Evaluate Vantage

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Another strong year for novel drug approvals is in the making

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Few signs of a tightening regulatory climate can be found in approval numbers for 2020 – but some big decisions are still pending.

A handful of unexpected knockbacks by the FDA this year had biopharma followers wondering whether the US regulator had sharpened its teeth. The raw numbers do not seem to support this idea, with 45 novel agents having received a green light so far in 2020, only four fewer than last year's total.

A further 21 hopefuls are awaiting decisions before year-end, according to *Evaluate Vantage*'s calculations; approvals all round would set something of a record. Still, the outcomes of high-profile applications are more likely to be considered barometers of the regulatory climate, rather than whatever the final tally comes in at – and the FDA has plenty of big calls still to make.

For example, Novartis will hear on the approval of its lipid-lowering agent, inclisiran, towards the end of the year. The group paid $9.7bn for the project's developer, The Medicines Company, just under 12 months ago. Given that another expensive buyout continues to cause headaches – the scandal-prone Avexis that Novartis bought for $8.7bn – the Swiss firm will not want to give investors any more reasons to question its M&A nous.

Impressive LDL cholesterol lowering seems to give inclisiran a good shot at approval; however, the RNAi technology by which the agent works is very novel. With a cardiovascular outcomes study, Orion-4, not due to read out until 2024, the FDA could choose to take a cautious stance here.

Roxadustat is another big project on which a decision should emerge towards the end of the year. The novel anaemia therapy is the first of its type to cross the FDA's path, but no advisory committee has been called; this has been read as a good sign by supporters of the developers, Astrazeneca and Fibrogen.

However, the project has not avoided controversy, so a green light is far from assured.

On the card: big US approval decisions still pending this year			
Product	**Company**	**Decision date**	**2026e US sales**
Inclisiran	Novartis	Late 2020	$1.3bn
Eysuvis	Kala Pharmaceuticals	October 30	$1.1bn
Roxadustat	Astrazeneca/Fibrogen	December 20	$875m
Liso-cel	Bristol Myers Squibb	November 16	$860m
DaxibotulinumtoxinA	Revance	November 25	$654m
Source: EvaluatePharma.			

Kala looks like a safer bet with its dry-eye project, Eysuvis, but it will not escape the notice of the FDA that the company had to run three phase III trials before getting the result it wanted (*Persistence pays off for Kala, March 10, 2020*).

Bristol Myers Squibb and former Celgene shareholders also have a nervous few months ahead. Approval of liso-cel by December 31 must occur for contingent payments pledged at the time of the Celgene takeout to be made. Another component of the contingent value right, ide-cel, received a refusal to file letter earlier this year; its new PDUFA date of March 27, 2021, is just four days before the CVR deadline.

Regulatory risk exists with all products, of course, no matter how easy the path to market appears to be. And of course whether any of these agents manage to meet sales forecasts is a separate but equally important question; sellside consensus numbers are frequently considered ambitious.

The rate of complete response letters will be watched carefully in the coming weeks. A previous analysis by *Evaluate Vantage* found little evidence of an uptick in these regulatory red lights; a string of high-profile knockbacks, including rejections for Gilead and Galapagos's filgotinib and Biomarin's valrox gene therapy, had prompted questions about a tightening in the regulatory climate (*Has 2020 been a big year for regulatory knockbacks?, September 17, 2020*).

It is improbable that all of the 21 projects up for review by year end will pass muster. It is also unlikely that year's approval tally of novel agents will drop dramatically. The outcome of applications detailed above will be of real interest, however – because should the FDA really become less friendly, biopharma would really have something to worry about.

Annual FDA novel drug approvals