LIFE SCIENCES INDUSTRY REPORT 2025

PART 7: BIOLOGICS & GENERICS

Uncover the transformative trends that will drive the life sciences industry ahead, backed by expert commentary and data-driven insights.

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Editors’ introduction

The importance of biosimilars only continues to grow, driven by the potential savings they are able to deliver to healthcare systems, providing an alternative to comparator products and lowering price through competition.

In Europe, for example, where authorities acted quickly to ingrain these treatments into the regulatory framework, biosimilars have managed to provide tens of billions of euros in savings since 2012, according to IQVIA. When the primary patent on a blockbuster drug expires, affordable generic or biosimilar competition is expected to balance the market, offering relief to patients who could not afford the high price tag associated with the brand-name drug. However, in reality, this is not always the case.

In Part 7 – the final instalment of our inaugural Life Sciences Industry Report – we look more closely at reporting from 2024 on the biosimilar and generics space, providing an overview of the landscape and the potential yet to be realised therein, as well as the caveats to possibilities.

From how the US Inflation Reduction Act can provide a positive boost to biosimilars and how drugmakers ‘game’ the US patent system, to the complexities of navigating the market for these therapies when it comes to rare and complex conditions, as well as innovations on the horizon in generics – some industry analysts suggest that less expensive biosimilars may be the solution to free up finances for novel, more expensive agents.

In pharmaphorum’s inaugural Life Sciences Industry Report 2025, Parts 1 through 7, we delved into the trends that propelled the pharmaceutical industry along in 2024, aiming to present truly informed insights into an industry very much at the height of its discovery and development capabilities, on the precipice of truly impressive, paradigm shifting innovation and, vitally, paving the way to broader access to treatments that will permit better quality of life and patient outcomes overall.

Where will we be as we enter 2026? Time shall tell. Be part of the conversation, and get in touch about our Life Sciences Industry Report 2026 today.

Eloise McLennan
Deep Dive Editor

Nicole Raleigh
Web Editor

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Life Sciences Industry Report 2025 Part 7: Biosimilars & generics

Approval trends

In 2024, 58 first generics and 17 biosimilars were approved, reflecting an increase due to patent expirations and regulatory advancements.

Market entry

Both first generics and ANDA have seen increased market entry in recent years, reaching a combined high of 1046 in 2023.

ANDA approvals

The number of ANDA approvals has been consistently high, with 956 approvals in 2023.

Biosimilar growth

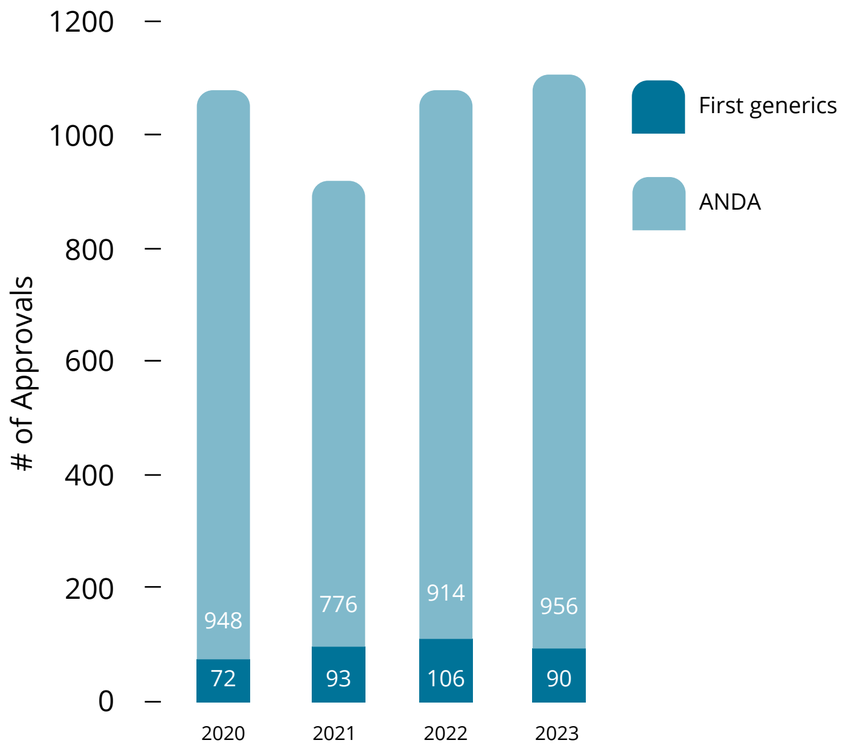
The approval of biosimilars has been steadily increasing, accounting for 5% of approvals in 2023

