Evaluate Vantage

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Upcoming events – Pivotal data for Galapagos and Cara

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Galapagos will discover if filgotinib can hang on to its reputation as one of the safest Jak inhibitors in the industry, while Cara is itching for pivotal trial success with intravenous Korsuva.

Welcome to your weekly digest of approaching regulatory and clinical readouts. Galapagos has already cleared one hurdle for its lead project, filgotinib, in the form of positive results from the pivotal Finch-2 trial in rheumatoid arthritis. The company now awaits imminent readout of the Finch-1 and Finch-3 studies.

Success in Finch-1 and Finch-3 will help to determine whether filgotinib, potentially the fourth-to-market Jak inhibitor for rheumatoid arthritis, will fly commercially. The results are also almost certain to move partner Gilead's shares, which have fallen 15% in the past six months following disappointing financial guidance and a recent failure in Nash.

The primary endpoint of both trials is the proportion of patients achieving a 20% improvement in the American College of Rheumatology score (ACR20) at either 12 or 24 weeks.

Study	Details	Control	Primary endpoint
Finch-1	Filgotinib + methotrexate in moderate to severe patients with inadequate response to methotrexate	Methotrexate +/- Humira	Proportion of patients achieving ACR20 at week 12
Finch-3	Filgotinib +/- methotrexate in moderate to severe patients naive to methotrexate	Methotrexate	Proportion of patients achieving ACR20 at week 24

However, it might be more important for filgotinib to show safety rather than efficacy, as its main selling point could be a cleaner safety profile than other Jak inhibitors. Both Pfizer's Xeljanz and Lilly's Olumiant carry black box warnings over serious infections, while the FDA only approved a lower dose of the latter after concerns about thrombosis.

As such, investors will be keenly watching for any adverse events in Finch-1 and 3 – thrombosis issues in particular. A win on the safety front could help differentiate filgotinib from upadacitinib, Abbvie's rival Jak,

which is expected to be approved for rheumatoid arthritis later this year.

So far filgotinib has only reported thrombotic events in two patients in much earlier trials. Analysts are, however, divided over whether or not a superior safety profile would help filgotinib: at the moment consensus forecasts still have Xeljanz leading the Jak pack.

Brakes on future sales of filgotinib are almost certain to come in the form of an increasingly tough commercial market, where competition is likely to bring prices down. There is also the not so small matter of Xeljanz coming off patent in 2025. Even if filgotinib does win on safety Galapagos and Gilead are likely to have a battle on their hands.

Outlook for the Jak inhibitor class

			Annual sales ($r	
Product	**Company**	**Target**	**2019e**	**2022e**
Xeljanz	Pfizer	Jak 1, 2 & 3	2,189	3,069
Upadacitinib	Abbvie	Jak 1	52	1,450
Olumiant	Lilly	Jak 1 & 2	396	1,002
Filgotinib	Gilead/Galapagos	Jak 1	-	446

Cara scratches at the door to success

Data due in the second quarter of this year will determine whether Cara Therapeutics can justify its inclusion on the list of small biotechs to watch in 2019. Interest in the group hinges on pivotal results with its lead, intravenous Korsuva for moderate to severe pruritus in chronic kidney disease patients receiving haemodialysis.

Pruritus, painful itching, is one of the side effects of kidney failure, liver disease and certain cancers. At present there are no approved therapies for chronic kidney disease-associated pruritus, so success in the Kalm-1 trial could not only reverse the 16% share price decline that Cara has seen over the past six months, but also open up the door to indication extensions.

The primary endpoint of Kalm-1, which is testing Korsuva at 0.5µg/kg, is the proportion of patients with an improvement from baseline of at least three points in the weekly mean of the daily 24-hour worst itch numeric rating scale (WI-NRS) at week 12.

An earlier phase II trial found that 64% of patients in the 0.5µg/kg group reported a three-point improvement on the WI-NRS compared with 29% of placebo recipients, setting the expectations for Kalm-1.

Alongside the US Kalm-1 trial, Cara is also running Kalm-2, which will recruit patients internationally. If all goes to plan the group should be on track for an early 2020 filing. Cara already has a promotion and profit-sharing arrangement with Vifor, and this could encourage use in US dialysis clinics run by Vifor's partner Fresenius.

Many expect that Korsuva will avoid having limits set on its pricing for two years, a common practice with bundled payments for dialysis treatment. Some sellside analysts forecast peak annual sales of as much as $500m in the haemodialysis population.

Cara is also looking at oral versions of Korsuva in non-dialysis CKD patients, potentially offering a much bigger treatment cohort. A phase II trial in chronic liver disease is expected to start later this year. As such, success of IV Korsuva will only increase confidence that the group’s ambitious expansion and commercialisation plans might come to fruition.

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