

## Interview - SetPoint off to a good start in the clinic



[Elizabeth Cairns](#)

When in 2013 Covidien, Boston Scientific and GlaxoSmithKline pumped \$27m into a preclinical-stage company attempting to treat rheumatoid arthritis with vagus nerve stimulation, it looked like a leap into the unknown. But SetPoint Medical has reported pretty decent results in its first human trial, and with a megabucks potential market the company might yet turn out to be a smart choice for its investors.

"I think we can say definitively that it works, and that it's an effective therapy for many patients," says SetPoint's chief executive, Anthony Arnold. Results from the 17-patient study are encouraging, particularly in drug-refractory patients, but the technology is still early, and the group has much to prove.

### Vagus, baby

Vagus nerve stimulation is approved in the US for epilepsy and depression, indications that are arguably more intuitive than RA as they are neurological. The technique has also been tried in non-neurological disorders including heart failure and obesity, but results here could charitably be described as mixed.

So SetPoint's aim of using neuromodulation to treat RA is slightly leftfield. But the science seems sound: stimulating the vagus nerve can block the production of TNF and other inflammatory cytokines, meaning that the tech exploits, among others, the same pathway as Humira and other blockbuster RA biologics.

Initially SetPoint's pilot trial, 005, recruited eight patients with "substantial disease" – people who had trouble buttoning their shirts or using utensils. They had never taken antibodies but had been treated with methotrexate.

Mr Arnold says that of these eight patients, after 42 days of treatment six had "very significant reductions in their American College of Rheumatology scores and their disease activity scores, meaning all their biomarkers went down substantially, which indicated improvement – and their signs and symptoms got much better too."

One of these patients was later found to have a different condition, Whipple's disease, and was excluded.

### Turn it off and on again

The trial then enrolled 10 more patients who had failed on anti-TNF biologics. "These patients were just as sick as before, but with the additional challenge that they'd been through every available therapy," Mr Arnold says. "They'd tried multiple drugs, some as many as nine, and they had failed."

Seven of those 10 patients got notably better, he says, with substantial improvements in quality of life.

There was no sham group in the trial, but in a paper [published in PNAS](#) the investigators state that "withdrawal of treatment" – the stimulator was switched off – "significantly worsened the severity of disease".

Reactivating the device on day 56 restored significant clinical improvement, they wrote.

The second cohort is particularly promising. Firstly it improves SetPoint's chances of approval – treating patients who have no further pharmacological options always makes a device more appealing to regulators. But it also could increase the size of the market – not that, at nearly \$25bn, the RA market is tiny in the first place.

### Game, SetPoint and match

The data might be positive, but they are early, and will not be enough for regulators. Future trials will require larger trials, in maybe 200 patients, with more rigorous sham control to show the extent of the technology's benefit.

"With the numbers we have we couldn't give you definitive proof of exactly what the response rate would be statistically," Mr Arnold says. Trial endpoints might include measures of quality of life as well as biomarkers, he says. "Then you'll use the European disease activity score, which is a very good indicator of improvement

because it's primarily composed of objective measures."

This will help convince payers as well as regulators, he says. And this will be necessary. Biosimilars to the anti-TNF biologics are on the cusp of approval in the US, and will shake up the cost-effectiveness calculations as regards drugs versus devices.

Mr Arnold is unperturbed. The branded antibodies cost around \$40,000 per patient per year, he says, whereas biosimilars ought to clock in at \$24,000 or so. SetPoint's device is expected to sell for around \$30,000 plus the cost of the surgery – say \$11,000 in Europe and \$17,000 in the US.

But the stimulator lasts for 10 years, and running costs are negligible, so SetPoint can make a case for long-term cost-effectiveness. There are other arguments it can marshal: it claims a better side-effect profile for the device over drug therapy, and once implanted patients do not notice it, perhaps an improvement over the regular jabs necessary with biologicals.

And Mr Arnold points out that the antibodies tend to lose efficacy over time. "Five years out more than half the people successfully treated with TFN-alpha inhibitors no longer respond," he says. "With the device we haven't seen that type of falloff – patients do seem to respond a lot longer."

### More money

The company has raised more than \$50m from venture backers so far, but with new trials in the offing SetPoint is about to embark on another fund raising, aiming to raise \$40-60m by early next year.

SetPoint's VC investment			
Date	Round	Investment (\$m)	Investors
September 2015	Series C (second close)	15.0	Action Potential Venture Capital, Boston Scientific, Covidien Ventures, Foundation Medical Partners, Morgenthaler Ventures, Topspin Partners
August 2013	Series C	27.0	Action Potential Venture Capital, Boston Scientific, Covidien Ventures, GlaxoSmithKline
May 2009	Series B	4.0	Undisclosed
June 2007	Series A	5.5	Morgenthaler Ventures, Foundation Medical Partners
	<b>Total</b>	<b>51.5</b>	

"It's a very challenging time to raise money," Mr Arnold admits, but he is confident that both existing and new investors will rush to put up some cash.

One reason for this bullishness is the fact that big medtechs are already on board, which Mr Arnold says signals their strategic interest in SetPoint's technology.

"It's possible. I'm gearing this company towards an IPO, but it could be that one of those companies wants to make an offer along the way."

If anything, the environment for IPOs is even more hostile than that for venture funding. Mr Arnold agrees but says that, as the only device alternative to biologicals, even snaring a tiny fragment of the RA market – or adding to it by treating refractory patients – is a multibillion-dollar proposition.

This is true. SetPoint's ability to carve itself out a niche rests on what it can show in larger, more carefully controlled trials.

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