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The Next Big Patent Cliff is Approaching

(Source: An article by Jessica Merrill for Drug Store News)

The pharmaceutical industry is in the midst of a steady period of moderate growth, but financial pressure will build toward the middle of the decade, as many key blockbuster brands face loss of exclusivity. The window for launching new growth drivers to fill the expected revenue gap is also narrowing.

Investors are increasingly concerned about the period from 2025-2030, when many large name brands will lose market exclusivity in the U.S. and Europe while also facing generic or biosimilar competition for the very first time. Big pharma companies generally appear to be on the defense for now, without the pipeline to make up this deficit, which may put more pressure on drug makers to rely on business development as the tool to fill it.

Industry experts forecast that the top pharma companies will lose more than US$200 billion between 2022 and 2030. The top 10 pharmaceutical manufacturers combined have more than 46% of their revenues at risk during that time frame, and five of those companies have more than 50% of their revenues at risk, as forecasted by ZS Associates. Factoring in analyst consensus estimates for projected pipeline drugs in 2022-2030 hardly moves the needle.

However, drug makers can sustain the lifespan of a brand through lifecycle-management strategies, and biologics typically experience less erosion from biosimilars than small molecules do from generics. Business development activity could also offset the loss of exclusivity if drug makers are able to bring in the new assets that can reach the market in the second half of the decade.

Loss of exclusivity challenges will mostly affect big biopharma companies, but some will feel more pressure than others. Pfizer, Inc., Novartis AG, Merck & Co., Inc., Eli Lilly and Company, and Bristol Myers Squibb are poised to face steep patent cliffs. Roche Holding AG, which already cycled through large loss of exclusivity issues in 2020 with biosimilar competition in three blockbuster-sized drugs, now appears well-positioned for the foreseeable future, after the anticipated launch of *Lucentis (ranibizumab)* biosimilars in the U.S. later this year. Sanofi is also largely protected from losses, with its core growth brand *Dupixent (dupilumab)* protected in the U.S. until 2031 with a possible patent term extension.

Abbvie, Inc. will usher in the start of the next big patent cliff with the loss of the mega-seller *Humira (adalimumab)* in the U.S. beginning in 2023. Already biosimilars to *Humira* were launched in Europe in 2019, taking a toll on brand sales (although Europe was already a substantially smaller market for *Humira* revenues than the U.S.)

Johnson & Johnson will have to navigate a challenging

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- **Cardinal Health** is expanding its presence in Ohio with plans to build a 574,670 sq. ft. medical distribution center in the Columbus, Ohio area. The new building will integrate automation and technology to to improve safety, service and quality while delivering operation efficiencies and better support for fluctuations in volume and labor. The new facility will replace Cardinal's current 235,000 sq. ft. facility in nearby Obetz, Ohio.
- **Pfizer** has signed on a new chief financial officer with significant dealmaking experience that could prove invaluable as it looks to deploy its COVID-19 vaccine and drug windfall. *David Denton* is joining Pfizer as chief financial officer on May 2nd, succeeding company veteran *Frank D'Amelio*. Dento was most recently CFO at American home improvement retail giant Lowe's. Prior to his tenure at Lowe's he served as CVS Health's CFO, playing a pivotal role in CVS's US$69 billion acquisition of Aetna.
- **NovartisAG** announced that it will integrate pharmaceuticals and oncology business units and create two separate commercial organizations with a stronger geographic focus – **Innovative Medicines U.S.** and **Innovative Medicines International.** The two units will have full P&L responsibility across all therapeutic areas and ownership of customer experience, marketing and sales, as well as market access for their respective markets. The goal is to strengthen Novartis' ability to achieve its goal of

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TAMER

The Tamer Group Becomes Newest Member of IFPW

IFPW is pleased to announce that The Tamer Group (Saudi Arabia) has joined IFPW as a wholesale member organization.

Tamer Group is the leading supplier of pharmaceutical products to the Saudi market, including ethical branded products, OTCs and generics. With its strong presence, the Group's reach covers all private pharmacies, private hospitals, government hospitals, and other healthcare institutions.

Tamer Group is also a leader in healthcare, beauty care, prestige products, laboratory diagnostic machines and reagents, interventional cardiology, radiology, and orthopedics, as well as a fast-moving consumer goods company responding to the growing needs of the Saudi and Middle East communities.

IFPW welcomes Tamer Group and looks forward to its team's unique insights and perspectives, both regionally and on a global scale.

Patent Cliff (cont.)...

period around the same time, with the company's top-selling drug *Stelara (ustekinumab)* expected to lose patent protection in the U.S. in 2023, followed by *Simponi (golimumab)* in 2024.

Later in the decade, Pfizer is headed over the cliff with the potential U.S. loss of the rheumatoid arthritis drug *Xeljanz (tofacitinib)* in 2025, the blood thinner *Eliquis (apixaban)* in 2026, and the cancer drugs *Ibrance (palbociclib)* and *Xtandi (Enzalutamide)* in 2027.

