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Go or no go? Ozanimod and Fintepla await FDA verdicts

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Big approval decisions pending in March include ozanimod in multiple sclerosis, where Bristol-Myers is likely to win a green light, while the safety of Zogenix's Fintepla will be scrutinised.

One of the most valuable US approval decisions due in March sits with the multiple sclerosis project ozanimod, which Bristol-Myers gained through its Celgene acquisition. The S1P modulator is likely to get a green light, but commercial challenges await.

Novartis's rival S1P modulator Gilenya has already lost patent protection, so ozanimod, which has shown similar efficacy in relapsing/remitting patients, will need to compete on safety. Gilenya comes with a requirement for cardiac monitoring and a liver warning, while ozanimod has shown a better side-effect profile on both these issues.

Gilenya aside, ozanimod will also struggle to compete against Roche's Ocrevus, which is expected to become the MS market leader by 2024, with forecast sales of $3bn in the relapsing/remitting setting, according to *EvaluatePharma* consensus. The anti-CD20 MAb has shown impressive efficacy and has a clean label, representing a high bar.

Notable first-time US approval decisions due in March			
Project	**Company**	**PDUFA date**	**2024e sales ($m)**
ITCA 650	Intarcia	Mar 9	-
ET-105	Aucta/Eton	Mar 17 (likely extended)	-
Fintepla	Zogenix	Mar 25	$700m ($261m in Dravet)
Ozanimod	Bristol-Myers Squibb	Mar 25	$966m ($584m in RRMS)
Rizaport/RNG-103	Intelgenx Technologies	Mar 26 (fourth review)	-
E-58425	Esteve	Estimated Mar 31 (adcom tied 13 for and 13 against approval)	-
Rimegepant ODT/Zydis ODT	Biohaven	Q1	$885m (rimegepant franchise)
Travivo	Fabre-Kramer Pharmaceuticals	Q1	-
Sources: EvaluatePharma, company releases			

Zogenix's Fintepla is awaiting a decision in Dravet syndrome, a rare form of childhood epilepsy, but regulators' opinions of safety could be tarred by association. Although no serious cardiovascular issues have been observed with Fintepla its active ingredient is fenfluramine, one half of the fen-phen obesity drug that was withdrawn in 1997 over links with serious heart problems.

Clinically Fintepla has the edge over rival GW Pharma's Epidiolex in Dravet, but the latter has the head start: Epidiolex was approved in both Dravet and Lennox-Gastaut syndrome, another form of childhood epilepsy, back in 2018.

Fintepla is also being studied in Lennox-Gaustat syndrome, but recent results saw it underperform Epidiolex. Evercore ISI analysts expect Zogenix to price Fintepla largely for the smaller Dravet population, reducing the competitive threat to GW.

Elsewhere, a decision on Biohaven's Zydis ODT, a fast-acting formulation of the oral CGRP rimegepant in acute migraine, is expected by the end of March. Allergan's Ubrelvy became the first oral CGRP antagonist to win approval at the end of last year.

Prior setbacks

After a complete response letter in 2017 Intarcia's ITCA 650 is back in front of the regulators. ITCA 650 is a matchstick-sized implant that slowly releases exenatide, the active ingredient in the GLP-1 receptor agonist diabetes drug Bydureon.

If ITCA 650 manages to reach the market the next challenge will be to persuade patients and physicians of the benefits of an implant over injectable GLP-1 options, some of which now offer once-weekly dosing. The implant also cannot claim a cardiovascular benefit, which could be a major drawback in this highly competitive space.

Intelgenx's long and tortuous path to approval first started with Rizaport seven years ago; the migraine project, an oral soluble film formulation of the triptan Maxalt, is undergoing its fourth review. The last CRL in 2019 was due to CMC issues, and before that the company had to perform a bioequivalence study.

Supplementary and other notable approval decisions due in March			
Product	**Company**	**Event type**	**Date**
Opdivo+Yervoy	Bristol-Myers Squibb/Ono	sBLA for 2nd-line hepatocellular cancer (Checkmate-040)	Mar 10
IV Triferic	Rockwell	sNDA for anaemia in chronic kidney disease	Mar 28
Imfinzi	Astrazeneca	sBLA for 1st-line SCLC (Caspian)	Q1
Vesicare	Astellas	sNDA for neurogenic detrusor overactivity in paediatric patients	Estimated Q1

Priority reviews

Lastly, *Vantage* has compiled a list of pending FDA approvals that have been granted priority review. The speed with which the regulator has been pushing this type of application through means that there is a high chance that these verdicts will come early.

Notable projects hoping for speedy decisions include risdiplam, an SMN2 splicing modifier from Roche. The oral agent has shown encouraging efficacy data and a clean safety profile in spinal muscular atrophy and threatens Biogen's Spinraza.

Incyte's pemigatinib, meanwhile, showed impressive survival results at last year's Esmo in an FGFR2-selected population in bile duct cancer. The kinase inhibitor is seeking approval in a tiny population: as a whole the cancer amounts to only 3,000 or so new cases a year worldwide, and FGFR2 drives 10-15% of these.

Upcoming first-time US approval decisions with priority review (to June)				
Product	**Company**	**Indication**	**PDUFA date**	**2024e sales ($m)**
UGN-101 (mitomycin gel)	Urogen	Low-grade upper tract urothelial cancer	Apr 18	82
Selumetinib	Astrazeneca/Merck & Co	Paediatric patients with NF1 plexiform neurofibromas	Q2	35
Risdiplam	PTC/Roche	Spinal muscular atrophy (Firefish, Sunfish)	May 24	809
Pemigatinib	Incyte	Relapsed cholangiocarcinoma with FGFR2 fusions or rearrangements (Fight-202)	May 30	204
C-Dec/ASTX727	Otsuka	Intermediate and high-risk myelodysplastic syndromes & CML (Ascertain)	Estimated June	80
Ocaliva	Intercept	Fibrosis due to Nash (Regenerate)	Jun 26 (adcom Apr 22)	1,855 (1,236 in Nash)
Sources: EvaluatePharma & company releases.				