Evaluate Vantage

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In less than a month, Regeneron's luck kicks in

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A clinical trial hold on fasinumab might just be a case of bad luck, but given Teva's poor R&D track record the suggestion that bad judgement was involved is unavoidable. It is less than a month since the Israeli group licensed this pain asset from Regeneron, and for such a setback to occur so soon suggests buyer's desperation.

At least Teva's major cash outlays have not yet been triggered, and the efficacy generated so far actually looks positive, and should allow a phase III protocol to be designed. But the occurrence of joint disease means that fasinumab now joins Pfizer/Lilly's tanezumab under the safety spotlight (see table below).

Fasinumab is an anti-nerve-growth factor MAb, and shares this mechanism with Pfizer's tanezumab and Amgen's fulranumab, for instance. The trial just halted is a phase II study in chronic lower back pain, with a case of arthropathy – joint disease – in a high-dose patient with osteoarthritis (OA) cited as the reason.

Of course, this drug class is hardly a stranger to adverse events, and safety signals have been linked to pre-existing rapidly advancing arthritis, among other factors. But the biggest worry is that fasinumab has merely highlighted a previously well-known problem that some were hoping might have been specific to tanezumab and only seen in OA patients.

Still, safety concerns have previously hit others in this class, and contributed to Regeneron losing Sanofi as a partner on fasinumab, and to Johnson & Johnson and Takeda walking away from Amgen's fulranumab. There are no active fulranumab trials recruiting, suggesting that this project has been discontinued.

Selected anti-nerve growth factor MAbs

Project	Company	Indication(s)	Trial ID
Fasinumab	Regeneron/Teva	Phase III in OA pain; phase II in lower back pain on hold	NCT02683239
Tanezumab	Pfizer/Lilly	Five Phase III trials in lower back pain or OA pain	NCT02528188
Fulranumab	Amgen	Four small phase III studies completed, likely discontinued	NCT02301234
ABT-110	Abbvie	Abandoned in phase I	–
CRB0089 & CRB 0022	Mylan	Preclinical	–

For now Teva and Regeneron can tout positive data seen in the phase II trial; because of the hold they decided to unblind it at 70% enrolment, and say they saw improvement in pain scores at eight and 12 weeks, with a nominal p value of under 0.01.

Based on this, they say a phase III lower back pain trial can be designed – excluding patients with OA. A separate 10,000-patient study in patients with pain due to osteoarthritis of the knee or hip is ongoing, but Bernstein analysts question whether physicians would commit to using a drug with this kind of side effect in either OA or lower back pain – both long-term, chronic conditions.

As such the occurrence of arthropathy has validated the view of some analysts that the deal was better for Regeneron than for Teva, allowing the former company to reduce spending on a troubled drug class and focus instead on launching Praluent (*In Teva, Regeneron finds its Sanofi for pain, 21 September 2016*).

Today the sellside was quick to say we told you so, with Bernstein's Ronny Gal opining that fasinumab was clearly a high-risk programme, and asking whether a company still operating at the borderline of profitability should commit itself to it. Leerink reduced its success probability for fasinumab to zero.

Evercore ISI's Umer Raffat went further, suggesting that Teva should take the opportunity to cut its losses and back away from the deal, especially before the cost of the phase III outcomes trial kicks in. Pulling the plug will not come cheap, however, and Regeneron looks like it has been lucky twice in less than a month.

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