Pfizer has been to prepared for the impending patent cliffs, vowing to be an active deal maker to replenish the portfolio with late-stage drugs. Earlier this year, CEO Albert Bourla said Pfizer is aiming to sign deals that will add US$25 billion of risk-adjusted revenues to the top line by 2030, and it has the ability to close significant deals from the success of its COVID-19 vaccine and related therapeutics. Pfizer recently bought one late-stage asset with the US$6.7 billion acquisition of Arena Pharmaceuticals Inc., which could deliver the selective sphingosine 1-phosphate receptor modulator *etrasimod* for ulcerative colitis and other immune-inflammatory conditions to the market in the future.

Bristol Myers Squibb markets *Eliquis* with Pfizer but will experience other losses as well, including *Revlimid (lenalidomide)* in Europe and Japan, as well as on a limited volume basis in the U.S. Others that could lose exclusivity include Y*ervoy (ipilmumab)* in 2025 and *Opdivo (nivolumab)* in 2028.

Meanwhile, Merck is working to reduce its dependence on *Keytruda (pembrolizumab)* which loses exclusivity in 2028.

Loss of exclusivity timeline estimates are not an exact science, and the expected life of a brand drug can be unexpectedly extended or shortened based on outcomes of patent litigation, patent reviews and delayed launches of biosimilars or generics. Biologic drugs usually retain a greater amount of market share post biosimilar entry while oral small molecule drugs can quickly erode following a generic entry. Although there have been several successful biosimilar launches in the U.S., particularly in cancer treatments, the next big patent cliff will be more heavily weighted to biologics.

EY partner and industry expert, Arda Ural, noted that the upcoming patent cliffs will differ from those seen in prior years, with monoclonal antibodies facing patent cliffs starting in 2023.

To replenish portfolios, pharmaceutical companies are expected to rely heavily on M&A and business development to fill the void in the aftermath of exclusivity losses. The challenge will be to find the right assets, at a value that investors won't consider overpriced.

"It comes down to each company's risk profile and the CEO's tenure and how they value their pipeline. It is very unique case by case," Ural said.

Several factors have made deal-making more challenging for big pharmaceutical manufacturers as of late, including the high value for assets, the cash-rich financing environment for biotechs, an onslaught of innovation that makes due diligence overwhelming, and the fact that more emerging biopharmaceutical companies are launching drugs independently.

Analysts remain optimistic, however, and are reassured about the industry's financial prospects as it cycles through this difficult period.

In Brief (cont.)...

becoming a top-five company in the U.S. in terms of sales while maintaining and growing its leadership position internationally.

- **CVS Health** is showcasing its work to create a healthier and more sustainable world by releasing the findings of its annual *Environmental, Social and Governance Report*. "In 2021, we made significant progress towards our Healthy 2030 goals, with a particular focus on addressing health equity and protecting the environment," said *Karen S. Lynch*, president and CEO of CVS Health. "We'll continue to utilize our community presence, diverse assets and expertise to improve the health of people and the planet." The company highlights how it has worked to improve health equity through its Health Zones initiative, which addresses six social determinants of health — housing, education, access to food, labor, transportation and healthcare access.
- A new COVID-19 variant, Omicron XE, has been detected in 637 patients, according to the **U.K. Health Security Agency**. Known as a "recombinant," it contains a mix of the previously highly infectious omicron BA.1 strain, which emerged in late 2021, and the newer BA.2 variant, currently the U.K.'s dominant variant. Health authorities said there is currently not enough evidence to draw conclusions on its transmissibility or severity.
- In the face of unprecedented lockdowns in Shanghai and now China's 3rd largest city, Guangzhou (under partial lockdown), the Chinese government is revising its course on the importation of foreign mRNA COVID-19 vaccines amid growing calls for more effective vaccines. Officially, the Shanghai lockdown is to end April 18th but is unlikely given China's zero case target and current case developments. China has already approved a recombinant protein vaccine from Chongqing Zhifei Biological Products Co. Ltd. for booster use.
- The **Medicine Patents Pool** has signed agreements with 35 companies to manufacture the generic version of **Pfizer's** oral COVID-19 treatment *nirmatrelvir*, which in combination with a low dose of *ritonavir* can be supplied in 95 low- and middle-income countries. The sublicense agreements are the result of the voluntary licensing agreement signed by MPP and Pfizer in November 2021 that will help enable the supply of the medicines to countries comprising approximately 53% of the world's population.
- The **U.S. Army** has signed a US$1 billion contract with the **U.S. Department of Defense (DOD)** for an unknown number of its BinaxNOW and ID NOW COVID-19 tests. The U.S. government also announced contract modifications with **Abbott** and **iHealth Labs** to purchase 176.8 million over-the-counter tests, a step toward the Biden administration's redoubled goal of delivering 1 billion free at-home tests following the rise of the Omicron variant.
- **Rutgers University** researchers concluded that the **Pfizer** antiviral drug *Paxlovid* is still effective against COVID-19 by jamming the cell machinery of a key protein, known as the "main protease" or Mpro, involved in replicating the virus. As COVID's Omicron variant spreads rapidly throughout the world, authorities have watched to see whether the virus evolves "resistance," evading the defenses provided by current medicines. Physicians are counting on treatments like Paxlovid to stem the spread.

(Sources: Business Wire, Drug Store News, FierceBiotech, FiercePharma, Scrip Intelligence, and World Pharma News)