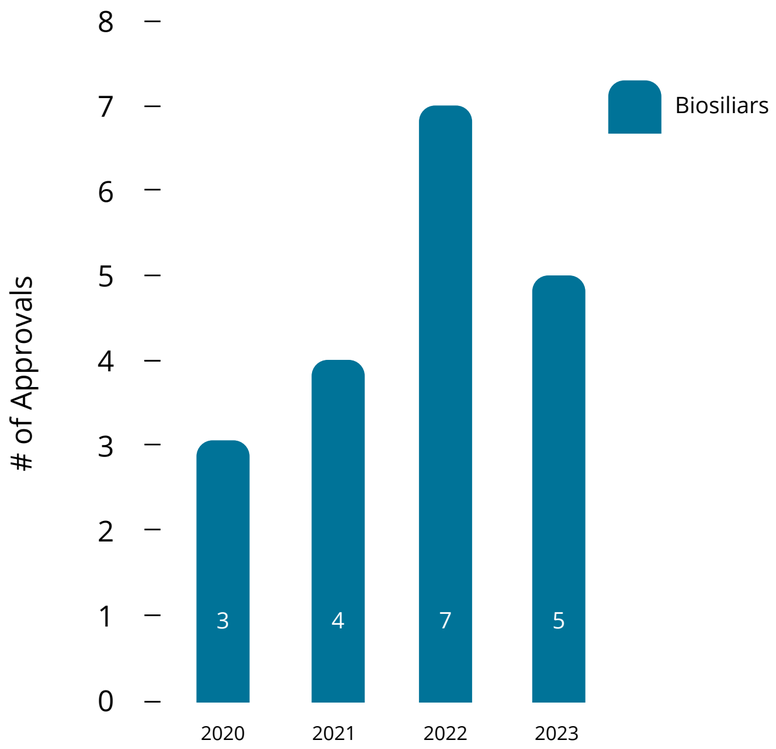
Data and insights powered by EVERSANA

USFDA ANDA approvals: Small molecules (first generics & ANDA generics) vs large molecules (biosimilars)

Both first generics and biosimilar approvals have increased over time due to patent expirations of brand-name drugs and advancements in regulatory pathways facilitating generic and biosimilar market entry

In 2024 58 first generics and 17 biosimilars have been approved*





Sources: FDA.gov; Office of Generic Drugs 2023 Annual Report; Accessed on 3rd December 2024

* First generics till 30th Sep 2024, and biosimilars till 30th Nov 2024

*Data and insights powered by **EVERSANA***

Inflation Reduction Act proves positive boost for biosimilars

For the pharma industry, the IRA has made headlines due to it allowing price negotiations on top-selling treatments. However, Ben Hargreaves finds that another provision within the Act was designed to encourage biosimilar uptake, and it seems to be working.

The US political system has settled on a consistent target of campaigning over the last few election cycles: the pharmaceutical industry. The centre of the debate has been on the cost of healthcare and the pricing of treatments that play a role in this. With the Inflation Reduction Act, the Biden-Harris administration took steps to give Medicare the ability to negotiate the pricing of some of the most commonly delivered treatments.

Another notable action of the IRA was to try to encourage the prescription of biosimilar treatments. Through the IRA, the Administration attempted to do this by allowing the Centers for Medicare & Medicaid Services (CMS) to provide a 2% payment increase for using qualifying biosimilars, which was effective in October 2022. Certara recently evaluated the impact of the IRA's measures on biosimilars to determine whether this change has helped or hindered uptake.

Playing catch up

The importance of biosimilars within the IRA is based on the potential savings they are able to deliver to healthcare systems. Biosimilars are drugs that have a similar structure and effectively the same treatment outcomes when compared to their originator, biologic product. The approval and introduction of biosimilar products onto the market is an effective way to create an alternative to the comparator product, thereby producing a reduction in price through competition.

In Europe, where authorities acted quickly to ingrain these treatments into the regulatory framework, biosimilars have managed to provide €50 billion in savings since 2012, according to IQVIA. Over a similar period, it was found that biosimilars accounted for a cost reduction of $12.6 billion in the US, representing an underperformance when compared to Europe. When considering that the North American market is more than double the size of the European market, it shows how much of an opportunity is left for biosimilars to make a significant impact.

