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Is biopharma getting better at accelerated approval conversions?

Amy Brown

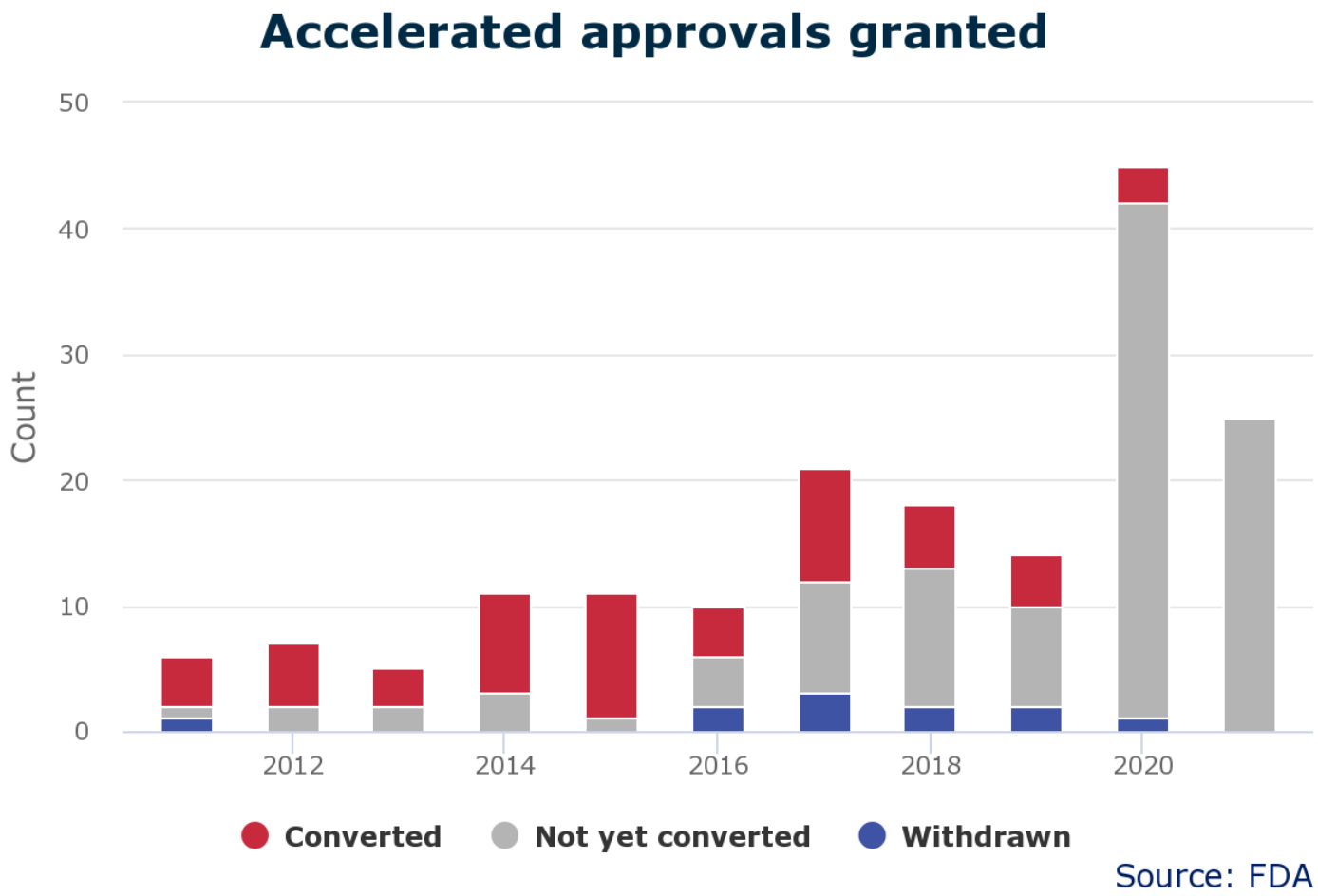
Amid ongoing pressure to reform the FDA's fast-track pathway, signs emerge that the criticism is being heard.

The FDA's accelerated approval pathway has been attracting mounting criticism, but change is on the way. Bills seeking to reform the process have been introduced as part of this year's reauthorisation of the biopharma user fee bill, while the agency's new commissioner, Robert Califf, has made no secret of his desire to rectify weaknesses.

The latest stats on this area suggest that recent criticism as well as longer-standing admonitions have not fallen on deaf ears. More CDER accelerated approvals were converted to full approval last year than in any other, and a trend for faster conversions seems to be emerging.

It is also notable that the conversions that happened over the past five and 10 years took a median of 3.1 years. This is much quicker than the five-year "expiration date" that has been proposed as part of one of the reform-seeking bills.

