Evaluate Vantage

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Archer misses the target

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Annexon’s failure in geographic atrophy could clear the way for its rivals.

If Annexon’s decision late yesterday to play down the failure of its geographic atrophy project ANX007 in a mid-stage trial was an attempt to forestall a drop in its share price, the strategy did not work. The company opened down 58% this morning.

Annexon is determined to press on, but expectations for ANX007 have clearly diminished. And other players here, including Novartis, Roche and Ionis, could stand to benefit.

Geographic atrophy is a late stage of macular degeneration. Lesions form in the retina as photoreceptor cells die, causing vision loss.

The Archer trial of ANX007 missed its primary endpoint, with the anti-complement factor C1q MAb showing no significant benefit over sham on the rate of change in geographic atrophy lesion area after a year’s treatment. But it did slow loss of vision, Annexon said.

Patients given the injection monthly showed a 72% reduction in risk of 15-letter loss, a measure of visual acuity, and patients in the every-other-month treatment group showed a 48% risk reduction. Annexon claimed significance for these versus sham and quoted p values – but since this was a secondary endpoint in a study that missed its primary goal, these are statistically meaningless.

This finding also raises the question of how the antibody protected against vision deteriorating when it had no effect on the lesions that cause that deterioration.

Annexon plans to discuss the project’s future with regulators, but investors do not seem to see much of a path forward here. At the end of March the group had cash reserves of $228m; today its market cap sits at $116m.

Rivals

This could give other groups a chance to seize the geographic atrophy market. There are more advanced products than Annexon’s, including the first drug to be approved in the disease, but they too leave room for improvement.

Apellis Pharmaceuticals’ Syfovre got the FDA nod three months ago based on two trials, Derby and Oaks, only one of which showed a reduction in the formation of new lesions. Since then Apellis has claimed vision benefits with Syfovre, but these came from a post-hoc analysis.

Another project is awaiting the FDA's verdict. Iveric, the group on which Astellas swooped in April in a deal worth just shy of $6bn, said that its project Zimura achieved reductions in the rate of vision loss, but again from a post-hoc analysis. The Gather1 and 2 trials both hit their primary endpoint, decline in the rate of lesion growth versus sham.

There is clearly room for an agent that can produce an unambiguous diminution of vision loss in geographic atrophy patients. The next most advanced projects are in phase 2, and data from the Explore study of Novartis's complement factor I gene therapy PPY988 could appear soon. Novartis got hold of this asset thanks to the acquisition of its originator Gyroscope Therapeutics in 2021. Not a great deal is known about PPY988, and gene therapy is a tricky area, so the readout will be watched with interest. A second study could yield data next year.

The antisense specialist Ionis is also active here, and hope has been kindled by Roche taking a license to its project back in 2018. The asset has another major advantage in that it is injected subcutaneously, rather than into the patient's eyes.

Another upcoming candidate could beat even that. Astrazeneca's danicopan is a pill, taken twice a day. Data on both these projects could emerge next year, and Annexon has left the goal wide open.

The mid-stage geographic atrophy pipeline

Project	Company	Description	Status
Syfovre	Apellis Pharmaceuticals	Complement factor C3 inhibitor, intravitreal	Approved in US Feb 2023
Zimura	Astellas/Iveric	Complement factor C5 inhibitor, intravitreal	Filed in US, Pdufa date 19 Aug 2023
ANX007	Annexon Bioscience	Anti-complement factor C1q MAb, intravitreal	Ph2 Archer failed May 2023, Ph3 planned
PPY988 (GT005)	Novartis (via Gyroscope)	Complement factor I gene therapy, intravitreal	Ph2 Explore & Horizon could report 2023 & 2024, respectively
IONIS-FB-LRX (RG6299)	Ionis/Roche	Complement factor B antisense, subcutaneous	Ph2 Golden could report 2024
Danicopan (ALXN2040)	Astrazeneca	Complement factor D inhibitor, oral	Ph2 (NCT05019521) could report 2024
VOY-101	Perceive Biotherapeutics	Undisclosed, intravitreal	Ph1/2 (NCT05380492) could report 2025
OpRegen (RG6501)	Lineage Cell Therapeutics/Roche	Retinal pigment epithelial cell therapy, surgical subretinal delivery	Ph2a (NCT05626114) could report 2029

Source: Evaluate Pharma & clinicaltrials.gov.