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Stock Watch: Class Of 2016 FDA Approvals

Seller Beware: Ignore Your Market At Your Peril

by Andy Smith

Revenues are still elusive for a surprising number of the novel drugs approved by the FDA five years ago. Emergent safety issues and confirmatory clinical trial failures were less common than lack of competitiveness as the main reason for revenue weakness.

In 2017, while working in a drug pricing and commercialization consultancy, I prepared a slide analyzing the 2016 sales of the 35 novel drugs that were approved in 2011. I have just repeated the exercise for the drugs approved in 2016. Five years may not always be enough to reach blockbuster status, but among the 22 drugs that were approved by the US FDA in 2016, five blockbusters had stretched away from eight with undisclosed or absent sales by 2020. And then there were those in between.

The Benefit Of Five-Year Hindsight

To demonstrate to smaller biotechnology companies the importance of conducting market research with payers, the slide I constructed in 2017 showed that 19% of drugs approved by the US FDA in 2011 had annual sales of less than $20m five years after approval. Those products were abject commercial failures. As my argument went at the time, it would have been better to find out they were likely to yield permanent losses before the significant investments in Phase III and launch activities were made. In Europe, the situation was worse, with 46% of drugs approved there in 2011 having sales below $20m in 2016. A 2001 *Nature Biotechnology* *article* described estimates of the value of biotechnology products as being "all too often clearly unrealistic" which fits with my experience as an investor where most CEOs suggested that their products could be blockbusters (i.e., generating annual sales of $1bn or more).

In both time periods, the FDA approved imaging agents, and two were excluded from the latest analysis, leaving 20 drugs under the spotlight.

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In 2020, five products had reached blockbuster status five years after their FDA approvals and it is probably no surprise that they all came from big pharmaceutical or big biotechnology companies. *Roche Holding AG*'s PD-L1 monoclonal antibody Tecentriq (atezolizumab) was first approved in 2016 for urothelial cancer. Subsequent approvals in other cancer indications including non-small cell lung cancer have ensured that with 2020 sales of CHF2.7bn (about $3.0bn), Tecentriq topped the 2020 revenue list of the class of 2016 FDA-approved drugs. Also unsurprisingly on the list of 2020 blockbusters approved in 2016 was *Biogen, Inc.*'s Spinraza (nusinersen) for spinal muscular atrophy, which generated $2.1bn in 2020. At a launch price of $750,000 for the first treatment year and $350,000 thereafter, Spinraza's status as a rare disease blockbuster was virtually ensured despite competition from *Novartis AG* and Roche and a cost-effectiveness critique from ICER. The other three 2020 blockbusters from the class of 2016 FDA approvals were *Eli Lilly and Company*'s* Taltz (ixekizumab), an IL-17A monoclonal antibody for the treatment of psoriasis, *Gilead Sciences, Inc.*'s direct-acting HCV combination antiviral Epclusa (sofosbuvir/velpatasvir) and hematological cancer drug Venclexta (venetoclax), marketed by *AbbVie Inc.* and Roche. Indeed, the success of Gilead's sofosbuvir-containing HCV franchise (in the patent courts and the markets) was responsible for the absence of reported revenues for *Merck & Co., Inc.*'s HCV antiviral Zepatier (elbasvir/grazoprevir) in 2020.

Lemons And Plums

We used to have a saying in venture capital that the lemons went bad before the plums ripened. This implies that if investments were going to fail, they usually did so fairly quickly, and long before the good investments matured and were realized. The same appears true of eight of the drugs approved by the FDA in 2016. Zinbryta (daclizumab), for example, an anti-CD25 monoclonal antibody for the treatment of multiple sclerosis, was approved in 2016 but withdrawn in 2018 by Biogen and AbbVie (which acquired Zinbryta's developer *Facet Biotech** for $450m) after reports of serious autoimmune encephalitis. Lilly's Lartruvo (olaratumab) for soft tissue sarcoma was withdrawn in 2019 after a confirmatory trial – required as part of the accelerated approval – failed to demonstrate a survival benefit. (Also see "*A Successful Failure? Lartruvo's Speedy Withdrawal Sets New Bar For Accelerated Approval Drugs*" - Pink Sheet, 25 Apr, 2019.)