It could be argued that even three years is too long, although some drug trials will always take longer than others. Perhaps a time limit on accelerated approval is too blunt an instrument; still, it might discourage some of the more extreme cases of foot-dragging by sponsors in terms of running confirmatory trials.



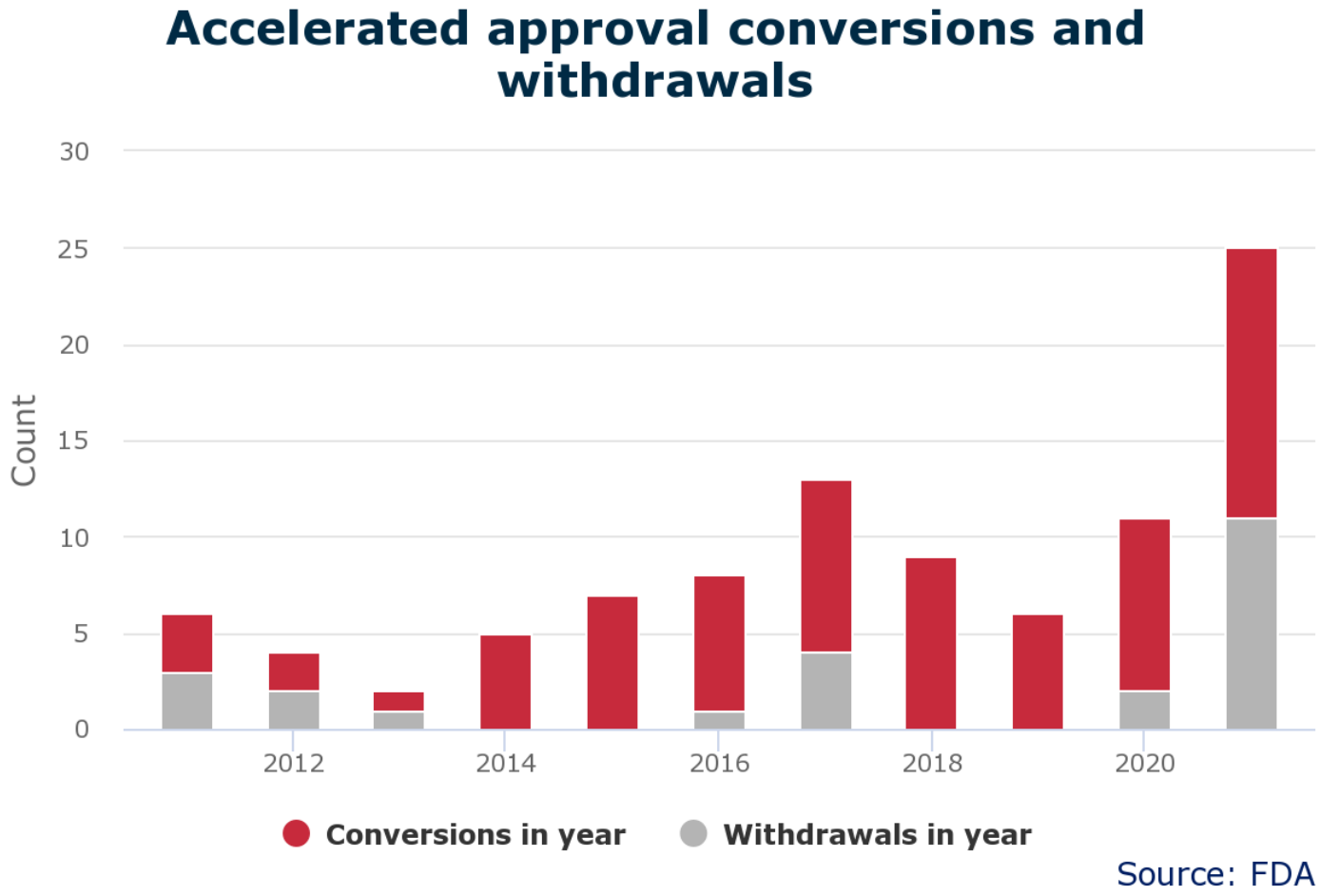
It is the more egregious examples that have given this pathway a bad name, of course, and these are in the minority.

Aduhelm and Exondys 51 are frequently held up as cases in point. Biogen will start screening patients for the confirmatory study of the Alzheimer's drug in May, almost a year after winning accelerated approval, while the confirmatory trial of Sarepta's Duchenne muscular dystrophy treatment is unlikely to yield data until 2026, 10 years after this drug's green light.

Recent moves from the FDA suggest that the regulator's patience is wearing thin. The agency seems to have decided that developers of PI3K inhibitors have been taking too long to prove their worth, for example, last month denying MEI's zandelisib access to the accelerated approval pathway.

