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Go or no go? Roche, Lilly and Teva await big regulatory readouts

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September promises at least eight notable US marketing decisions, including a crucial lung cancer ruling for Roche's Tecentriq and verdicts on Lilly and Teva's competing migraine therapies.

September looks set to be a busy month for the influential US drug regulator, with several reviews of novel mechanisms slated to wrap up. Among the most notable, Lilly and Teva will be hoping to follow Amgen onto the market with their anti-CGRP migraine therapies, setting the scene for a fierce marketing battle.

Lung cancer could also see some new arrivals: Roche hopes to be given a green light to start marketing Tecentriq in the lucrative first-line non-small cell lung cancer space, while Pfizer is poised to launch its offensive against Astrazeneca's grip on the market for EGFR-targeted drugs. Among the smaller companies awaiting news, Insmed and Antares are expecting pivotal decisions, due towards the end of the month.

Notable September approval decisions				
Product	**Company**	**PDUFA date**	**Product NPV ($bn)**	**Market cap ($bn)**
Tecentriq	Roche	5 Sep (sNDA)	16.38	211.4
Emgality	Lilly	End Sep (date unknown)	3.14	112.9
Fremanezumab	Teva	14 Sep	2.38	23.9
Damoctocog Alfa Pegol	Bayer	Sep (Evaluate estimate)	1.35	89.9
Dacomitinib	Pfizer	Sep (date unknown)	1.23	243.7
Moxetumomab pasudotox	AstraZeneca	Third quarter (date unknown)	0.93	97.9
Alis	Insmed	28 Sep	0.68	1.7
Xyosted	Antares Pharma	28 Sep	0.05	0.6
Source: EvaluatePharma.				

A three-month manufacturing delay for Teva's asset means that its FDA decision deadline will come the same month as Lilly's. Both are striving to follow Amgen and Novartis's Aimovig, which arrived in the US in May. All are anti-CGRP antibodies: prophylactic, injected treatments for patients with very severe migraines, a class that has exhibited broadly similar effectiveness. As such, neither will want to delay reaching the lucrative US market. While the Lilly decision is not seen as particularly risky, Teva's manufacturing issues add an element of danger.

Roche could kick off September's PDUFA decisions, however: the Swiss pharma giant is waiting to find out whether its shot at a first-line US lung cancer label has hit the mark. Use in this specific indication accounts for the vast majority of the drug's forecast sales, and will allow it to start competing with Merck & Co. The specific label sought is first-line non-squamous NSCLC, in combination with Avastin, and given the positive readout of Impower-150 and the FDA's keenness to greenlight anti-PD-(L)1 agents it would be surprising for the agency not to approve it. For more details on this decision see our detailed article: *US agency to rule on Tecentriq's most important use, August 15, 2018*.

Also in lung cancer, Pfizer hopes to challenge Astrazeneca's grip on the EGFR-targeting space with dacomitinib, and data generated in a first-line setting look strong enough for approval. The tyrosine kinase inhibitor easily beat Iressa in the Archer 1050 trial, reducing the risk of disease progression or death by 41% and improving survival by over seven months in untreated lung cancer patients. Astra's newer pill Tagrisso is the real target, however, and is already approved front line; the Flaura study, also against Iressa, found a 54% reduction in the risk of progression or death though overall survival data has yet to emerge.

Astrazeneca has its own decision pending: the UK drug maker has guided to a third-quarter decision for its antibody-drug conjugate moxetumomab pasudotox, which has been filed as a last resort treatment for hairy cell leukaemia. The decision represents a rare regulatory test of the ADC approach – despite much promise, few projects have managed to advance to this stage. Substantial unmet need in this rare blood cancer bodes well for approval. At Asco this year Astra presented results from the supportive pivotal '1053' study, which found that 30% of patients achieved a durable complete response, meeting the primary endpoint.

Elsewhere, Bayer should learn whether its long-acting recombinant human factor VIII, or damoctocog alfa pegol, has passed muster as treatment for haemophilia A. The Protect VIII trial showed that the clotting agent offered patients protection from bleeds when used prophylactically once every seven days, five days, or twice per week. The project is the German conglomerate's attempt to stay in the blood factor game, where its former blockbuster Kogenate has been overtaken by long-acting therapies from rivals in the last few years.

Among the smaller players, Insmed is likely to receive a green light for Alis – an inhaled form of an aminoglycoside antibiotic to treat non-tuberculous mycobacterial (NTM) disease caused by *Mycobacterium avium* complex – but the approval could be tinged with disappointment. In August an advisory committee voted 21-2 in favour of the product in refractory NTM patients, but 2-12 against its use in a front-line setting.

This will drastically limit the addressable patient population, assuming that the FDA follows this advice.

Concerns about whether the surrogate primary used is a reliable indicator of efficacy could also prompt the regulator to demand further trials, though the unmet need in the refractory population means that there is a good chance of this being a post-marketing requirement.

Finally, tiny Antares awaits the outcome of the FDA's second review of Xyosted, a once-weekly testosterone auto-injector that the company hopes will prove more popular than intramuscular injections and topical gels. The agency issued a complete response letter in October 2017, citing concerns about the potential for the product to cause blood pressure to rise, and occurrences of depression and suicidality.

The fact that a new PDUFA date was issued quickly, and that the agency did not convene an advisory committee to review the data, could be viewed as good omens for approval, but the controversial history of testosterone replacement means that the risk of the FDA remaining unsatisfied cannot be ruled out.

Supplementary approvals and others estimated for September		
Product	**Company**	**Details**
Filgrastim	Adello Biologics	Neupogen biosimilar filed in Sep 2017, BSUFA date unclear.
Fycompa	Eisai	Decision due by Sep 28 on sNDA in partial-onset or primary generalized tonic-clonic seizures in children.
Grastofil	Apotex	Neupogen biosimilar filed in 2015, BSUFA date unclear.
Nucala	Glaxosmithkline	Decision due by Sep 7 on sNDA in eosinophilic COPD, but approval unlikely after negative adcom vote.
Symjepi	Adamis	PDUFA date of Sep 27 for a low-dose version of already approved higher dose.