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Galapagos flies with more Finch data

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Filgotinib could be the safest Jak inhibitor yet, but Galapagos will need to make the most of this as it squares up to Abbvie.

Galapagos and Gilead might be late to the Jak inhibitor party, but they now have a decent shot at going up against their more advanced competitors. New data with the partners' contender, filgotinib, suggest the project has slightly lower efficacy than its main rival, Abbvie's upadacitinib but, perhaps more importantly, a better safety profile.

The latest results, from the Finch 1 and 3 trials in rheumatoid arthritis, set up the prospect of an intriguing battle against Abbvie, which had once had an option over filgotinib but chose to focus on upadacitinib, which it developed in house. There are still some questions around how soon filgotinib might get approved, and at what dose, but hopes that it could become a strong contender sent Galapagos's stock up as much as 18% today, while Gilead climbed 2%.

Manta delay?

The timing of filgotinib's filing with the FDA depends on how willing the agency is to review the project ahead of data from an ongoing safety trial, called Manta, which is evaluating filgotinib's impact on the sperm counts of male patients with ulcerative colitis. Results could come later this year, but the study has previously been delayed by slow enrolment.

The FDA asked for the trial after animal studies found a link between filgotinib and decreased sperm counts. Galapagos's chief operating officer, Bart Filius, told *Vantage* that this issue had only been seen in animals treated with doses over 200mg, the highest dose used in clinical trials, and that it had not been observed in human trials so far.

Analysts do not expect filgotinib to get a warning over testicular toxicity, given the history of other drugs that have been linked with this problem in preclinical studies and gone on to be approved.

However, if the FDA wants to see the Manta data before filing, this could push filgotinib's launch back to as late as 2022, Leerink analysts estimated – versus a 2020 launch in the best-case scenario.

Mr Filius said the timing of filgotinib's US filing should become clearer once Gilead has met the FDA to discuss the Finch results. The Manta data should not be needed for European and Japanese approved, he added.

High dose

Another big question is whether Gilead and Galapagos can get approval for the high dose of filgotinib, which would be a coup. The FDA limited approval of Lilly's Jak inhibitor Olumiant to a low dose because of concerns about thrombosis, while Abbvie is only seeking approval for a lower 15mg dose of upadacitinib, with an FDA decision due in the third quarter.

Abbvie has not explained its decision to drop a higher 30mg dose, but the Leerink analysts noted an increased rate of herpes zoster infection with this dose in phase III.

This does not appear to be as big an issue with filgotinib – and neither does thrombosis, which has been seen with other Jak inhibitors.

Best in class? Jak inhibitor safety signals in rheumatoid arthritis				
	Filgotinib (Galapagos/Gilead)	**Upadacitinib (Abbvie)**	**Olumiant (Lilly)**	**Xeljanz (Pfizer)**
Serious infections	1.8%	2.7%	2.9%	2.5%
Herpes zoster	1.5%	3.4%	3.3%	3.6%
DVT/PE	0.1%	0.4%	0.5%	n/a
DVT: Deep vein thrombosis; PE: Pulmonary embolism. Source: Bernstein note March 29, 2019.				

As for efficacy, filgotinib looks to have fallen slightly short of upadacitinib, although the usual caution about cross-trial comparisons applies.

Notably, in the Finch 1 trial filgotinib did not show superiority over Abbvie's Humira, something that upadacitinib managed to do in its analogous study, Select-Compare. Both trials added a Jak inhibitor to methotrexate in patients with an inadequate response to methotrexate.

Cross-trial comparison of Finch 1 vs Select-Compare							
	Finch 1 (NCT02889796)				**Select-Compare (NCT02629159)**		
	Filgotinib 200mg	Filgotinib 100mg	Humira 40mg	Placebo	Upadacitinib 15 mg	Humira 40mg	Placebo
ACR20 response (%)	77*	70*	71	50	71*†	63	36
**p<0.001 vs placebo †p<0.05 vs Humira. All at 12 weeks. Source: Company releases.*							

In Finch 3, testing filgotinib alone or plus methotrexate in methotrexate-naïve patients, filgotinib monotherapy did not impress. Still, the responses with Humira in Finch 1 and methotrexate monotherapy in Finch 3 were particularly high, Bernstein analysts noted.

The Finch 1 and 3 results add to a win from the Finch 2 trial in September, in patients with an inadequate response to biologics (*Angst for Abbvie as Gilead scores with cast-off, September 12, 2018*).

If both upadacitinib and filgotinib get approved – which now looks likely – the choice of which to prescribe could come down to a delicate balancing act between efficacy and safety. Getting payers onside will also be key; here Abbvie's experience in rheumatoid arthritis with Humira should not be sniffed at.

Currently, *EvaluatePharma* consensus puts 2024 revenues for filgotinib at $1.1bn, while upadacitinib is expected to hit $2.5bn that year. Galapagos and Gilead still have a big battle ahead, but at least the latest Finch data have given them a good chance of making a mark.

Cross-trial comparison of Finch 3 vs Select-Early in methotrexate-naïve patients				
	Finch 3 (NCT02886728)			**Select-Early (NCT02706873)**
	Filgotinib 200mg + MTX	Filgotinib 100mg + MTX	Filgotinib 200mg monotherapy	Upadacitinib 15mg monotherapy
ACR20 response (%)	9.6**	8.8*	6.7	20**
**p<0.05 vs MTX, **p<0.001 vs MTX. All at week 24 and adjusted vs methotrexate alone. Source: Company releases.*				