The Big Read US companies

The looming ‘patent cliff’ facing Big Pharma

When blockbuster drugs lose IP protections it can wipe out billions of dollars in revenue for companies

Hannah Kuchler in London and **Patrick Temple-West** in New York

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Every year, thousands of patients sit in doctors’ offices with needles in their arms receiving a dose of a wonder drug called Keytruda. The cancer medicine is one of the world’s best sellers, earning Merck $29.5bn in sales last year. But drip by drip, the US pharmaceutical company’s time is running out.

In 2028 Keytruda’s patent ends, allowing rivals to sell the same drug at a cheaper price. Investors are spooked and Merck’s shares have sunk 35 per cent over the past 12 months. While the company has been at pains to show it is prepared, Daina Graybosch, an analyst at Leerink, says the so-called patent cliff is hanging over the business. Merck has a “massive hole” in its revenue to fill. “They can’t fill it with one drug,” she adds.

Merck on Wednesday appeared to take a step towards addressing the looming Keytruda patent cliff. The company is closing in on a $10bn deal to buy London-based biotech Verona Pharma, which has an approved respiratory disease drug that analysts predict could generate peak annual sales of approaching $4bn.

Losing the intellectual property rights for blockbuster drugs is a long-standing ritual for pharmaceutical companies. Drugmakers can earn fortunes when new discoveries are first sold to patients. Governments grant them about 20 years of patent life per drug.

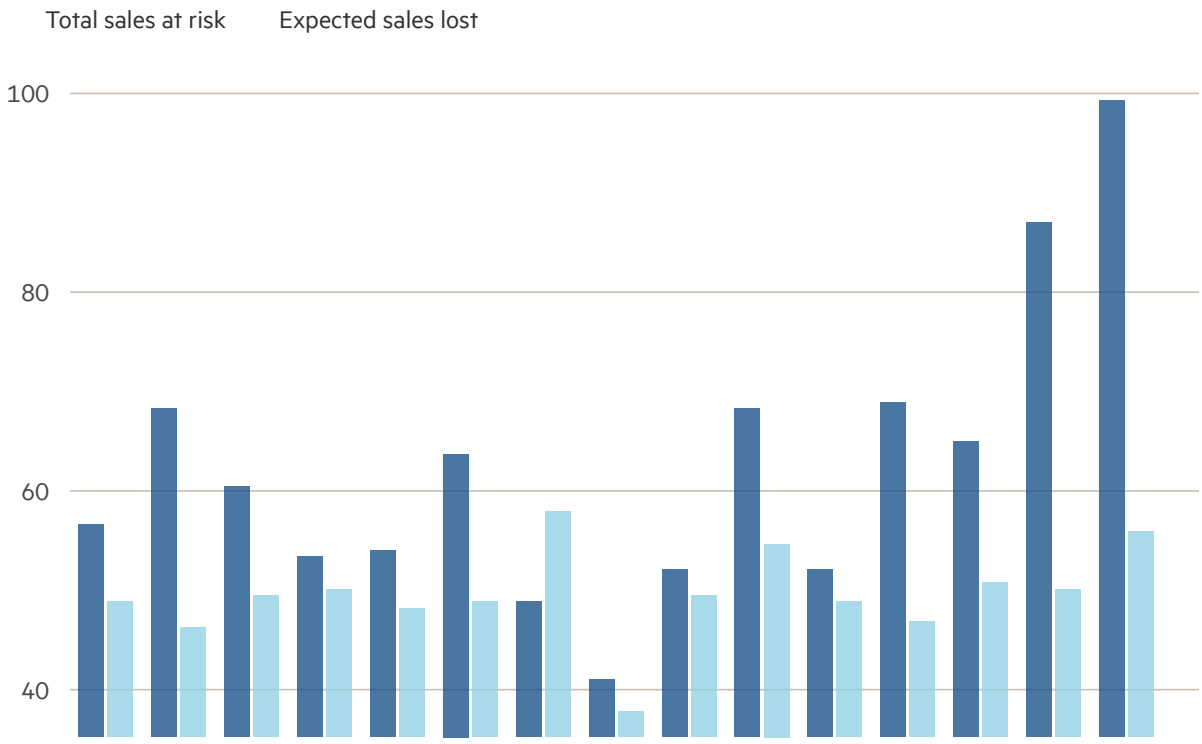
But up to half of that time can be used before the drug gets to market, during development. When the patent is up, competitors are allowed to release generic rivals, potentially wiping out billions of dollars of revenue for the original proprietor.

