

## US approval sets up Zilretta for a life of mediocrity



[Jacob Plieth](#)

After overcoming a phase II failure Flexion had two more tricks up its sleeve: it pulled one off on Friday, managing to persuade the US FDA of the approvability of Zilretta for osteoarthritis knee pain based on a pivotal trial that showed the drug to be no better than standard triamcinolone, a cheap steroid.

The first had been to convince the sellside that Zilretta could become a strong seller even though triamcinolone has been available as a generic for years. With Flexion's stock up 10% on Friday the big losers were short sellers – over 20% of the float had been sold short – who had bet on the FDA telling the group to start again.

Also losing out were investors in Vericel, which fell 8% after a strong run-up in September. Vericel's autologous chondrocyte product MACI is approved for a different use – knee cartilage replacement – and Zilretta might cut into this vanishingly small market.

### Best bet

Right now Flexion's best bet is to play up Zilretta's status as a reasonably safe, non-surgical product that is not an opioid – a hot issue given sensitivity about abuse potential of these painkillers.

It would do well not to mention the fact that its pivotal trial showed Zilretta, an extended-release triamcinolone, to be no better than the immediate-release generic ([Second time around, Flexion makes the case for a generic steroid, February 17, 2016](#)). Some four million OA knee pain patients are on immediate-release steroids at present.

What is worse, the shortcoming appears spelled out on [Zilretta's label](#), along with a useful graphical representation. As these fears set in after an analyst call today Flexion lost 7% in early trade this morning.

The group has made much of the new drug's admittedly strong benefit over placebo, the pivotal trial's primary efficacy measure, and the suggestion that it could avoid disruptive blood glucose spikes that can be seen with immediate-release steroids in type 2 diabetics who have knee OA.

And the sellside has largely gone along with this optimism, and *EvaluatePharma* numbers reveal consensus 2022 sales expectations of \$457m. In February Wells Fargo analysts went as far as to suggest that Zilretta, effectively Flexion's only asset, "could be a game changer [and] a potential \$1bn+ product".

Flexion priced Zilretta at \$500 per dose – roughly on a par with Synvisc-One, an injection that supplements knee fluid to help lubricate the joint. At \$500 for Zilretta the group needs to capture at least half of the four million patients on immediate-release steroids to reach blockbuster sales.

It is not immediately clear how payers will support this in light of Zilretta's lack of benefit over standard triamcinolone. Even bullish banks like Raymond James expect a slow sales trajectory, in spite of factoring in up to four injections per patient – current approval is for just one – price increases and growth in the underlying market.

### Profitability

Even before considering the threat of cheap generics, given such dynamics can a \$500 product ever become profitable?

In the absence of a partner costs will be considerable: on today's analyst call Flexion said it had hired 103 reps. The sellside expects these to target the 9,000 orthopaedists and rheumatologists who account for more than 75% of injections given for OA knee pain.

Some of the enthusiasm had been driven by unsubstantiated rumours earlier this year that Sanofi was interested in buying Flexion, but like Zilretta itself that now looks like a tough sell.

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