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Go or no go? A delayed decision on Evrenzo

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March will see big US decisions for Evrenzo and ide-cel, while tanezumab goes in front of an advisory committee.

A three-month delay to a US FDA verdict on Biogen's aducanumab means that March will be decidedly quieter than expected on the approvals front. However, there are two valuable decisions still to come concerning Evrenzo, the anaemia pill from Astrazeneca/Fibrogen, and Bristol/Bluebird's multiple myeloma project ide-cel, both of which carry big sellside forecasts.

The Pdufa date is also approaching for Keytruda's perioperative use in triple-negative breast cancer, though a negative advisory panel makes approval unlikely. And, over a decade since its clinical development started, Pfizer/Lilly's troubled pain project tanezumab will be up for discussion.

Delayed verdict

Astrazeneca/Fibrogen's Evrenzo, which contains the active ingredient roxadustat, has 2026 forecasts of $2.4bn, making the decision on its approvability, due by March 20, the biggest of the month in terms of potential sales. The verdict was supposed to have come at the end of last year, but the FDA requested further clinical data analyses.

Analysts believe that Evrenzo, which is already on the market in Japan and China, will get US backing in dialysis-dependent and independent chronic kidney disease, although the calibre of the label will be important. A black box warning is likely, Leerink analysts believe, possibly encompassing the risk of overcorrecting haemoglobin or more worrying issues including infection, malignancy, or cardiovascular events.

If the label does warn of increased risk of cardiovascular events the impact would likely be modest in dialysis-dependent patients, Leerink states. In this group Evrenzo is intended to replace erythropoiesis-stimulating agents (ESAs), which already have a cardiovascular warning. That said, if the safety of Evrenzo and ESAs is considered similar, doctors could favour the older, cheaper drugs.

In non-dialysis-dependent patients a cardiovascular black box would be more of a problem. Less than 15% of these patients receive ESAs precisely because of this risk, so use of Evrenzo would be limited too.

Competition

The second most potentially valuable decision will be that for Bristol Myers Squibb's and Bluebird's BCMA-targeting Car-T project ide-cel in late-line multiple myeloma. The filing was based on the phase II Karmma

study, which showed an 82% overall remission rate at the highest dose tested.

Glaxosmithkline's Blenrep became the first anti-BCMA therapy approved for relapsed or refractory multiple myeloma last year, despite underwhelming efficacy and severe ocular toxicity. Blenrep, an antibody-drug conjugate, can only be used in patients who have received at least four prior therapies, and approval came with a black box warning and requirement for a REMS programme.

Ide-cel's real competition could come from J&J and Legend Biotech's cilta-cel, another BCMA-directed Car-T therapy whose rolling submission started at the end of last year. In terms of efficacy cilta-cel looks unbeatable, having shown a 97% overall remission rate, though neurotoxicity has been an issue.

Safety concerns

After 13 years and 39 clinical trials Pfizer and Lilly's pain project tanezumab is up before an FDA panel next month as the companies seek approval of a 2.5mg dose in moderate to severe osteoarthritis.

Safety will be big on the agenda: the anti-nerve growth factor's past has been blighted by incidences of rapidly progressive osteoarthritis that led to a partial clinical hold. Dosing in studies had to be lowered, leading to lower efficacy *(New tanezumab pain for Pfizer and Lilly, October 24, 2018).*

The balancing act for regulators will be whether doctors desperate for non-opioid options for pain relief can overcome their concerns over toxicity. If tanezumab does get approved a boxed warning looks likely.

The result of the panel will also have read across to Regeneron's similarly-acting fasinumab. Data from that project's long-term phase III safety study are due in the first half of this year.

The tables below list first-time and supplementary US approvals and advisory meetings due, with consensus forecasts from *EvaluatePharma*.

Notable first-time US approval decisions due in March				
Project	**Company**	**PDUFA date**	**2026e sales by indication ($m)**	**Note**
KP145	Kempharm/ Aquestive	Mar 2	-	ADHD treatment, prodrug of Ritalin
Evrenzo (roxadustat)	Astrazeneca/Fibrogen/ Astellas	Mar 20	2,423	Delayed from December over clinical data analysis issues
Ide-cel (idecabtagene vicleucel)	Bristol Myers Squibb/ Bluebird Bio	Mar 27	1,336	Anti-BCMA Car-T for multiple myeloma patients who have received at least three prior therapies, based on Ph2 Karmma study
Dasiglucagon HypoPal Rescue Pen	Zealand Pharma	Mar 27	268	For treatment of severe hypoglycaemia in people with diabetes
Mirabegron oral suspension	Astellas	Mar 28	589*	Treatment of neurogenic detrusor overactivity in patients aged three years and older
Fotivda	Aveo	Mar 31 (resubmission)	155	2013 US complete response letter, additional clinical study needed; company ran Tivo-3
Ponesimod	J&J/Idorsia	Q1	-	J&J gained the project, for relapsing MS, through its acquisition of Actelion
Dostarlimab	Glaxosmithkline	H1	446	Had been expected by the end of 2020 but there was a manufacturing inspection delay owing to Covid-19
Rolontis	Spectrum	No new date given yet	344	Action deferred in October 2020
DaxibotulinumtoxinA	Revance	No new date given yet	632	Action deferred in November 2020
**Includes sales for tablet version (Myrbetriq). Source: EvaluatePharma & company releases.*				

Advisory committee meetings in March				
Project	**Company**	**Adcom date**	**2026e sales by indication ($m)**	**Note**
Tanezumab	Lilly/Pfizer	Mar 24-25	111	Filed for moderate to severe osteoarthritis in adults for whom other analgesics are ineffective/inappropriate; Pdufa had been set for Dec 2020 but FDA scheduled adcom
Source: EvaluatePharma, FDA ad com calendar				

Supplementary and other notable approval decisions in March			
Product	**Company**	**Indication (clinical trial)**	**Date**
Yescarta	Gilead	Relapsed or refractory follicular lymphoma and marginal zone lymphoma after two or more lines of systemic therapy (Zuma-5)	Mar 5
Arcalyst (rilonacept)	Kiniksa	Recurrent pericarditis (Rhapsody)	Mar 21
Exparel	Pacira	Postsurgical analgesia in children aged six and over (Play)	Mar 22
Mybetriq (mirabegron tablets)	Astellas	Treatment of neurogenic detrusor overactivity in patients aged three and over (NCT02751931)	Mar 28
Keytruda	Merck & Co	TNBC chemo combo as neoadjuvant, also single agent as adjuvant therapy (Keynote-522)	Mar 29 (negative adcom in Feb)
Xolair	Roche	Self-administration option across all approved US indications	Q1
Source: EvaluatePharma & company releases.			