But post-launch safety and efficacy-related withdrawals were comparatively rare: more commonly, products appear to have failed in a competitive sense. With manufacturers failing to

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report 2020 sales for six of the class of 2016 approvals, it looks like this 30% are unlikely to have generated meaningful revenues. While most of these products came from pharmaceutical companies, biotechnology companies were often involved. *Sanofi*'s GLP-1 receptor agonist Adlyxin (lixisenatide) was licensed from *Zealand Pharma A/S*. Sanofi last recorded Adlyxin sales in 2018, when they amounted to $66m. Adlyxin's obscurity in Sanofi's more recent annual reports is likely to be a reflection of its uncompetitive profile. A similar reason for the absence of revenue reporting could be leveled at *Pfizer Inc.*'s* Eucrisa (crisaborole) for psoriasis, which came with the $5.2bn acquisition of *Anacor Pharmaceuticals, Inc.* Eucrisa has not been completely absent from Pfizer's financial statements, however: it has been responsible for $5.2bn in asset impairment charges since 2019. Also in the group of 2020 revenue no-shows were Merck's Zinplava (bezlotoxumab) for the treatment of Clostridioides difficile infections, Anthim (obiltoxaximab), an anti-anthrax toxin antibody from the private company *Elusys Therapeutics, Inc.*, and Cinqair (reslizumab), *Teva Pharmaceutical Industries Ltd.*'s anti-IL-5 antibody for the treatment of severe asthma, where revenues are buried somewhere in its 'other products' line.

10 Drug Launch Flops Of The Decade

By Jessica Merrill

08 Jan 2020
The view from 2020: *Scrip* looks back over the last decade at the drug launches that defied expectations – for the worse.

Read the full article here

The Long And Winding Tail

In the 2017 analysis, the $20m in annual sales was an arbitrary cut-off that fitted the data for that year. Companies may have avoided reporting sales below or above $20m in 2020 to limit any stigma. In any year, blockbuster status provides a firm success boundary but I did take a closer look at those seven products approved by the FDA in 2016 that reported sales in 2020 of less than $1bn to determine whether these were also successes. These range from *Clovis Oncology, Inc.*'s PARP inhibitor Rubraca (rucaparib) with 2020 sales of $165m, to *Sarepta Therapeutics, Inc.*'s Exondys 51 (eteplirsen) for Duchenne muscular dystrophy (DMD) with 2020 sales of about $450m; none had sales of more than $500m. Sarepta, like Biogen with Spinraza, has exploited the rare disease card with a $300,000 per annum price. Sarepta's $456m in 2020 revenue also included its second DMD product Vyondys 53 (golodirsen), which was launched in 2020 and priced at parity to Exondys 51. Most of the products with sub-$500m 2020 revenues in the class of 2016 FDA approvals do not have the rare disease pricing advantage of Spinraza and Exondys 51. *Intercept Pharmaceuticals, Inc.*'s Ocaliva (obeticholic acid) came close, however, with a launch price of $69,350 per annum when it was approved for the treatment of primary biliary cholangitis in 2016. Ocaliva generated $313m in 2020, but Intercept's recent failure to expand its indications to NASH, and the FDA's more recent safety warning on its use in cirrhosis patients, may now crimp growth, outside of price increases. (Also see "*Intercept Drug's Market Standing In PBC Undermined By Safety Woes*" - Scrip, 27 May, 2021.)

For four of the seven companies (Clovis, Sarepta, Intercept and *ACADIA Pharmaceuticals Inc.*) whose products were approved by the FDA in 2016 and which reported sales of less than $500m in 2020, the approvals were their first drugs to reach the market. Two products – *Jazz Pharmaceuticals plc*'s Defitelio (defibrotide) and *UCB S.A.*'s Briviact (brivaracetam) – joined bigger franchises, while Xiidra (lifitegrast) has since changed hands from *Shire Pharmaceuticals Group PLC* (acquired by *Takeda Pharmaceutical Co. Ltd.*) to Novartis. The four companies that won their first approval in 2016 remain loss-making despite achieving annual sales of $100m or more. It is likely that many of the risky preclinical companies that have come to the market in recent years are unrealistically valuing their franchises. Should any of their products gain FDA approval, many will continue in the footsteps of this subset of four from the class of 2016 and continue to make losses beyond the investment horizons of most investors.

*Andy's pensions hold Pfizer and Lilly and he managed a fund that held Facet prior to its acquisition in 2010.

Andy Smith gives an analyst and investor's view on life science companies. He joined the independent research house Equity Development in October 2019 having previously been an analyst at Edison group and a Senior Principal in ICON PLC's Commercialization, Pricing and Market Access consulting practice. Smith has been the lead fund manager for four life science–specific funds, including 3i Bioscience, International Biotechnology and the AXA Framlington Biotech Fund, and was chief investment officer at Mannbio Invest. He was awarded the techMark Technology Fund Manager of the year for 2007 and was a global product manager at SmithKline Beecham Pharmaceuticals until 2000.