

## Cholesterol fears rock Immunovant



[Lisa Urquhart](#)



### **Immunovant and other FcRn-players must hope that a potential safety signal turns out to be indication rather than class specific.**

Immunovant's decision yesterday to pause clinical trials of IMVT-1401 in thyroid eye disease following signals of increased cholesterol and LDL levels not only caused its own shares to plunge. The news sent ripples though the anti-FcRn space, a field that has attracted huge expectations.

Preliminary unblinded 12-week data from approximately 40 patients enrolled into Immunovant's phase IIb Ascend Go-2 trial showed LDL-C increases of about 65% in the 680mg arm, 40% in the 340mg arm, and 25% in the 255mg arm, compared with no increases in the placebo cohort. This prompted fears that the dose-dependent rise in cholesterol could be a class effect for the anti-FcRn mechanism.

Such was the concern that Argenx wasted no time in [issuing a press release](#) to put clear blue water between its FcRn asset efgartigimod and IMVT-1401. The group said it had measured total cholesterol, HDL and LDL in two separate trials involving 384 patients and seen no difference in levels compared with placebo.

Argenx's rush to defend efgartigimod's honour was not surprising given its announcement yesterday that it would be [tapping shareholders for a staggering \\$1bn equity offering](#).

### **Broad benefits**

Targeting FcRn has gained increasing interest recently because of its potential to address a range of hard-to-treat autoimmune diseases. This broad utility is [one reason why J&J paid \\$6.5bn for Momena](#) last year.

In a conference call yesterday, Immunovant said no LDL-C changes had been detected in myasthenia gravis (MG) or immune thrombocytopenia (ITP) studies conducted by the group's China partner, Harbour Biomed. Neither had a link been found in a search of scientific literature of FcRn trials, execs added. This led Leerink to speculate that the rise in LDL and cholesterol could be an on-target effect restricted to thyroid eye disease (TED), the condition being evaluated in Ascend Go-2.

IMVT-1401 is the most advanced FcRn asset in development for TED. The condition is associated with Graves' disease, which causes hyperthyroidism, which can lead to LDL-C increases, further cementing the theory that the cholesterol rises could be indication specific.

As such, Immunovant's decision to run cholesterol tests on stored serum from previous trials in MG and Graves' disease could provide an important answer regarding any read across to other indications.

Ascend Go-2 patients eventually saw their cholesterol levels fall to normal by 20 weeks, leading Leerink analysts to suggest the elevations could theoretically be managed with statins, opening up a way to continue trials.

IMVT-1401 is not dead in the water but, after plummeting 42% yesterday, Immunovant's stock has barely recovered today. It seems that investors remain unconvinced about the way forward.

### The FcRn pipeline - leading contenders

| Project                | Company                 | Projected launch | 2026e sales | Lead clinical development overview  |
|------------------------|-------------------------|------------------|-------------|---|
| Efgartigimod           | Argenx                  | 2021             | \$2.6bn     | Filed: MG; Ph3 ITP, PV ongoing  |
| Rozanolixizumab        | UCB                     | 2022             | \$409m      | Ph3 MG, ITP ongoing   |
| Nipocalimab            | J&J                     | 2022-24*         | n/a         | Ph2/3 WAHA ongoing  |
| IMVT-1401 (batoclimab) | Immunovant              | 2023             | \$1.3bn     | Ph2 MG, TED ongoing   |
| ALXN1830               | Alexion Pharmaceuticals | tbc**            | n/a         | Ph1 in healthy volunteers poised to start with SC formulation. Ph1/2 trials in WAHA and PV terminated with IV formulation |

*\*based on company's estimate of NME filing, 2021-2023. \*\*development paused due to Covid-19, trials to resume shortly with subcutaneous formulation. ITP = immune thrombocytopenia; MG = myasthenia gravis; PV = pemphigus vulgaris; TED = thyroid eye disease; WAHA = warm autoimmune haemolytic anaemia. Source: EvaluatePharma & company statements.*

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