Evaluate Vantage

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Olumiant setback opens the door to rivals

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Rejection of Lilly's Olumiant by US regulators might go down as one of the biggest surprises of 2017, with the FDA's complete response letter citing dosing and safety data coming just two months after European officials signed off on the rheumatoid arthritis drug.

The Jak-1/2 inhibitor was projected to become the fifth-biggest RA product by 2022, explaining the billions erased from Lilly and Incyte's market values yesterday. However, a look at the pipeline in this disease area shows that the partners have as much to worry about from competitors as they do from their own setback (see table below).

Should Olumiant be delayed in the US to 2020, as many analysts now assume, Abbvie's ABT-494 and Gilead and Galapagos's filgotinib could be in the frame for launch on a similar timeframe. Both also inhibit the janus kinases, although Olumiant hits both Jak-1 and 2. Pfizer's Xeljanz, the first of this class to reach the market, hits Jak-3.

By 2020, the launches of Kevzara and sirukumab will also presumably be well under way. Although these injected antibodies have a different mechanism of action, they will also be competing for patients in what is already a very crowded space. This is before considering the prospect of Humira biosimilars.

Novel entrants to the RA market

				Global RA sales ($m)		
Product	**Company**	**Pharma class**	**US launch**	**2017**	**2020**	**2022**
ABT-494	Abbvie	Jak-1 inhibitor	2019e	-	447	1,223
Sirukumab	Johnson & Johnson	Anti-IL-6 MAb	Q4 2017	49	525	1,020
Kevzara	Sanofi	Anti-IL-6 MAb	Q1 2017	74	440	686
Filgotinib	Gilead Sciences	Jak-1 inhibitor	2020e	-	10	162

Source: EvaluatePharma.

Of course, the rival Jaks in development could also now be facing heightened FDA scrutiny of their safety, although the companies involved have the advantage of being forewarned.

Lilly did not disclose the specific reasons for the FDA's decision, citing in a press release additional clinical data "needed to determine the most appropriate doses" and to "characterise safety concerns across treatment arms".

The EU's label for Olumiant, which contains the active ingredient baricitinib, could provide some clues. It warns generally of infections, elevated liver enzymes and neutropenia, as is common with many immunosuppressive drugs. As for dosing, the EU recommends 4mg, which can be reduced to 2mg when the disease is under control, and even lower doses in patients over 75 years old, at higher risk of infection or with impaired kidney function.

A major concern now is that the FDA will only allow the lower 2mg dose to be marketed, which would erase much of Olumiant's efficacy advantage over competitors.

Notably, Olumiant appears to be following the reverse path to Pfizer's Xeljanz, which got a first-cycle US OK in 2012, but failed to get European approval until last month.

Off the table

The setback knocked $3.9bn off Lilly's market capitalisation, roughly equal to Olumiant's net present value as calculated from *EvaluatePharma's* sellside consensus. The current sellside forecast puts Olumiant sales at

$1.6bn, with $988m coming from the US.

These numbers are now off the table, although the big royalty stream that Lilly owed Incyte meant the product was never going to be a huge profit driver for the pharma giant.

Shares in Incyte tumbled 10% yesterday, knocking $3bn off its valuation. The FDA's decision delays a $100m approval milestone and slows its 20% royalty stream to a trickle; in addition, the co-development structure of the licensing deal has Incyte assisting in R&D costs through regulatory approval, while $150m in sales-based milestones are likely in jeopardy.

Both groups must now hope that other pipeline prospects can fill the gap. For Lilly this means its diabetes and oncology products – Trulicity and abemaciclib in particular. Incyte, meanwhile, needs its immuno-oncology candidate epacadostat to live up to high hopes (*Incyte dramatically ups the immuno-oncology combo ante, April 3, 2017*).

For now, being on the wrong side of what was seen as a low-risk event will be a drag on investor sentiment. Olumiant's competitors will move to make the most of this delay, which could prove fatal to its blockbuster potential.

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