Evaluate Vantage

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Argenx sets a high bar with a novel drug class

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A new mechanism for certain autoimmune conditions takes a big step forward with impressive pivotal data on Argenx's efgartigimod.

The Belgian biotech Argenx has attracted some pretty lofty expectations over the past two years and, happily for investors who bid up the company's market cap to a similarly exuberant $7bn, the first set of data on its lead project have not disappointed.

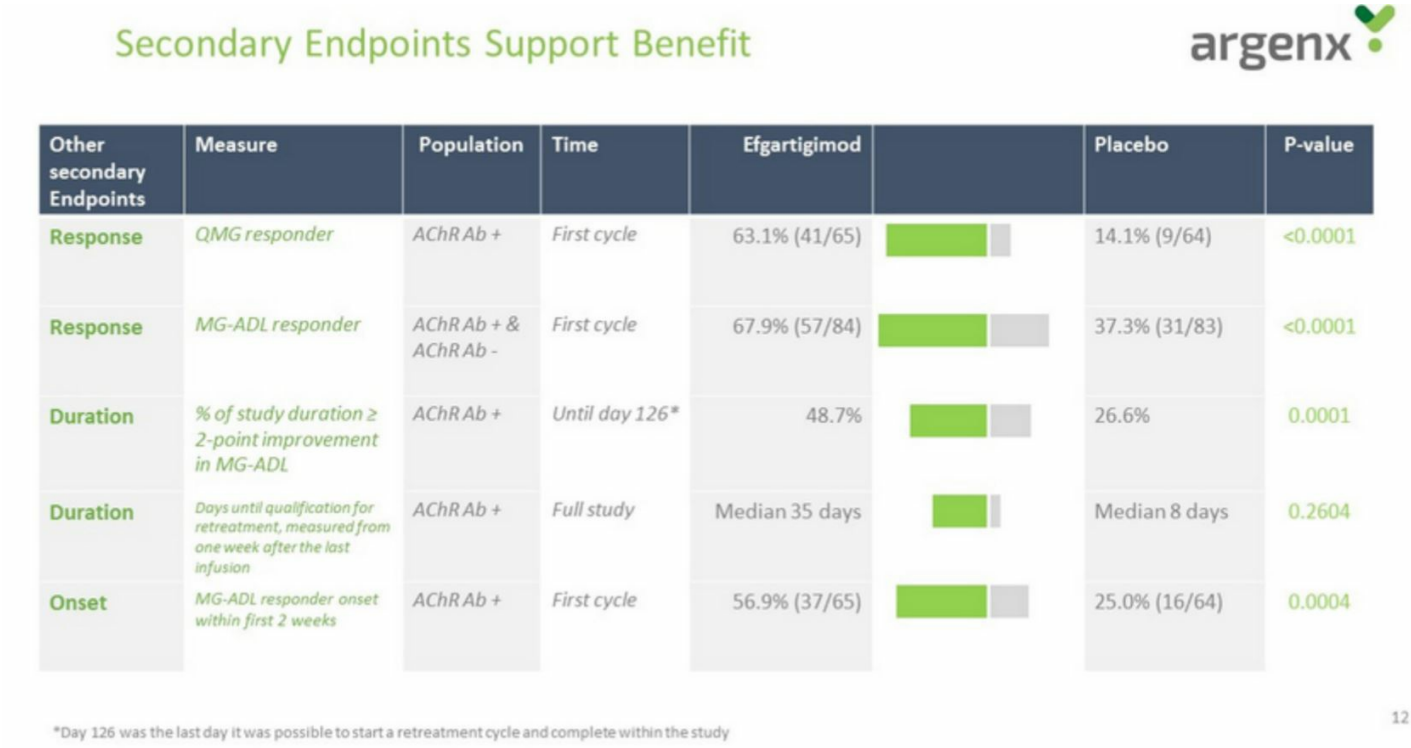
Efgartigimod, an antibody fragment that blocks FcRn, improved symptoms in a big proportion of patients with myasthenia gravis; regulatory approval in the US will be sought later this year. Rivals are nipping at Argenx's heels in what is shaping to be a highly competitive space, but for now the company looks to be comfortably out in front.

The Adapt study tested efgartigimod against placebo in 167 patients with advanced myasthenia gravis (MG), a neurological condition that causes certain muscles to weaken progressively. The primary endpoint was the percentage of patients that improved by at least two points on the MG-ADL symptom scale over eight weeks, and significantly more efgartigimod-treated patients hit this measure than those in the placebo group ($p<0.0001$).

Almost 70% of subjects met this criterion in the active arm, versus almost 30% in the placebo cohort, and the 40-point difference is likely to provide a yardstick of sorts for projects coming up behind. Safety also looks hard to beat: Argenx described efgartigimod as similar to placebo, and indeed the most common events – headache, stuffy nose and nausea – were reported at similar rates in both arms.

Secondary endpoints were also almost unequivocally positive. Only duration of effect over the full 26 weeks of the study missed statistical significance, and on a call this afternoon company executives blamed the use of a log rank test for this failure. But, with 34% of patients responding for 12 weeks or more, and 57% for 8 weeks or more, durability seems unlikely to be a concern.

Adapt trial secondary endpoints



Source: Argenx presentation.

These results suggest that efgartigimod is odds on for approval, although a remaining question is whether this will be granted in all patients. For the vast majority of patients, around 85%, it is autoantibodies against AChR that drive MG, and it was in these patients that the primary endpoint was measured.

However, the trial allowed all patients to be enrolled, and one secondary endpoint did look at responses in all-comers. This hit significance, although executives pointed out a surprisingly high placebo response, and said a broad label remained a point of discussion with regulators.

Still, the 33% surge in Argenx stock this morning, adding another $2bn or so to the company's valuation, indicates that investors are unconcerned by this or indeed any other potential issue.

It seems that only superior signals from competitor projects could burst this bubble, and first up is likely to be phase II data from Momenta's antibody nipocalimab. Stifel analysts have suggested that this project could demonstrate deeper and more durable responses than efgartigimod, though of course it is substantially behind in development.

A closer rival can be found in UCB, whose rozanolixizumab should generate pivotal MG data next year. The Belgian company also recently paid $2bn to access a different MG-targeted mechanism, Ra's zilucoplan, which should also yield pivotal data early next year, and could make for a nervous period for investors buying into the Argenx advance today.

Still, as things stand the race is Argenx's to lose in MG. And already lofty expectations – helped in no small part by sellside sales forecasts that sit at $1.8bn in 2026 – just got even higher.

FcRn targeted projects: the progress so far			
Project	**Pharmacology**	**Company**	**Next steps**
Efgartigimod	Anti-FcRn Ab fragment; IV and SC in earlier development	Argenx	US filing due by year end
Rozanolixizumab	Anti-FcRn MAb; SC	UCB	Phase III readout expected H1 2021
Nipocalimab	Anti-FcRn MAb; IV	Momenta	Phase II MG trial due to read out by Q3 2020
IMVT-1401	Anti-FcRn MAb; SC	Immunovant/ Hanall Biopharma/ Harbour Biomed	Phase IIa due in MG and thyroid eye disease over next 12 mth
ALXN1830	Anti-FcRn MAb; IV and SC in earlier development	Alexion (Syntimmune)	Paused owing to Covid-19, to restart 2021, SC formulation prioritised
ABY-039	Anti-FcRn bivalent Ab mimetic; SC	Affibody	Alexion handed back rights in Feb 2020; phase I ongoing
Source: EvaluatePharma, company statements.			