Evaluate Vantage

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FDA keeps the faith in surrogate endpoints

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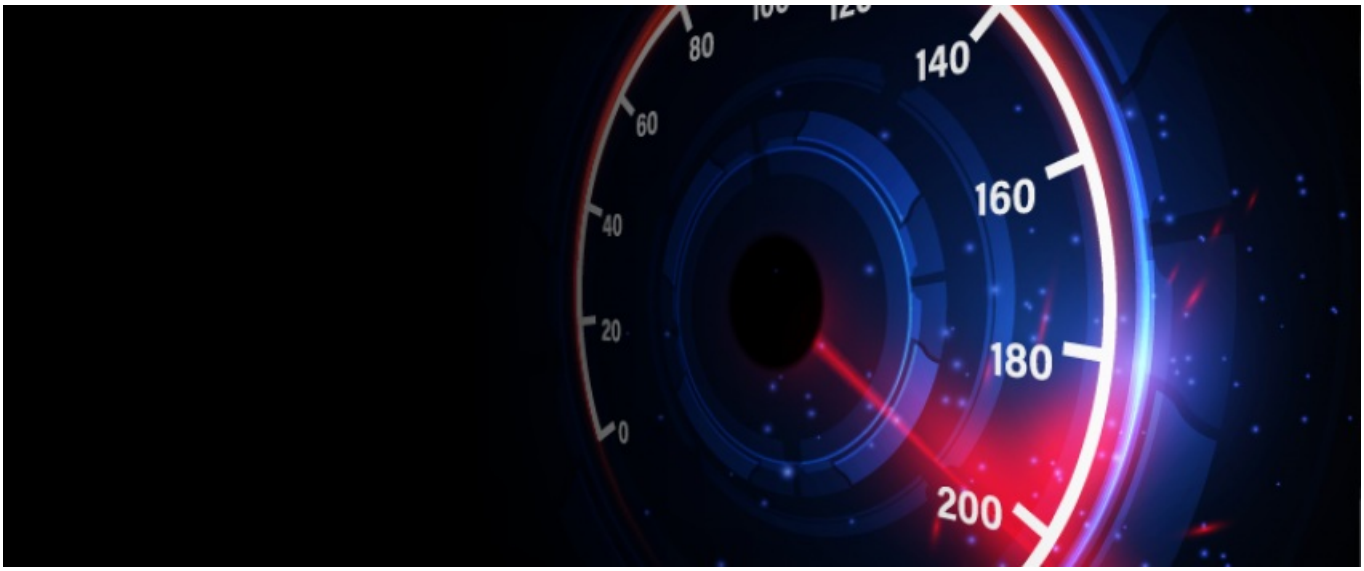
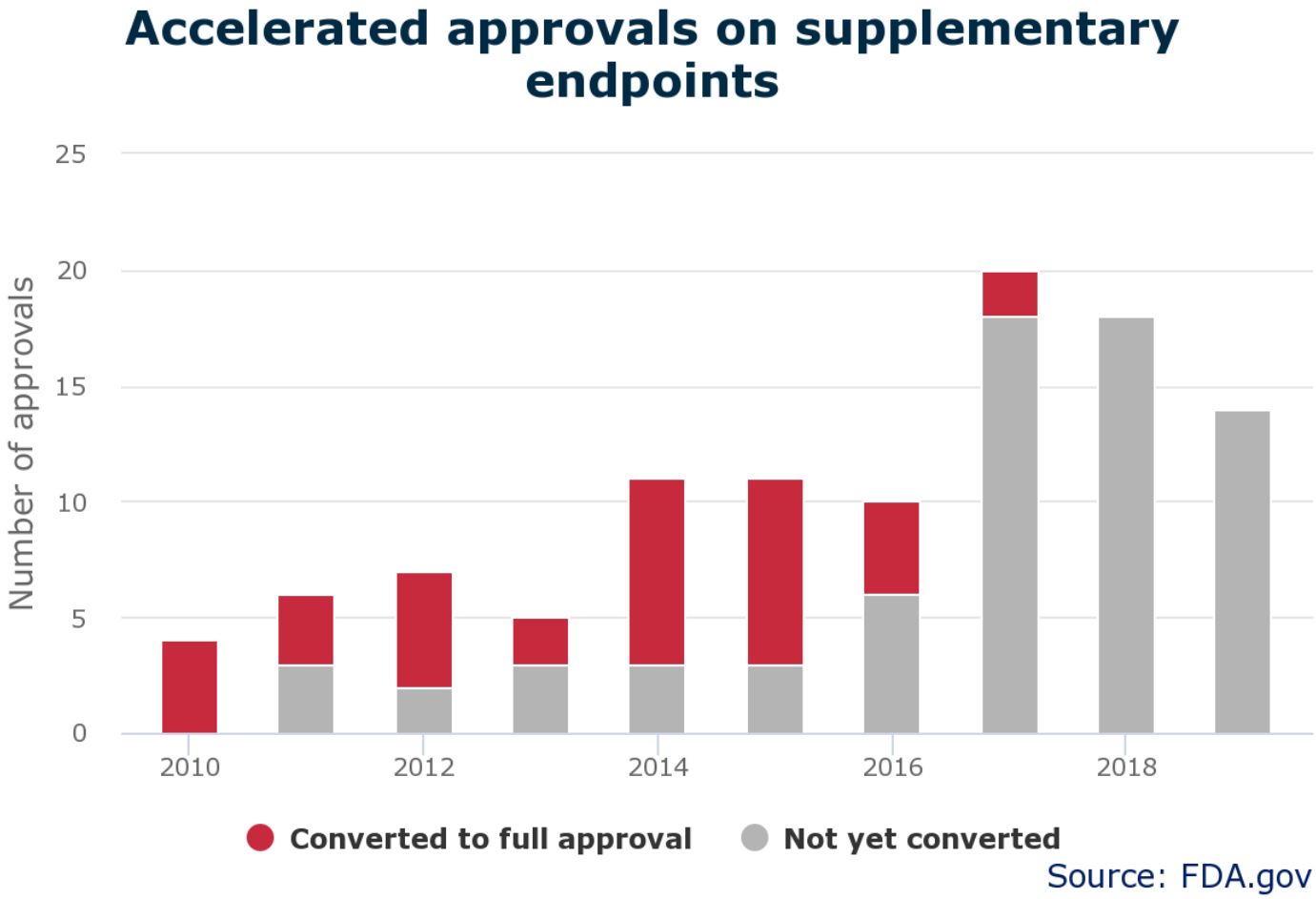