One of the reasons that there is such a difference is because of how quickly Europe embraced biosimilars, being the first to approve biosimilars and then maintaining a steady rate of approval. However, the US market is beginning to mature and the recent introduction of biosimilars to Humira (adalimumab) could prove a turning point for biosimilar revenue generation.

Providing incentive

However, despite the potential for savings, there has been a slow shift in switching to biosimilars due to the additional administrative burden. If the biosimilar product does not offer a substantial enough reimbursement benefit, the healthcare provider may choose to avoid moving patients from their existing treatment simply by avoiding the complexity involved.

This is why the IRA offers to reimburse 108% of the originator product's Average Selling Price

32% of respondents noted that reimbursement incentives provided by the CMS were also a major driver of biosimilar use.

(ASP), a boost on the standard reimbursement of 106% of ASP. The additional savings provided could be enough to gently encourage providers to switch to a biosimilar product. In the long-term, once biosimilars have become an accepted part of the system, there may be a reduced need for such incentives, as familiarity and understanding of the products could be established – with the latter factors remaining an issue for uptake. In the IRA, the provision allows for this added 2% reimbursement to be in place for a temporary, five-year term.

Broad awareness

To understand the impact of this provision after two years of being in place, Certara surveyed 79 facilities about 17 oncology and supportive care biosimilars, and five reference products. The findings revealed that stakeholders are 'moderately aware' of the changes brought about by the IRA, with a comprehensive 95% of respondents suggesting their administration is at least partially aware of the provision. The report found that facility size and awareness are correlated, with respondents from larger facilities being more likely to rate themselves informed about the reimbursement plans when compared with smaller facilities.

The survey found broad utilisation of biosimilars, with 91% using at least one of the biosimilars referenced. Of the 17 biosimilars included, the average number used per facility was six. The facilities that indicated no use of biosimilars cited reimbursement challenges and provider choice as the principal reasons for not adopting the products.

Certara also inquired as to the reasons for the facilities' use of biosimilars and, overwhelmingly, the reason was net price. The respondents cited net price and contracting as the most common reason (65%) for use, with clinical equivalency appearing as the next most important reason (45%).

The IRA impact

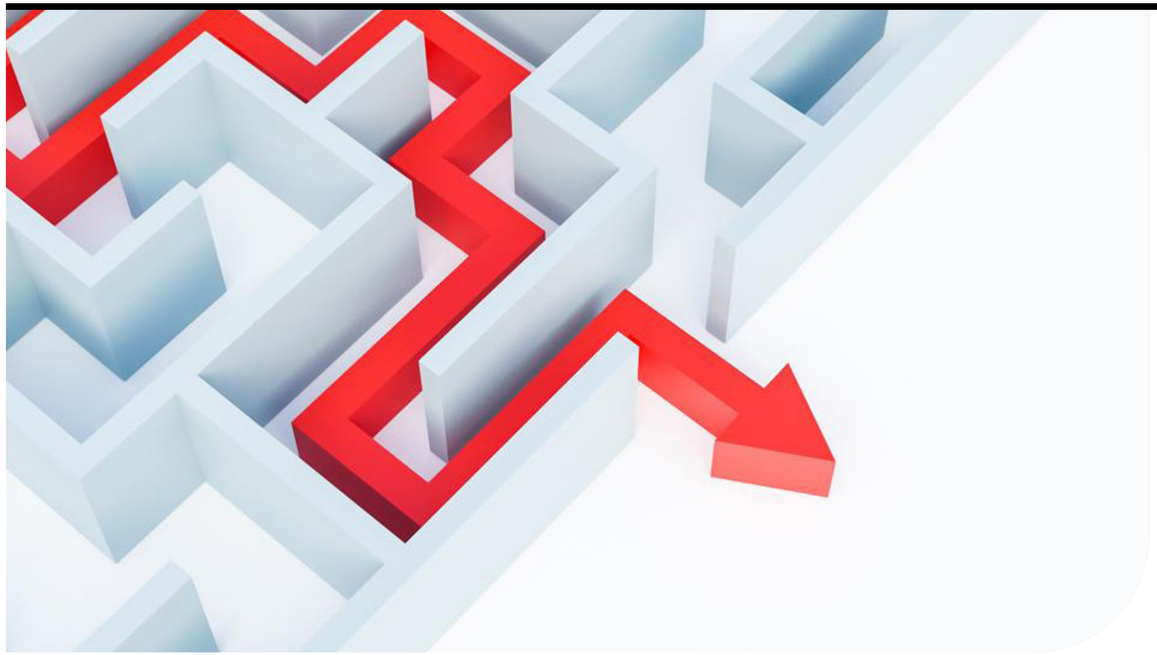
Importantly for the changes to the IRA, 32% of respondents noted that reimbursement incentives provided by the CMS were also a major driver of biosimilar use. Even more significantly, there was a link between greater familiarity with IRA add-on payments and the number of biosimilars used in a facility. At those facilities where respondents suggested leadership was highly aware of the IRA change, there were an average of eight biosimilars used; by comparison, at those where there was a low or complete lack of awareness, the average worked out at 5.4 biosimilars used.

