

## Regeneron nips at Amgen and Pfizer's heels in pain drug race



[Jonathan Gardner](#)

Johnson & Johnson might have joined Sanofi and AstraZeneca in giving up hope on the anti-nerve growth factor class, but not everybody has. Regeneron Pharmaceuticals now has the support it needs for its massive pivotal trial of fasinumab, with positive phase II/III data on treating arthritis-related pain.

The safety issues that have dogged these antibodies still exist, as patients treated with the Regeneron project experienced nerve and musculoskeletal side effects. Yet with pressure on the FDA to take steps to reduce the misuse of pain-killing opioids, it seems like the agency should be keen to let the phase III trial proceed with a careful eye on safety.

### Low doses good

Patients taking fasinumab reported significant improvements in arthritis-specific pain scores across four doses at 16 weeks compared with patients taking a placebo. The difference from baseline scores ranged from 3.35 points on the WOMAC scale at the lowest 1mg dose to 3.65 at the 9mg highest dose.

Given the long-term safety concerns on these anti-nerve growth factor (NGF) agents, these data would point the way towards a lower dose ([Tanezumab's return shows pharma has held its nerve](#), March 24, 2015).

Regeneron's filing of a 10,000-patient phase III trial at [clinicaltrials.gov](#) states that there will be two dosing regimens but does not specify the level.

The adverse events data from the just-reported trial affirm the need to be careful with the phase III dose and vigilant with any signals from the pivotal trial. Nerve and musculoskeletal side effects such as joint pain, numbness, or peripheral oedema were recorded in 17% of the patients taking fasinumab.

Because of disease exacerbation resulting from use of anti-NGF agents, Regeneron conducted imaging tests to screen patients at risk and identify those developing joint damage. Of screened patients, 2% were excluded from the trial because of pre-existing fractures or osteonecrosis.

In the trial, no osteonecrosis cases were identified in patients taking fasinumab, but researchers identified six cases of osteoporosis-related fractures and three cases of rapidly progressing osteoarthritis; importantly, none of these side effects appeared in the 1mg dose group.

### Class outlook

With its phase III trial reportedly recruiting, fasinumab is drawing close to Pfizer's tanezumab in the race to a regulatory submission. The Regeneron agent could report data in 2018, trailing tanezumab by a few months or so in the osteoarthritis indication, although a third agent, Amgen's fulranumab, is nearing some key phase III readouts.

Survival of the fittest - fate of the anti-nerve growth factor antibodies			
	Project	Company	Status
Active	tanezumab	Pfizer	Phase III
	fasinumab	Regeneron Pharmaceuticals	Phase III
	fulranumab	Amgen	Phase III
Abandoned	ABT-110	AbbVie	Abandoned in phase I
	MEDI-578	AstraZeneca	Abandoned in phase I

Pfizer is testing its antibody in a number of indications outside arthritis – for example in cancer pain and low-

back pain - which could put tanezumab on the market with some clear daylight. Tanezumab is the only anti-NGF project that has an *EvaluatePharma* consensus forecast - \$105m in 2022 - although Leerink Research expects \$400m for fasinumab in 2020.

Safety issues, clinical holds and other regulatory activities have seen AbbVie and AstraZeneca give up on ABT-110 and MEDI-578; meanwhile, J&J last month handed back to Amgen rights to fulranumab, something Sanofi did to Regeneron with fasinumab four years ago ([Pfizer steps out of J&J's shadow to get a tan, April 11, 2016](#)).

Still, three agents are left standing and active in phase III, which might have been seen as an unlikely scenario four years ago. If they succeed in the clinic the commercial promise of these drugs might be limited by strict labelling and risk-mitigation procedures; however, they could be attractive as a non-addictive option to treat arthritis pain.

Study	Trial ID
Phase II/III trial in 375 patients with osteoarthritis pain of the knee or hip	NCT02447276
Phase III trial in 10,000 patients with osteoarthritis pain of the knee or hip	NCT02683239

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