The US regulator granted 14 accelerated approvals in 2019, fewer than in the previous two years, and the sector remains slow at conversions.

The introduction of US breakthrough designation in 2013 marked a big jump in accelerated approvals; the latest data released by the FDA show that 14 happened last year. This is a dip on the previous two years, though it seems unlikely that biopharma companies are cooling on this fast-to-market strategy.

This regulatory pathway allows for drugs to be approved quickly based on trials relying on surrogate endpoints, rather than directly measuring clinical benefit. The ultimate aim is to get important new therapies to patients quickly, and this appears to be working, although critics claim that these products' real effectiveness is not established soon enough.

The data below, which were released by the FDA, include first time and supplementary approvals. Cancer drugs dominate, particularly in more recent years. Keytruda, for example, has received 14 approvals based on surrogate endpoints, according to the regulator's list, only four of which – those in lung, head and neck and melanoma settings – have converted to full approval.



As would be expected, the chart above shows that few recent arrivals have converted to full approval. The real concern lies with products that have been on the market for some time, whose approvals are still backed by insufficient evidence.

True, in some cases the science has probably moved on, and a particular drug is no longer used. This is not always the case, however, and some have raised significant concerns. The regulator has come under pressure to remove Amag's preterm birth treatment Makena from the market, for example – this was granted accelerated approval back in 2011.

It is also notable that Keytruda failed in liver and gastric cancer trials last year, though the FDA has been silent on whether Merck & Co should have these accelerated approvals rescinded. Withdrawals do happen – Lilly pulled Lartruvo only last year after a confirmatory trial failed to show a benefit in patients with soft tissue sarcoma – but these seem to be the exception rather than the rule.

Foot dragging?