When asked directly about whether IRA's reimbursement enhancement had led to changes in biosimilar utilisation, a large part of the respondents stated that it had led to a slight increase (45%). There were also 14% who suggested that it had led to a significant increase. Only 21% responded that there had been a significant or slight decrease, with 20% noting that there had been no change. However, as the reimbursement period is set to last five years, an important metric is how this could be set to change over the coming years. A large majority (89%) believe that biosimilar use will increase in the next five years, with 74% of respondents of the opinion that the IRA add-on payments will be a factor in this increase.

"Oncology and supportive care biosimilars have achieved significant market share, saving the US healthcare system millions of dollars. While most of these savings are attributable to other causes, our primary research and market data analysis suggest that the IRA's Medicare reimbursement boost for qualifying biosimilars is a small but measurable contributing factor," the report authors concluded.

About the author

Ben Hargreaves is an established freelance life sciences writer, whose experience includes such publications as the BioProcess Insider, BioPharma-Reporter, BioSpace, Outsourcing-Pharma, pharmaphorum, and Motley Fool, among others.



Part Two: Navigating the complexities of global market access for rare and complex conditions

The journey to global market access for innovative therapies is fraught with challenges that vary significantly across the world. Drug manufacturers must adeptly navigate ever-changing regulatory frameworks, cultural expectations, and commercial landscapes to maximise the potential of novel treatments.

This complexity is especially pronounced in the realm of rare diseases, where the emphasis on cost-effectiveness and value can differ widely from one market to another. As decision-makers prioritise different criteria for reimbursement, understanding the intricacies of these varied landscapes becomes essential for manufacturers seeking to ensure that therapies reach the patients who need them most.

Challenges in global market access

At the heart of global market access lie the strategies and processes that drug manufacturers use to navigate the complex regulatory, cultural, and commercial landscapes unique to each target country or market. By mastering the art and science of global market access, companies can optimise the commercial potential for novel therapies, open new opportunities, enhance engagement with diverse rare disease communities and leverage the vast potential available in various global markets.

The emphasis on cost-effectiveness also differs from one region to the next. One study assessing the importance of criteria to decision makers in multiple countries has quantified some of these differences, showing that criteria, such as cost-effectiveness, may be valued extremely high in some jurisdictions, but deemed irrelevant in others.

Within the EU, each Member State is individually responsible for managing its own healthcare system, and there is great variation in market access conditions, local pricing, and reimbursement policies. Consequently, certain products may be accessible to patients in some Member States, but not others, based upon their perceived value and impact on health budgets. As seen in the introduction of CAR T-cell therapies, some therapies are considered unaffordable or not cost-effective, either because product efficacy is unproven or because the established value does not justify the price tag.

Global pricing and demonstration of value for rare disease therapies

To determine the perceived value for money a new drug delivers compared to the cost of other available interventions, decision-makers rely upon incremental cost-effectiveness ratios (ICERs) that contrast newer medicines to the current standard of care. The ratio, known as quality adjusted life year (QALY), is a measure of how well medical treatments improve or lengthen patients' lives.

QALY has been the standard measure in economic evaluations and is used widely in many countries where the HTA guides decision making, enabling payers and regulators to benchmark new products to the QALY threshold. If a drug falls under a designated threshold, it theoretically provides a cost-effective use of financial resources vs the available treatments that it may displace.

RWE plays an essential and increasingly prominent role in helping drug developers to demonstrate the value of their products.

While the cost-effectiveness threshold varies by country, it is often expressed as the upper limit of a payer's readiness to pay for a perceived health gain. There are also some countries that have a higher QALY if a product is indicated for a rare or orphan disease.