Merck is not alone. The pharmaceutical industry is facing some of its steepest patent cliffs to date. Drugs worth about $180bn of revenue a year are going off patent in 2027 and 2028, according to research firm Evaluate Pharma, representing almost 12 per cent of the global market. Bristol Myers Squibb and Pfizer are also facing 2028 patent expirations for top-selling drugs.

While patent cliffs are visible years ahead, investors are often not that “far sighted” and can be “surprised” when they come, says Tim Opler, a managing director in Stifel’s global healthcare group. “The pressure on pharma to find some way to augment the revenues is extremely high.”

The looming patent cliff puts $180bn in pharma sales at risk in 2027 and 2028

Global sales at risk from patent expiration ($bn)



The boom and bust cycle is the result of an uneasy compromise in how we fund innovation that is expensive to create but cheap to copy. Governments would rather grant limited monopolies to the private sector than fund much of this essential but risky work themselves. Stephen Haber, a professor of political science and history at Stanford, says that without patents, medicines would not exist.

But often no one is entirely happy with the compromise. Investors and pharma companies do not always feel adequately rewarded in a sector where failure is common. They particularly resent other measures to cut drug prices during the patented period, feeling these undermine the deal.

Healthcare systems balk at expensive new drugs, given to more people as populations age. Developing countries struggle to access the innovation until patents expire.

Policymakers tweak around the edges, often proposing adjustments to the number of years of patent protection. Yet few are committed to a completely different model.

Bhaven Sampat, an economist at Johns Hopkins, says the current system is “a blunt tool to incentivise innovation”. “It overcompensates some inventions and undercompensates other things,” he says. “No one thinks we have it exactly right.”

To get through bust periods historically, pharma companies would go on spending sprees, buying up smaller biotechs, where many innovative drugs are discovered, to fill their pipelines ahead of the patent expiry.

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Bhaven Sampat, economist at Johns Hopkins

Merck continues to hunt for targets to grow its business through acquisitions. “We are currently advancing the largest and most diversified pipeline in company history,” including a late-stage pipeline that has tripled since 2021, Merck tells the Financial Times. The potential commercial opportunity has been estimated to be $50bn from these late-stage candidates alone by the mid-2030s, it adds.

An uncertain political climate has resulted in the sector at large moving cautiously. First, companies feared that former US president Joe Biden’s aggressive Federal Trade Commission could stop deals in their tracks. Then came Trump’s threat of tariffs on the sector. The industry also lacks clarity on how much they will be able to charge for drugs, as politicians pressure them to cut prices.

Linden Thomson, a healthcare portfolio manager at Candriam, an asset manager, says companies are doing due diligence on deals but many are probably holding back because of global tumult.

But they will have to face the cliff soon. “It doesn’t surprise me that companies are being somewhat thoughtful on what the risk is of outlaying billions when they don’t know where they stand on tariffs, European pricing, and US pricing,” she says. “But it’s absolutely going to happen, it has to.”

The patent system was established in Britain during the industrial revolution and was first formalised in law in the US, according to Haber of Stanford.

Intellectual property protections were essential to the development of the pharmaceutical industry in the late 19th century and to it thriving in countries like the US, UK and Germany. “It’s not an accident that there’s only a few countries in the world that are huge pharmaceutical developers,” Haber says.

When a drug goes off patent, other companies can seek approval for their copycat versions. These are usually made based on reverse engineering and are informed by the proprietor’s patent filings. The copycats are then tested to ensure they are equivalent to the branded medicine. But crucially, they do not need to go through the expensive clinical trials process again.

While all innovations can be patented, the pharma industry suffers from patent cliffs in ways that others such as the tech industry do not. This is mainly because the key active ingredient in a drug is covered by one main patent, which is hard to invent around, and chemical formulas are relatively easy to copy.

Sampat of Johns Hopkins says the median number of patents per drug is around three to five, not the hundreds or thousands that cover, for instance, an iPhone. “So any given patent expiring doesn’t matter all that much for something like the iPhone, as it would for a drug,” he says.

Also unlike the iPhone, few patients are loyal to their brands and healthcare systems are eager to cut costs by moving to generic versions quickly after they are released. Many countries have laws allowing pharmacists to automatically swap out branded prescriptions with generics.

