Evaluate Vantage

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Why Abbvie might think twice before exercising Ablynx option

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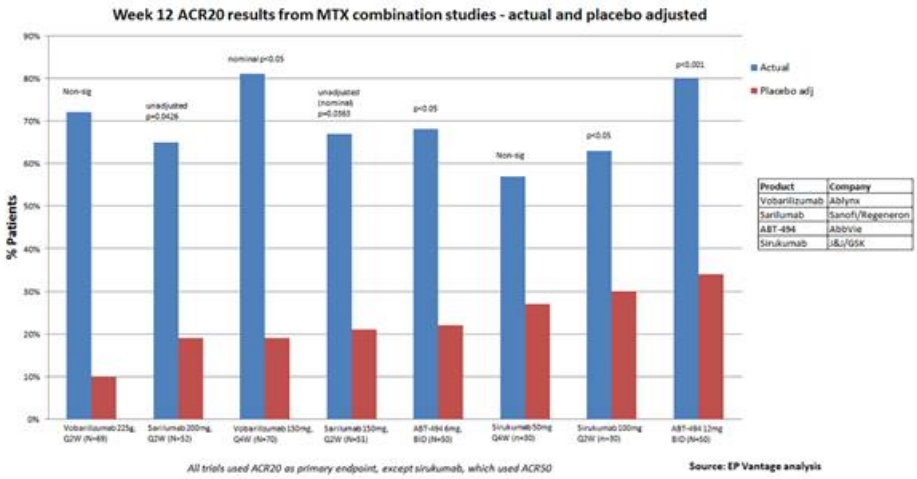
It is looking increasingly hard to see why Abbvie would want to pull the trigger on a full licensing deal over Ablynx's vobarilizumab. A crucial phase IIb trial has failed to meet its primary endpoint, two other agents in the same class backed with more rigorous phase III data are approaching the market, and Abbvie's internal rheumatoid arthritis pipeline is looking healthy.

True, the results released to date on the molecule are hard to interpret – a surprisingly strong placebo response was blamed for the trial miss – and maybe the RA giant will glean its potential. However investors were not comforted by Ablynx's efforts to defend its asset – shares have dropped 13% since a conference call yesterday – possibly on executives' insistence that they will push on alone should Abbvie head for the door.

As Ablynx's crosstown rival Galapagos found last year, after Abbvie turned down its RA candidate filgotinib, this outcome would not necessarily be a bad thing. A mere three months later Gilead licensed the JAK-1 in a much improved deal that included $300m up front, a $475m equity investment and an obligation on the junior party to fund just 20% of the phase III programme.

The situation is different here in that Abbvie chose its own internal JAK-1, ABT-494, over filgotinib. At an R&D presentation in June the company presented a meta-analysis that showed ABT-494 to be clearly more efficacious than filgotinib and Lilly's baracitinib, another rival JAK-1.



Vobarilizumab, meanwhile, is an anti-IL6R nanobody. It has no precedent in Abbvie's pipeline, which arguably has a gap in the mid-stages, particularly after ABT-122 was quietly abandoned last month. Four phase II trials were completed of ABT-122 but the dual targeted bispecific antibody, against TNF and IL-17, was insufficiently differentiated from other pipeline candidates, such as ABT-494, Abbvie said.

The US company last year also returned rights to another mid-stage candidate, Biotest's anti-CD4/CD25 antibody. As such, even though vobarilizumab would bring presence in a new class, it will likely be held up to the same high bar as ABT-122, filgotinib and BT-061 before it.

Nominally positive?

It is also worth remembering that filgotinib generated unequivocally positive data. So, while Ablynx went to great lengths to highlight the promising signals seen in the phase IIb study, the fact remains the trial failed on the primary endpoint of ACR20 at week 12.

A couple of measures did hit a nominal p value of under 0.05 – nominal because of the topline miss – and response rates, as measured by ACR20, 50 and 70, look strong on the surface. Compared with other projects in this class, as the table above shows, the absolute response rates do look competitive.

However, an incredibly high placebo response confounded the statistical analysis. Ablynx blamed the trial design: non-responders had to be discontinued at regulators' insistence, so the fact that doctors and patients were aware of this could have contributed to a strong response in the placebo arm, executives speculated on a conference call.

Executives emphasised less subjective measures of disease activity – DAS28CRP and ESR – that showed more noticeable differences between placebo and active arms. The project's less frequent dosing schedule – once monthly looks possible – and a relatively clean safety profile compared with others in the class also stands it in good stead, they said.

While Ablynx would be "absolutely delighted" if Abbvie choses to push on, chief executive Edwin Moses said "if they don't we would be prepared to start phase III ourselves".

Cash commitment

The data on vobarilizumab aside, Abbvie will also be considering the crowded class in which it will enter. Johnson & Johnson and GlaxoSmithKline are gearing up to file sirukumab while sarilumab, a Regeneron asset partnered with Sanofi, will hear on FDA approval in October.

Financial analysts forecast 2022 sales of $1bn and $800m respectively, while the market incumbent, Actemra, long-considered an also-ran in RA, is still forecast to be selling $1.3bn that year.

Ablynx presented data to show that on certain measures vobarilizumab has shown stronger efficacy than these far more advanced candidates. Maybe Abbvie will concur.

But having already committed to the huge ABT-494 pivotal programme, and with the legal bills around Humira no doubt racking up, Abbvie will likely think long and hard about committing another pile of money to RA.

Product	Trial ID
Vobarilizumab	NCT02309359
ABT-494	NCT02066389
Sarilumab	NCT01061736
Sirukumab	NCT00718718

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