in each arm, and it will be interesting to see if there are any differences here when full data are reported.

A bigger question hovers around the dosing schedules used in Norse Two. ONS-5010 was administered monthly, while Lucentis was given monthly for the first three months, followed by quarterly dosing. Outlook rightly pointed out that this Lucentis dosing schedule is detailed on the drug's label. However, the label also states that this regimen is not as effective as once-monthly dosing, the recommended schedule, and in fact leads to an average five-letter loss in visual acuity benefit versus monthly dosing.

Finally, the drug to beat these days is not Lucentis but Regeneron/Bayer's Eylea. If ONS-5010 does make it to market, Outlook could have more cut-price rivals soon: Eylea is set to lose US patent protection in 2023.

ONS-5010 has already shown non-inferiority to Lucentis in the smaller Norse One trial, and Outlook now plans a filing with the FDA in the first quarter of 2022. Perhaps getting approval will be an easier hurdle to clear than marketing the drug, particularly as Outlook only had $37m in cash at the last count.

The fact that the company needs to raise money explains why Outlook's stock, after soaring 45% in early trading, ended closing up a more muted 7% yesterday – and is down 10% this morning.