Big Pharma has seen a drought of megadeals since 2019 but is sitting on substantial liquidity that can be deployed

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Sources: Oppenheimer, CapitalIQ, company filings • 2025=through end-June

This means pharma companies have to focus relentlessly on refilling their pipelines before their bestsellers lose patent protection.

At present companies actually have plenty of money to spend on deals due to the success of the drugs going off patent plus an industry-wide move to slim down operations. EY estimates that companies are sitting on $1.3tn in dealmaking firepower.

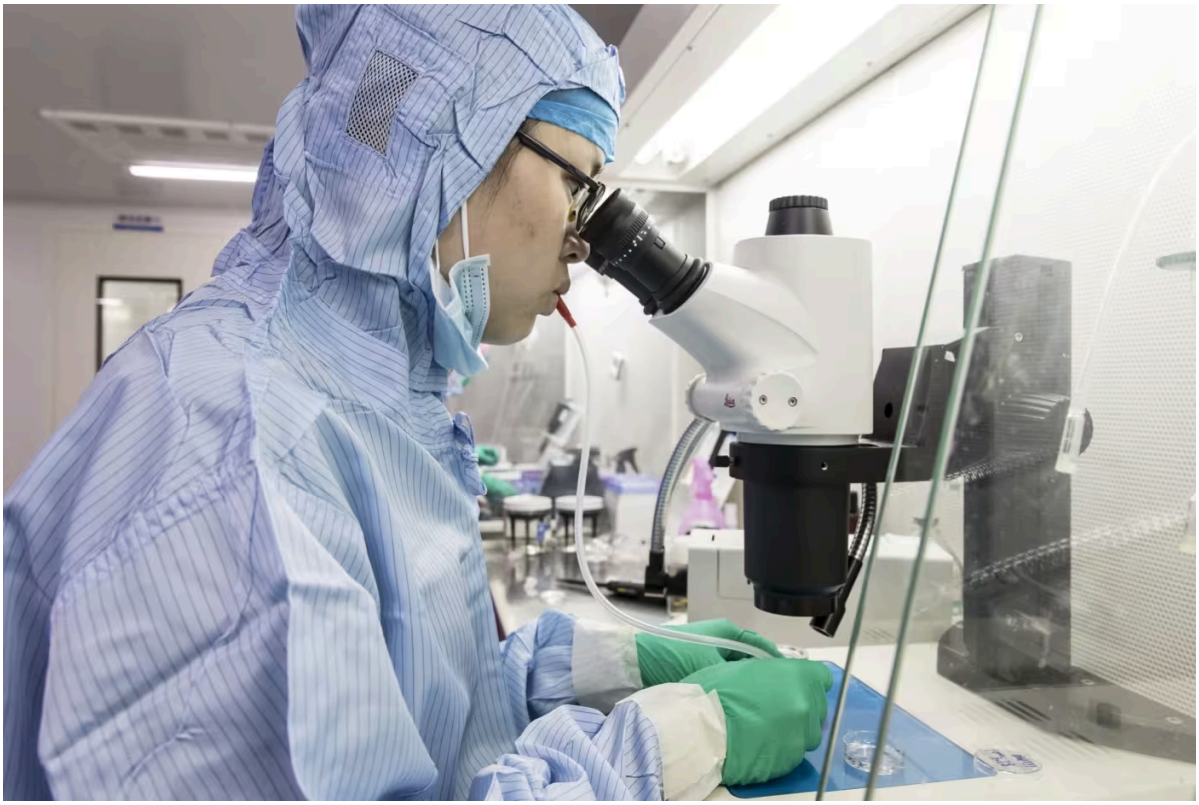
But after a big dealmaking year in 2023, which included Pfizer’s $43bn acquisition of oncology-focused biotech Seagen, and Amgen’s $28bn purchase of autoimmune drugmaker Horizon Therapeutics, the past 18 months have been quiet.

Companies are searching for the “Goldilocks” targets, neither too big nor too small.

In 2009, ahead of the last major patent cliff, there were several megamergers: Pfizer bought Wyeth for $68bn, Merck bought Schering-Plough for $41bn and Roche acquired Genentech for $47bn.

But there has not been a megamerger in pharma since 2019, when Bristol Myers Squibb bought Celgene for $90bn. These huge deals have fallen out of favour with many investors, who worry about antitrust scrutiny and see them as tough to integrate.

Gareth Powell, a healthcare investor at Polar Capital, reflects many others when he says he believes companies should hold back from megamergers and cost-cutting, and focus on long-term revenue growth to drive earnings.



