Evaluate Vantage

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Go or no go? Pandemic looms over FDA timelines

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Approval decisions are due for Jazz, Gilead and Galapagos in July, while Glaxo is preparing for a panel.

The early approval of Ultragenyx's Dojolvi for long-chain fatty acid oxidation disorders yesterday takes the first-to-market approval tally so far in 2020 to 29. That is well above the 18 new arrivals given a greenlight at the halfway point last year. However, as the FDA continues to shift resources and focus on pandemic-specific treatments, approval goals and timelines could well be knocked in the coming months.

The impact of the pandemic is already evident − Nabriva blamed travel restrictions for its CRL last month, with the FDA citing unresolved manufacturing issues at a European facility. The decision on Novartis's new subcutaneous formulation of ofatumumab was also delayed and, though no specific reason was given, the Covid-19 outbreak could well have played a part.

Despite advisory committees going virtual, many have been postponed. A panel meeting to discuss Glaxosmithkline's belantamab mafodotin is, for now, scheduled for July 14.

The anti-BCMA antibody-drug conjugate has produced underwhelming data in relapsed/refractory multiple myeloma, falling short of rival projects. The pivotal Dreamm-2 study yielded an ORR of only 31% including a 3% rate of complete remissions. Bluebird/Bristol's Karmma study of ide-cel yielded a 73% ORR and 31% CR rate in the same setting.

Safety will also be in focus: serious instances of keratopathy, a toxicity involving changes in the eye's corneal epithelium, have been reported.

Another of Glaxo's oncology efforts is up for approval: a PDUFA date for the anti-PD-1 dostarlimab has been set for the second half of the year. The filing was based on the phase I/II Garnet study in women with advanced or recurrent endometrial cancer with microsatellite stable (MSS) or microsatellite instability-high (MSI-H) tumours. The remission rate in MSI-H patients was an impressive 49%.

If approved dostarlimab will be a latecomer to the PD-1 class. Fortunately endometrial cancer is not as competitive as some tumour types: Merck's Keytruda is the only PD-1 with endometrial cancer on its label, but in tumours that are not MSI-H or mismatch repair-deficient, a different population to Glaxo's dostarlimab. However, Keytruda is also approved in MSI-H tumours irrespective of tumour type.

Competition ahead

Gilead and Galapagos's filgotinib is due a decision in rheumatoid arthritis this month. A big question is whether

its label gets a black box warning for thrombosis, similar to that seen with the older Jak inhibitors Xeljanz and Olumiant.

The hope had been that the new generation of Jaks would avoid this; however, Rinvoq, Abbvie’s rival project, received a black box when it was approved for arthritis last year.

Filgotinib looks to have slightly lower efficacy that Rinvoq but a better safety profile, with an incidence of deep vein thrombosis/pulmonary embolism of 0.1% versus 0.4% for Rinvoq, though this cross-trial comparison comes with the normal caveats.

Another company hoping to get a handle on the competition is Jazz, with a decision expected by July 21 for its narcolepsy project JZP-258. The product is a low-sodium follow-on project to Xyrem.

Xyrem is big business for Jazz. Forecasts are set to peak this year at $1.7bn but fall to $339m by 2026 with the entry of generics. The sellside doesn’t seem convinced that JZP-258 can compete with Xyrem's copycats and 2026 forecasts sit at $323m.

The tables below list first-time and supplementary FDA approvals due in July, with consensus forecasts from *EvaluatePharma.*

Notable first-time US approval decisions due in July				
Project	**Company**	**PDUFA date**	**2026e sales by indication ($m)**	**Note**
Camcevi	Foresee Pharmaceuticals	Est July	-	Used 505(b)(2) pathway
E-58425	Esteve	Est July	-	In January FDA adcom voted 13 for and 13 against approval
Vocabria (cabotegravir)	Shionogi/GSK	Est July	-	Cabenuva, the cabotegravir and rilpivirine combo received a CRL in December
Byfavo	Cosmo/ Paion/ Acacia Pharma	Jul 5	319	Additional data submitted earlier in the year caused a delay to June.
Ryanodex	Eagle	Jul 8 (resubmission)	4	-
VP-102	Verrica	Jul 13	310	At the end of June the FDA issued letter over CMC-related requests
Belantamab mafodotin	GSK	Panel meeting Jul 14	1,251	See text. PDUFA due in August
RVL-1201	Osmotica	Jul 16	309	For acquired blepharoptosis, also known as droopy eyelid
Wynzora	MC2 Therapeutics	Jul 20	-	-
JZP-258	Jazz	Jul 21	323	See text
Somapacitan/ NN8640	Novo Nordisk	Q3	318	Once weekly long-acting recombinant growth hormone in adult-onset growth hormone deficiency. Novo has a once-daily growth hormone, norditropin on the market
Dostarlimab	GSK/ Anaptysbio	H2	512	See text
Filgotinib	Gilead/Galapagos	H2	1,255	See text
Fostemsavir	GSK/Bristol Myers Squibb	H2	285	For use in heavily treatment-experienced adults with multidrug-resistant HIV-1 infection
Sources: EvaluatePharma & company releases.				

Supplementary and other notable approval decisions in July			
Product	**Company**	**Indication (clinical trial)**	**Date**
Xiaflex	Endo	Cellulite (Release 1 and 2)	Jul 6
Qutenza	Averitas	Neuropathic pain associated with diabetic peripheral neuropathy	Jul 19
Epidiolex	GW Pharmaceuticals	Tuberous sclerosis (GWPCare6)	Jul 31
Spravato	Johnson & Johnson	Major depressive disorder who have active suicidal ideation with intent	H2
Trelegy Ellipta	GSK	Asthma (Captain)	H2
Tremfya	Johnson & Johnson	Psoriatic arthritis (Discover-1 and -2)	H2
Xolair	Novartis	Nasal polyps (Polyp 1 and 2)	H2
Sources: EvaluatePharma & company releases.			