Evaluate Vantage

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Upcoming events – Pivotal data readouts for Galapagos and Bayer

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Galapagos and Bayer/Orion will both report phase III data this quarter – the former with filgotinib in arthritis and the latter with darolutamide in prostate cancer.

Welcome to your weekly digest of upcoming events. Safety will be the key to determining whether Galapgos's filgotinib can make headway in an already crowded rheumatoid arthritis market.

The Gilead-partnered drug is expected to yield results in the third quarter from the phase III Finch 2 trial, which pits filgotinib against placebo in patients on conventional disease-modifying anti-rheumatic drugs who have failed on a biological RA treatment.

Most analysts expect filgotinib to show efficacy roughly in line with other Jak inhibitors in RA but, crucially, with a cleaner safety profile; Stifel cited a lack of safety issues in the long-term Darwin 3 study.

This will matter as analysts have recently delayed the expected launch of the product from 2020 to 2021, as they expect Gilead to need time to collect sufficient safety data. This would make filgotinib the fourth Jak inhibitor to reach the market.

Consensus outlook for JAK inhibitor market						
					Annual sales ($m)	
Company	**Product**	**Mechanism**	**Status**	**US launch**	**2017**	**2024e**
Pfizer	Xeljanz	Jak 3 inhibitor	Marketed	2012	1,345	3,154
Abbvie	Upadacitinib	Jak 1 inhibitor	Phase III	2019	-	2,184
Lilly	Olumiant	Jak 1&2 inhibitor	Marketed	2018	46	1,339
Gilead	Filgotinib	Jak 1 inhibitor	Phase III	2021	-	1,279
Astellas	ASP015K Oral	Jak inhibitor	Filed	-	-	40
Source: EvaluatePharma.						

Xeljanz's first-mover advantage is reflected in the drug's 2024 forecast sales, despite a black box warning over serious infections and malignancies. Meanwhile, Lilly's Olumiant got the go-ahead from the FDA in June but only for the lower, 2mg dose, after concerns about thrombotic events.

Abbvie's upadacitinib, due to launch next year, has also been linked with thrombosis, although recent trial results appear to have assuaged some of these worries. As if this competition were not enough, filgotinib might not have long on the market before it goes up against generics, too: Xeljanz's patent is set to expire by the end of 2025.

Success in Finch 2 would bode well for the remaining Finch 1 and 3 RA trials, due to read out in 2019. Investors might also become more optimistic about filgotinib's success in other indications including chronic dermatitis, ulcerative colitis and ankylosing spondylitis; results from the phase II Tortuga study in the last indication are due this quarter.

Study	Setting	Trial ID
Finch 2	Rheumatoid arthritis	NCT02873936
Finch 1	Rheumatoid arthritis	NCT02889796
Finch 3	Rheumatoid arthritis	NCT02886728
Tortuga	Ankylosing spondylitis	NCT03117270

Bayer/Orion's darolutamide is also late to the party, as the war for domination in prostate cancer has been waged between Johnson & Johnson's Zytiga and Pfizer/Astellas's Xtandi, both established in metastatic, castration-resistant disease. This battle has additionally encompassed J&J's follow-on drug, Erleada.

Darolutamide, which as an antiandrogen works the same way as Xtandi and Erleada, is also making a play in prostate cancer: the first of two pivotal darolutamide trials, Aramis, could read out shortly.

Darolutamide has 2024 sales projections of $851m, according to sellside consensus compiled by *EvaluatePharma*, giving it an NPV of $2.7bn. Judging by prostate cancer market dynamics this looks rich (*Yes, Pfizer is taking the threats to Xtandi seriously, August 23, 2018*).

The struggles of competing against expected Zytiga generics have been amplified by Zytiga's success in the

academic-run Stampede trial in an early prostate cancer setting – hormone-sensitive disease – in which it is now additionally approved.

As such, with Erleada J&J pursued a brand new early indication, non-metastatic, castration-resistant prostate cancer, securing approval here in February. Pfizer/Astellas followed suit and succeeded in July in extending Xtandi's label to this indication, which is also the focus of darolutamide's Aramis trial.

Aramis recruited 1,502 subjects, and its primary efficacy measure is 72-month metastasis-free survival (MFS) versus placebo. In the same non-metastatic setting Erleada and Xtandi showed median MFS of 40.5 and 36.6 months in the respective Spartan and Prosper trials, versus a 16.2 and 14.7-month placebo response, with no overall survival benefit.

Like Xtandi and Erleada darolutamide is also being studied in hormone-sensitive prostate cancer, but its Arasens trial in this setting will not read out until 2022. It needs to prove itself in Aramis first.

Selected prostate cancer readouts				
Project	**Company**	**Study**	**Trial ID**	**Primary completion**
Non-metastatic, castration-resistant prostate cancer				
Xtandi	Pfizer/Astellas	Prosper	NCT02003924	Completed, approved
Erleada	Johnson & Johnson	Spartan	NCT01946204	Completed, approved
Darolutamide	Bayer/Orion	Aramis	NCT02200614	Sep 2018
Hormone-sensitive prostate cancer				
Xtandi	Pfizer/Astellas	Arches	NCT02677896	Late 2018
Erleada	Johnson & Johnson	Titan	NCT02489318	Nov 2020
Darolutamide	Bayer/Orion	Arasens	NCT02799602	Aug 2022