A technician at a laboratory outside Shanghai. Big Pharma is increasingly attracted to Chinese assets because they have smaller upfront costs than western deals © Qilai Shen/Bloomberg

Smaller targets can be relatively cheap as the biotech market is down 50 per cent since its peak in February 2021, and many early-stage companies are trading below cash.

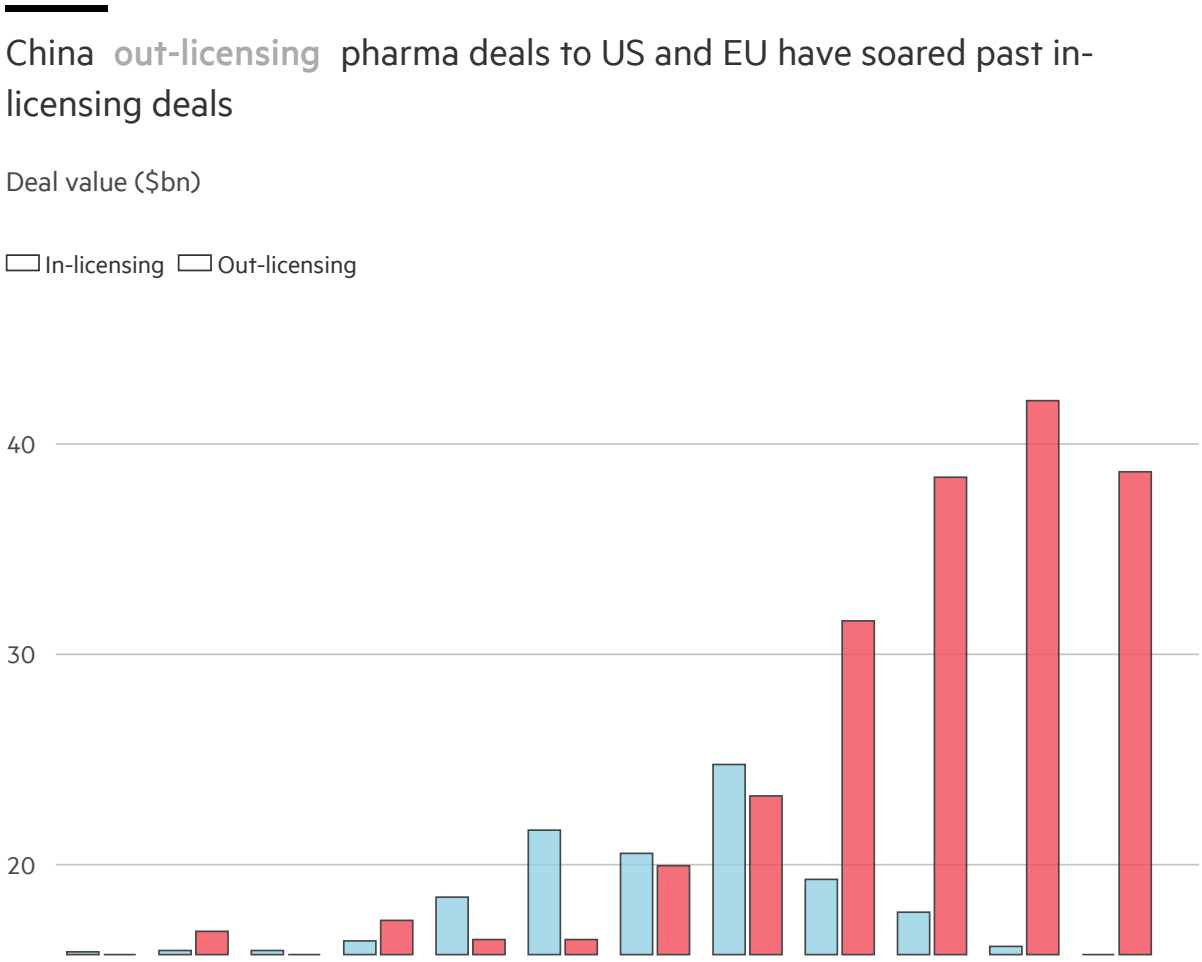
But ideally Big Pharma is looking for biotechs with drugs that could come on to the market soon — and sell in their billions.

Thomson says valuations might look “super compelling” across the biotech sector, but there are few companies with late-stage drugs that could sell several billions in revenue.