Another sign of a tightening up was last year's panel looking at "dangling" accelerated approvals for various checkpoint inhibitors.

It is worth noting that 2020 was boosted by 16 accelerated applications by Merck & Co for alternative Keytruda dosing regimens. Even removing these, the 29 accelerated approvals represents a record high.



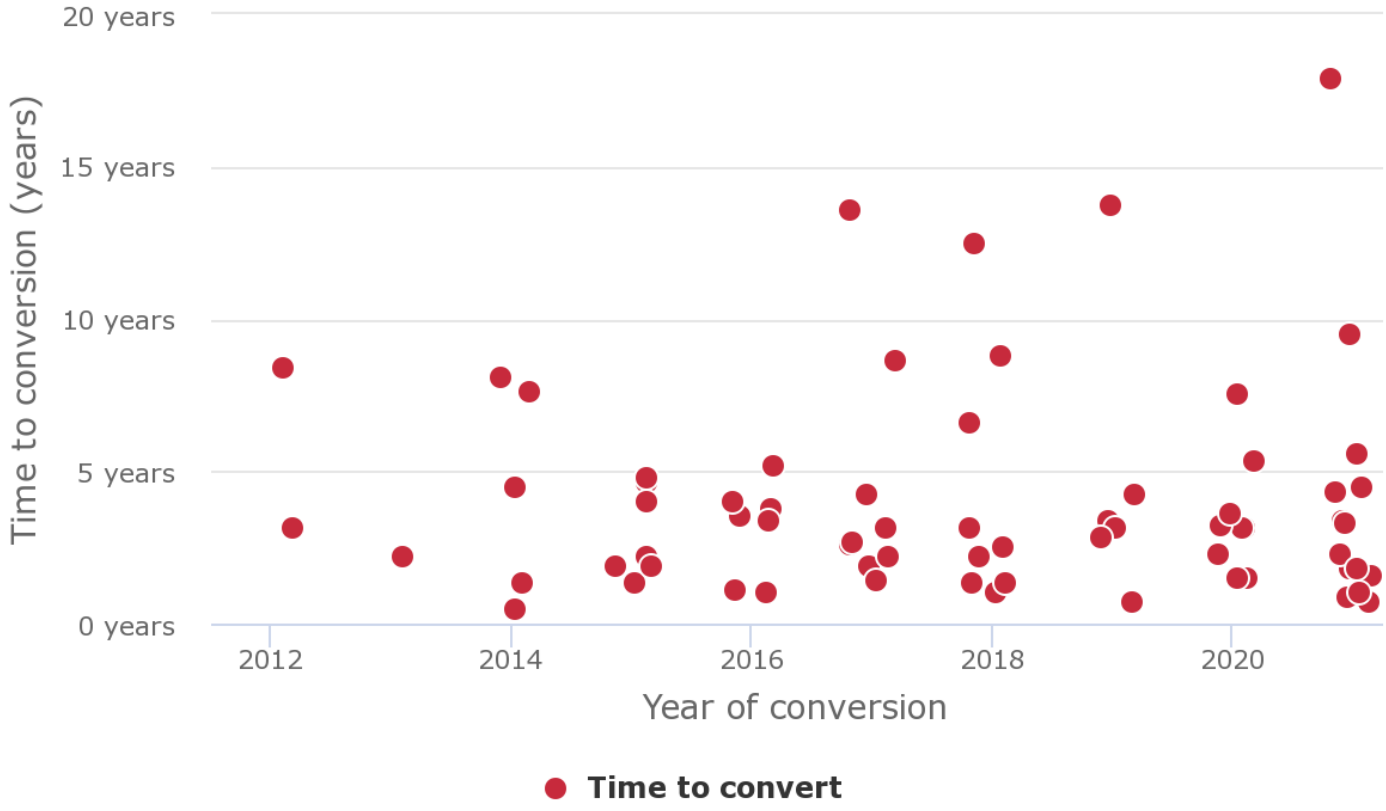
The chart above shows that a record number of conversions happened last year. This analysis, which considers CDER approvals only, is certainly encouraging, although a more sobering statistic is the number of drugs whose efficacy still needs confirming.

Of the 167 accelerated approvals granted in the past 10 years almost two thirds remain “dangling”. Meanwhile, the jump in withdrawals last year was largely a result of the FDA’s checkpoint inhibitor panel, which ultimately led to six of 2021’s exits.

The final chart here suggests that conversions are getting faster. Each dot is a conversion, showing the year full approval was granted and the time that this took to achieve. More recent years do seem to contain a higher density of faster approvals.

Pressure to improve on these statistics is only going to grow in the coming years, particularly if the use of the pathway continues to expand. Few would argue against more concerted efforts to purge the bad apples.

Time to convert



Source: FDA