

## Upcoming events - Roche's Avastin heir and vTv's oral GLP-1



[Joanne Fagg](#)

Welcome to your weekly digest of approaching regulatory and clinical readouts. Phase II data for Roche's Avastin successor vanucizumab are expected before the end of the year, and with biosimilars set to enter by 2019 Roche's strength in lifecycle management will need to come into play.

vTv Therapeutics is also expecting phase II results: a trial of its oral GLP-1 receptor agonist TTP273 is to report by the end of the year. It will need to emphasise the project's delivery and safety benefits in a crowded injectable diabetes market, and while interest remains in its Alzheimer's candidate the pipeline needs to impress to rally shares.

### Avastin follow-on

The phase II trial of Roche's vanucizumab, previously known as RG7221, has enrolled 198 patients with untreated metastatic colorectal cancer, and data are expected this year.

The double-blind study pits vanucizumab against Avastin, both in combination with Folfex chemotherapy. The primary endpoint is progression-free survival, with secondary measures including overall survival, objective response rate, duration of response and adverse events, and the data should provide a go/no-go decision on phase III.

Two phase I trials in solid tumours are also recruiting, studying vanucizumab in combination with Tecentriq or the CD40 agonist RO7009789.

Colorectal cancer is Avastin's most lucrative indication, and while this drug inhibits VEGF alone vanucizumab is an anti-Ang2-VEGF bispecific. Both targets are involved in blood vessel formation.

Consensus forecasts from *EvaluatePharma* show Avastin sales peaking at \$7.2bn in 2018, before dropping by more than a third by 2022 with the entry of biosimilars. It is unlikely that vanucizumab will be on the market in time for Avastin biosimilar entry.

But Roche also has Tecentriq, an anti-PDL1, which looks poised to pick up the baton as Roche's biggest growth driver. 2022 sales of Tecentriq are forecast to reach \$5.5bn by 2022, according to *EvaluatePharma* data. Tecentriq is marketed for bladder cancer, filed in lung cancer and in phase III for colorectal cancer.

Roche is well rehearsed in planning for lifecycle management thanks to its efforts with both Herceptin and Rituxan, although the latter's replacement, Gazyva, has not performed quite as well in the clinic ([Roche finds Gazyva not a complete Rituxan replacement, July 18, 2016](#)).

Roche will want the vanucizumab data to help validate Avastin's strategy too.

### Crowded market

Meanwhile, the phase II Logra trial of vTv's TTP273 is under way in 156 type 2 diabetes patients on metformin, and should read out by the end of the year. It measures as primary endpoint change from baseline in HbA1c at three months. TTP273 is being given orally at 150mg once or twice daily, and assessed versus placebo.

In a phase Ib trial the project effectively reduced plasma glucose levels at 75mg twice daily, and showed a numerical reduction in body weight, blood pressure and plasma triglycerides. Rates of nausea and vomiting, a common side effect that has hampered injectable GLP-1 use, were low.

The diabetes market is crowded, and vTv needs to make its candidate an attractive alternative to current injectable treatments. However, big players are already leading the way - for example, Novo Nordisk's oral semaglutide project OG217SC is in phase III ([Novo's oral GLP-1 looks sweeter, August 27, 2015](#)).

vTv also has an oral glucokinase activator in development: TTP399 recently showed a statistically significant

change from baseline in HbA1c at six months in its phase IIb trial. This was originally licensed from Novo.

But vTv's Alzheimer's asset azeliragon is where most of the interest lies. Azeliragon is a small-molecule antagonist of the receptor for advanced glycation endproducts, or RAGE. The Steadfast phase III trial in 800 patients with mild disease should produce topline data by the beginning of 2018 ([vTv paddles out to catch summer Alzheimer's wave, July 21, 2015](#)).

The company completed its \$117m IPO last year, but shares are off 29% since. Upcoming catalysts need to impress to restore investor sentiment.

Project	Study	Trial ID
Vanucizumab	McCave	NCT02141295
TTP273	Logra	NCT02653599
TTP399	Agata	NCT02405260
Azeliragon	Steadfast	NCT02080364

To contact the writer of this story email Joanne Fagg in London at [joannef@epvantage.com](mailto:joannef@epvantage.com) or follow [@JoEPVantage](#) on Twitter

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[+81-\(0\)80-1164-4754](tel:+81-(0)80-1164-4754)

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