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# Argenx’s independent streak approaches its biggest test

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**Armed with the first approval for an FcRn antagonist, the Belgian company’s chief executive remains convinced by a solo strategy.**

Small developers rarely manage to cross the regulatory finish line without falling to either mishap or predator – and even fewer make a success of the launch. But investors showed little inclination to flee from Argenx this week when the Belgian company announced FDA approval for efgartigimod in generalised myasthenia gravis.

Conditions remain rough for US biotech stocks so this suggests a lot of confidence in the company, and some big expectations for Vyvgart, as the project is now trademarked. It is the leading FcRn antagonist so perhaps this is understandable; the novel mechanism could prove useful in around 100 settings, Argenx's chief executive Tim Van Hauwermeiren tells *Evaluate Vantage*, predicting that the class “could be as big as the anti-TNFs”.

Argenx boasts a $17bn market cap, showing that some investors share this hope. But it is also true that company has much to do to justify that valuation. Most pressing is to prove that a more convenient subcutaneous formulation of Vyvgart works as well as the intravenous product just approved; the AdaptSC study designed to show this will report early next year.

This head-to-head trial is designed to show non-inferiority, using IgG reduction as its primary endpoint. IgG autoantibodies, which the FcRn antagonists are designed to block, are thought to be at the root of a wide range of autoimmune conditions.

“We are very keen to turn the data card,” says Mr Van Hauwermeiren. Success is crucial for Vyvgart to live up to hopes. Higher demand in the long term is expected for the SC option, though Mr Van Hauwermeiren says the IV route might still be preferred by some patients and physicians – who can make more money from IV products.

**Double-barrelled**

Next year will also see the emergence of pivotal data in other diseases, and the company wants SC and IV options available in all settings. The more convenient SC is being pushed forward first, however.

“That strategy is paying off because patients don’t need to go into hospital for these trials. So they have continued to enrol throughout the pandemic,” Mr Van Hauwermeiren says.

The SC product was created using Halozyme's delivery technology, and is considered a novel combination product by the FDA. As such, a larger safety database is required for approval than AdaptSC can provide, so a second safety trial is ongoing. When a filing might happen is something Mr Van Hauwermeiren is keeping close to his chest.

"We feel good where we are on that, but we have not said anything publicly," he says.

**Approaching clinical readouts for Argenx and Vyvgart**

| Trial | Setting | Data |
|---|---|---|
| AdaptSC | Head-to-head trial of SC vs IV in GMG | Early H1 2022 |
| AdaptSC+ | Long-term safety study of SC formulation in GMG | TBC (needed to complete SC filing) |
| Advance | Pivotal trial of IV formulation in ITP | 2022 |
| AdvanceSC | Pivotal trial of SC formation in ITP | 2022 |
| AdvanceSC+ | Long-term safety study of SC formulation in ITP | TBC |
| Address | Pivotal trial of SC formulation in pemphigus | Late 2022? |
| Address+ | Long-term safety study of SC formulation in pemphigus | TBC |

*Note: SC=subcutaneous; IV=intravenous; GMG=generalised myasthenia gravis; ITP=immune thrombocytopenia. Source: company statements.*

Selling Vyvgart will present another big test for Argenx. Mr Van Hauwermeiren expects a "gradual, but consistent" launch; analysts note that company executives have seemed to rein in some of the loftier sales forecasts for the early years of the rollout.

"There's a ton of education for us to do, and we could only start that after approval," Mr Van Hauwermeiren says. "Navigating the Covid pandemic is another test. It's not trivial to launch a drug [in these circumstances]."

Argenx wants to position Vyvgart as the first infused therapy for GMG, which means getting ahead of Astrazeneca's Soliris, the complement inhibitor blockbuster formerly owned by Alexion. The follow-on drug Ultomiris could present an even greater challenge. Astra has used a priority review voucher to speed up Ultomiris's approval in GMG, it was revealed this week, a signal of intent from the pharma giant.

Mr Van Hauwermeiren is confident that once physicians and patients gain experience with Vyvgart its benefits over complement inhibitors will become clear.

"You need to follow the logic of the biology of the disease. If you eliminate the autoantibodies you eliminate all downstream effects including, but not limited to, complement. GMG is not a complement-mediated disease," he says.

**Closer to home**

Other FcRn antagonists coming behind also pose a threat to Vyvgart, though these projects are yet to yield phase 3 data. UCB is closest with rozanolixizumab, recently toplining its pivotal GMG study and outlining plans to file later next year. In 2020 Johnson & Johnson kicked off a broad pivotal clinical programme with nipocalimab, the former Momenta asset.

Rozanolixizumab is infused subcutaneously over one to two hours. Nipocalimab is an IV project, and while J&J has said a SC version is in the works details have yet to appear.

Mr Van Hauwermeiren says Vyvgart's tailored dosing schedule, which both patients and payers "love", and a subcutaneous shot that takes 30 seconds, "should not to be underestimated. We have set the bar very high on efficacy, safety and convenience."

All of which prompts the question: why has Argenx not been bought by product-hungry big pharma? Price is the obvious answer: the company's valuation is demanding for a mechanism that in reality needs proving, commercially if not clinically. Mr Van Hauwermeiren's independent streak is also well advertised.

"The real question is … who can best serve patients and who can create shareholder value in the fastest amount of time? The speed and quality by which we execute… I think it is all boding well," he says.

With a launch and crucial development milestones looming, Argenx could soon find its investors' support for a solo strategy tested like never before.

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