Evaluate Vantage

November 12, 2019

Astrazeneca looks to power lupus effort over the finish line

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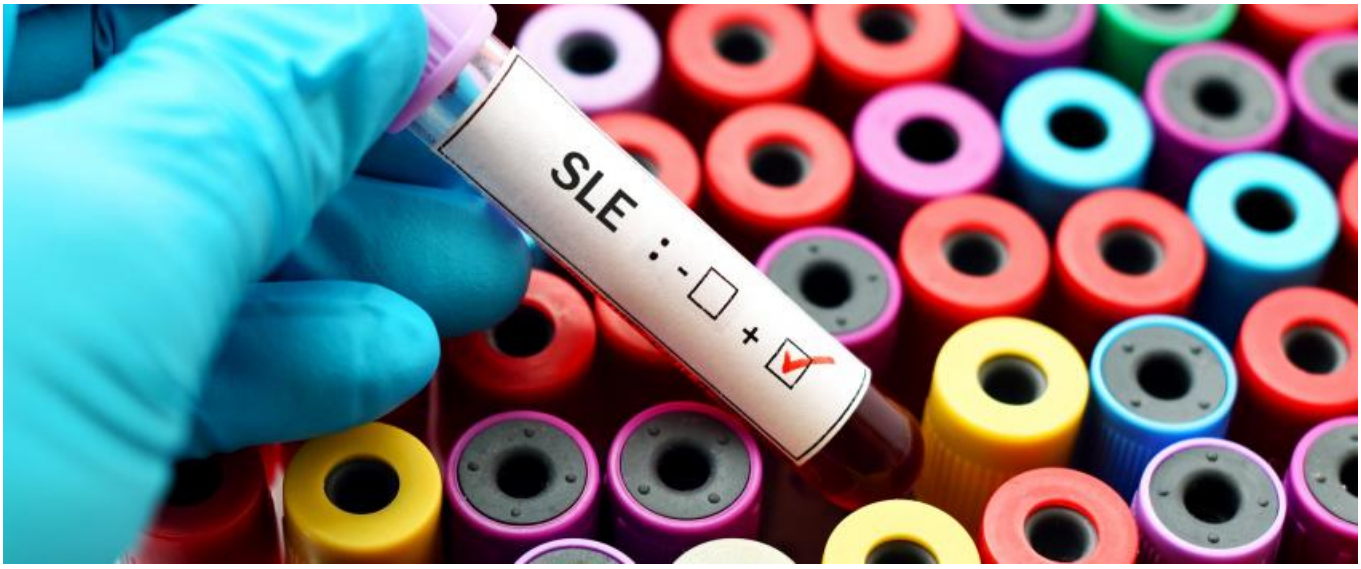

Astrazeneca's goal of bringing the second new lupus drug in over half a century to the market is a step closer, but all hangs on the FDA accepting mixed clinical data.

After reporting detailed results from its Tulip-2 trial in systemic lupus erythematosus (SLE), Astrazeneca is confident that anifrolumamb could hit the market as early as 2021, notwithstanding an earlier phase III failure.

There had been fears that the group might need to do another confirmatory trial following the Tulip-1 flop, potentially pushing approval out for several more years. Speaking to *Vantage* today Richard Marshall, senior vice-president of late-stage R&D at Astra, brushed aside suggestions of any delay, and said the UK group would move rapidly to get anifrolumab in front of the regulators and to patients as soon as possible.

Achieving these filing and launch ambitions will depend on US and European regulators accepting a data package that includes the positive readout from the phase II Muse trial, a sub-analysis of Tulip-1, and full phase III data from Tulip-2, with its amended endpoint. What might play well here are the limited treatment options in lupus.

Tulip-2 had already been toplined as positive, and yesterday it was revealed that anifrolumab had led to 48% of patients showing reduced disease activity, versus 32% in the placebo arm, as judged by the BICLA composite measure.

It should be remembered that both Tulip-1 and Tulip-2 initially had similar trial designs, with a primary endpoint of the number of patients achieving an SLE responder index score of 4 (SRI-4) or greater at week 52, versus standard of care. Following Tulip-1's failure, but before Tulip-2 was unblinded, Astra changed the primary endpoint for the latter to BICLA.

Let's flip for it

There remains some debate in the industry as to which of the two measures best reflects efficacy in this notoriously hard to treat condition. While BICLA requires only partial improvements, these have to be seen in all organs, whereas SRI-4 is measured on complete response, but only in some lupus symptoms.

Today, Mr Marshall said BICLA was the more stringent measure because it captured "the totality of the disease", and that on this measure anifrolumab had "shown compelling evidence of efficacy on disease activity consistently across all three trials".

However, he was also keen to point to anifrolumab's SRI-4 win in the Muse trial. "Both measures are validated by regulators, and we have shown an impact across both measures," he said.

What regulators are prepared to validate is the crux of the issue here, and one of the most important drivers is going to be unmet need. Mr Marshall is very much aware of this, stating: "Anifrolumab represents a new, first-in-class treatment for a disorder with a high disease burden."

There is also historic precedent of the FDA being generous when it comes to diseases with few alternatives. Glaxosmithkline's Benlysta won US approval on the basis of unmet need, despite one of its pivotal trials failing to beat placebo.

The next hurdle

But, as Glaxosmithkline has found, regulatory success does not always add up to a commercial win. Much was made of Benlysta being the first new lupus treatment in over 50 years when it was launched, but its sales have never really lived up to initially lofty expectations; recent increases have been mainly driven by the launch of a self-injectable subcutaneous formulation.

After launching in 2011, Benlysta sales are finally forecast to tip over the $1bn mark in 2023, according to *EvaluatePharma*. If anifrolumab can make it past the regulators and is priced competitively, the opportunity could be huge.