Under “immense pressure” from shareholders and their boards, companies are beginning to rethink this strategy and realise they may have to invest earlier, when drugs are still in initial clinical trials, says Zahid Moneer, global head of healthcare investment banking at BNP Paribas. “In response to the patent cliffs, Big Pharma guys are looking at phase 2, or even earlier, if they really believe it is transformational,” he says.

One difference since the last major set of patent cliffs is that companies are now looking for drugs to buy in China. They often buy ex-China rights to early-stage innovative medicines and then conduct the later-stage trials themselves, so they can provide global data to western regulators. So far this year, there have been licensing deals between Chinese companies and US and European partners worth up to $35bn, according to data from EY.

Nanna Lüneborg, general partner at Forbion Capital, a European venture capital firm that has done several deals in China, says the rise of the Chinese sector has been “absolutely phenomenal”. “I think all of us have just been completely amazed by the scale and the quality of the assets coming out of China,” she says.



But China also makes buyers nervous, she adds, because if they are doing due diligence on a US or European company, they have little idea if there is a good competitor in China, which could enter the market and undercut business.

Daniel Parisotto, managing director in healthcare investment banking at Oppenheimer, says Big Pharma is attracted to Chinese assets — typically the rights to develop and sell the drugs outside China — because they have smaller upfront costs than western deals, where much of the price is tied to a drug reaching certain milestones, like trials, or approvals.

Drugmakers pay less upfront than they would in the west. “But ultimately the jury is still out on whether those Chinese assets have a higher failure rate or the same success rate as western assets,” he says.

While M&A is the most obvious method of recovering from a patent cliff, pharma also deploys strategies to extend the life of its existing drugs. Robin Feldman, a law professor at the University of California San Francisco, says the record for extending a patent beyond the original expiry is more than 30 years.

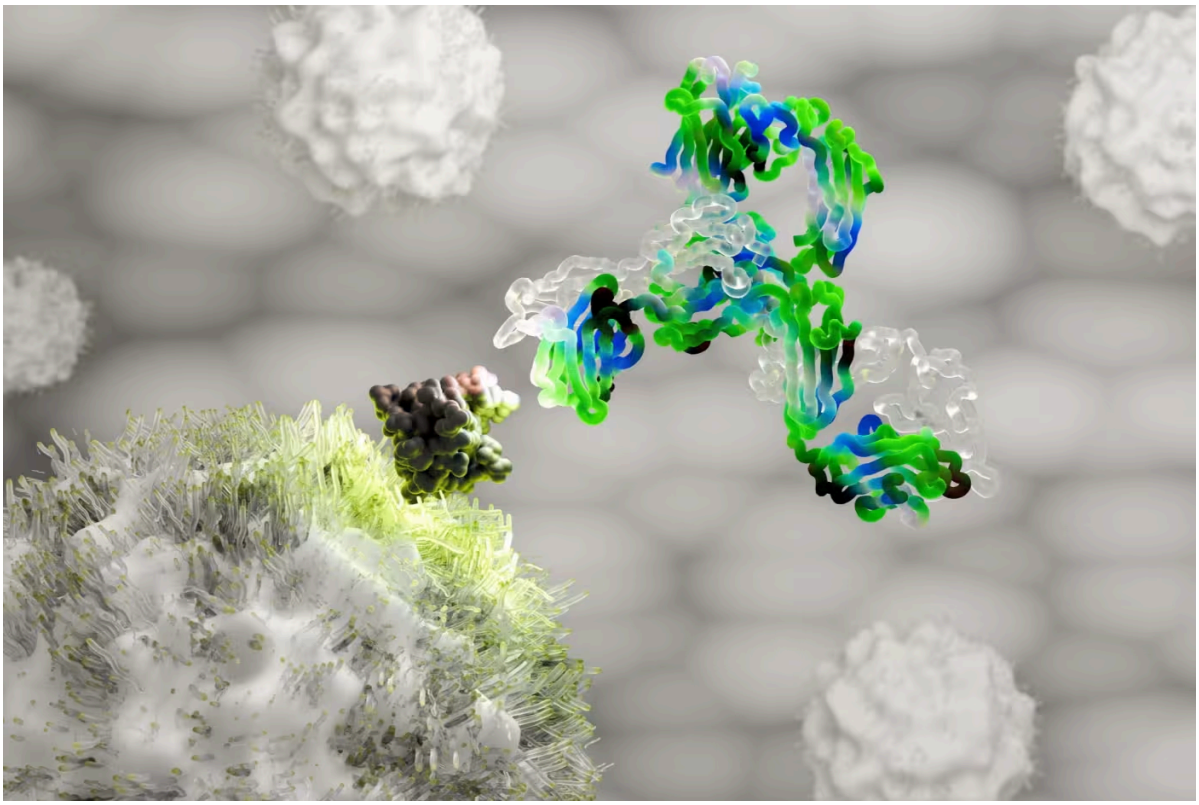
Before Keytruda, the world’s bestselling medicine was AbbVie’s Humira, a wonder drug that fights arthritis, Crohn’s disease and other inflammations. In 2020, AbbVie earned $16bn in the US alone from Humira, and it was charging $77,000 a year for the drug, according to a 2021 congressional report.