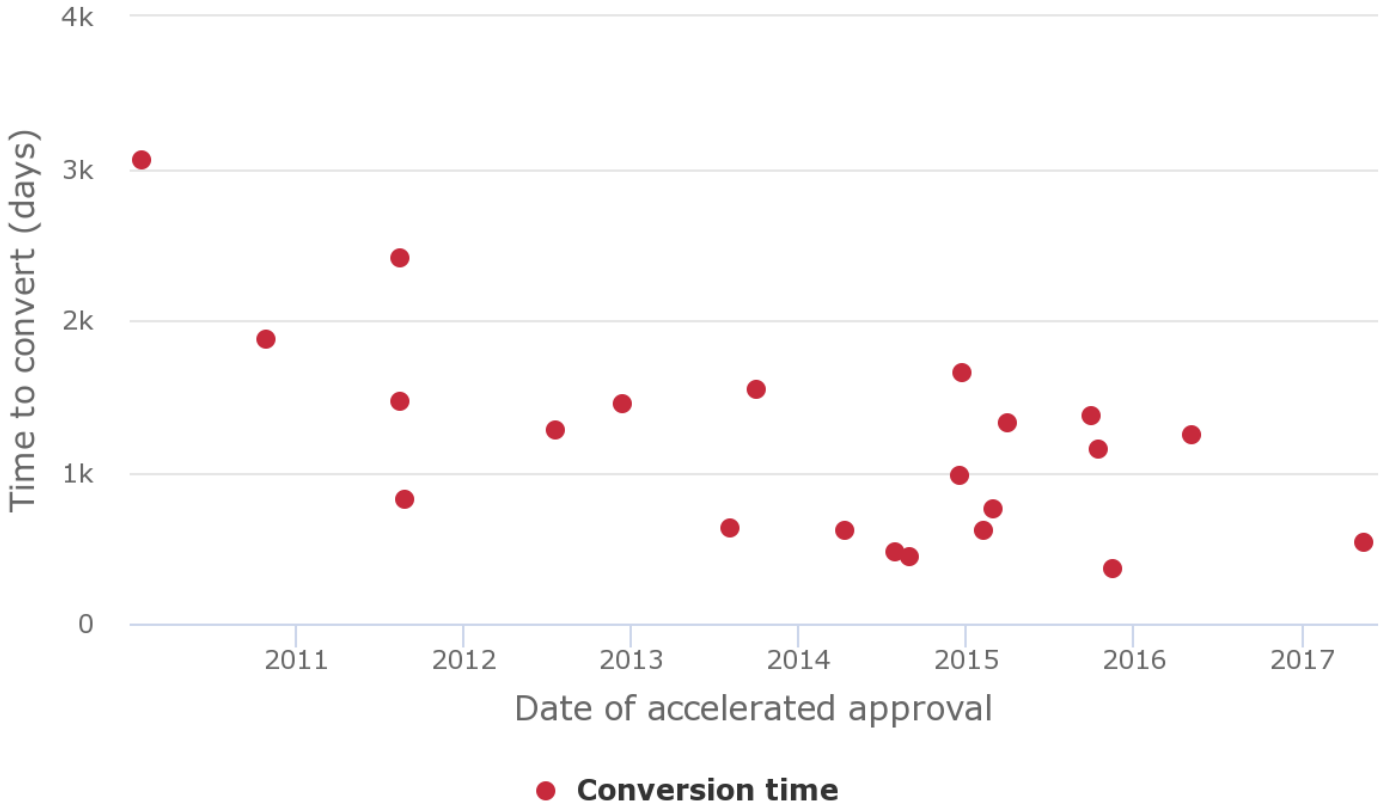
Little urgency can be detected on industry's part to convert these licenses to full approval, the graph below suggests, although there has perhaps been some improvement from a decade ago.

On the far top left sits Tykerb; Glaxosmithkline, which then owned it, took more than eight years to convert a 2010 accelerated approval in post-menopausal breast cancer patients to a full licence. Not that this mattered much, as mediocre effectiveness had already sealed this kinase inhibitor's fate.

Most of the elderly accelerated approvals that have not yet converted are now commercially insignificant, though many are still actively marketed: the enzyme-replacement therapy Elaprase that Takeda acquired from Shire, for example, or Lundbeck's Northera. US sales of these products are forecast to reach $364m and $177m respectively this year.

The benefit to developers in foot-dragging is plain to see, while apparently patients and physicians must wait for evidence that their medicine has real value. Criticism of the FDA for not chasing up confirmatory studies with sufficient vigour looks like a fair rebuke in some cases.

Conversion times for accelerated approvals



Source: FDA.gov