The Chicago-area company tried for years to hang on to its drug. Humira’s basic patent expired in 2016, but AbbVie obtained 132 other patents for administering and making the drug, essentially fortifying Humira’s exclusivity with a “patent thicket.” The last of these patents expires in 2034.

US lawmakers balked at the lingering high cost for Humira and sued AbbVie. The city of Baltimore alleged people were paying millions of dollars unnecessarily to AbbVie and that its patent strategy violated antitrust law. In May 2021 the company’s CEO, Richard Gonzalez, sat for three-and-a-half hours to face fire from members of Congress.

But in 2022, a US appeals court ruled for the company, saying there is nothing wrong with holding a lot of patents. Big technology companies have much larger patent caches, the three-judge panel said.

Nevertheless the pharmaceutical industry is facing renewed political scrutiny for such tactics. Trump has railed against high drug prices. Two of his allies in the Senate introduced legislation in March to attack patent thickets.



The looming expiration of the patent on cancer drug Keytruda has spooked investors, causing Merck’s shares to fall 35 per cent over the past 12 months © Science Photo Library/Alamy

Other strategies companies can deploy to protect drugs from competition are “trade secret” barriers, says Indradeep Bhattacharya, a partner at Baker McKenzie, a law firm. While patents are typically public, trade secrets law involves keeping an invention private.

In Europe, some antitrust and competition regulators are getting more active, Bhattacharya says, “looking at pharmaceutical companies that are trying to game the patent system to unfairly extend their monopolies”.

Another strategy once an off-patent version reaches the market is to try to prevent it from being covered by insurance. Opler of Stifel’s healthcare group says that in the US, pharma companies have been able to keep rivals off the market by offering discounts to wholesalers and pharmacy benefit managers across a range of drugs, in return for not carrying the cheaper rival to the now off-patent branded drug.

“You can use your power to keep the market for longer,” he says.

Despite predictions of a dramatic drop in sales, the 2027-28 cliff could be more like a “steep hill”, says Frank Lichtenberg, professor of healthcare management at Columbia Business School.

The blockbuster drugs going off patent are almost all biologics — infusions derived from biological, not chemical, processes — and they are harder to replicate than pills. Lichtenberg thinks it could take five years for sales to slump as much as 75 per cent, far longer than the months it took for some best-selling tablets to be replaced by generics last time.

Ultimately the jury is still out on whether those Chinese assets have a higher failure rate or the same success rate as western assets

Daniel Parisotto, managing director in healthcare investment banking at Oppenheimer

Biosimilars — generic versions of biologics — are harder to reverse engineer and are subject to different laws, which mean branded drugmakers only share broad information about the manufacturing process.

When biosimilars get to market, US pharmacists cannot by law to automatically swap them in as cheaper alternatives, like they can with generics. And when they do, the price drops are not as steep. Lichtenberg estimates they sell for about half the price of the branded drug, rather than 10 or 20 per cent of the price for a generic.

The US has been far slower than Europe in adopting biosimilars but that may soon change. The FDA was already speeding up its process of approving biosimilars and a recent Trump executive order directed the regulator to find ways to accelerate approvals further.

The Trump administration is also working on policies that would make it easier for pharmacists to substitute biosimilars for a branded drug, as is already done in Europe.

For companies like Merck, all these potential policy changes only add to the uncertainty around how severe their patent cliff will be.

Over a decade ago, researchers hailed Keytruda as a "giant leap" forward for patients. Its "intelligent and ambitious" clinical development helped Merck make Keytruda the bestselling cancer drug, says Lüneborg of Forbion Capital.

It is going to be hard to find another drug that can treat so many patients — or generate so many billions. Merck is now in the same position as countless other pharma companies that have braced for a drop in revenue after a successful product goes off patent, says Lüneborg. Ultimately they become "victims of their own success".

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