Value and importance of real-world evidence for optimal reimbursement

While manufacturers have traditionally relied upon clinical trials for drug development, real-world evidence (RWE) has become a vital source of information in global reimbursement processes. RWE provides clinical evidence regarding a medical product's safety and efficacy, derived from real-world data (RWD) collected during routine healthcare delivery.

RWE includes data derived from electronic health records, medical claims, product or disease registries, and other sources, such as digital health technologies. The key distinction is that this data is not collected in a controlled research environment; instead, it reflects how a drug performs in real-world conditions, providing a crucial foundation for evaluation.

The exponential increase in electronic data and improved analytics tools that are now available to all stakeholders will also boost reliance upon RWE for determining drug performance. New methodologies for leveraging RWE are expected to influence decision-making and enable greater understanding of how factors such as demographics, comorbidities, geography, and lifestyle can help healthcare providers decide the right product to prescribe for specific subpopulations, as is the case with precision medicine.

Furthermore, as manufacturers assess the value and comparative effectiveness of their products, they will also need to collect and use patient-reported outcomes (PROs) to enhance RWE generation. PROs are typically the best source of information about how a person is feeling and managing outside of the clinic, and can provide valuable information from the patient perspective on the effectiveness, safety, and tolerability of health interventions.

RWE documents value

Today, manufacturers, regulators, and payers increasing rely upon RWE to demonstrate the value of new drugs and gain a deeper understanding of their safety and effectiveness across diverse patient populations beyond the confines of clinical trials. Multiple survey articles indicate that RWE is now integrated throughout the product lifecycle, supporting both regulatory access and reimbursement submissions.

RWE plays an essential and increasingly prominent role in helping drug developers to demonstrate the value of their products to regulators. By providing data-driven insights into the drug's actual benefits and risks in everyday clinical settings, manufacturers can advance both clinical and financial objectives, highlighting competitive advantage for their products.

Real-time, RWD analysis enhances the understanding of specific diseases, supporting in the development of treatment approaches and identifying opportunities to support coverage decisions. Increasingly, HTA bodies are seeking RWE to help address uncertainty and generate more longitudinal data that verifies the durability of the clinical responses over time. This is particularly vital for securing optimal reimbursement, especially when clinical trial data alone may not be sufficient.

RWE is utilised from early opportunity assessments to launch planning, evidence generation, brand management, commercial optimisation, and post-marketing assessments. RWE supports regulatory decision-making in post-marketing surveillance to further document the product's safety profile and gather supplemental evidence needed to support ongoing market access and reimbursement.

Addressing pricing sustainability

Groundbreaking cell and gene therapies (CGTs) are offering new treatment options for patients with previously untreatable rare diseases and are set to transform the treatment landscape. As part of precision or personalised medicine, CGTs are designed to tailor treatments to a patient's specific genetic profile, environment, diet, and lifestyle. This approach enables a more targeted strategy for disease treatment based on each person's unique characteristics.

However, these treatments are often associated with high upfront costs, largely associated with complex, time-consuming and costly manufacturing processes that carry requirements for specialised equipment, staff and facility costs, high-cost raw materials, and skilled labour. Collectively, these expenditures drive up the production costs and ultimately affect pricing and reimbursement strategies.

In response to the sometimes multi-million-dollar price tags associated with these novel, life-changing therapies, payers and biopharmaceutical manufacturers are increasingly engaging in value-based agreements and negotiating alternative payment models to improve affordability. These financial solutions connect reimbursement, coverage, or payment to the effectiveness and real-world performance of treatments over a specified time period.

Lower-cost biosimilars

With limited drug or health budgets, some industry analysts suggest that less expensive biosimilars may be the solution to free up finances for novel, more expensive agents. However, the potential for creating future biosimilar competition for CGTs to lower prices and improve patient access may be challenging. This is largely due to the complexity of CGTs, the regulatory requirement to demonstrate high similarity with no clinically meaningful differences, as well as challenges related to intellectual property and market size.

Other industry experts regard gene therapies as better candidates for biosimilar development than cell therapies. They assert that biosimilarity can be achieved when gene therapy biosimilars contain the same genetic sequence as a reference product, and the variability in the vector meets the high similarity standard.

Regulatory pathways and accelerated approvals

While there is no current international standard or regulatory framework for the approval of CGTs, there are expedited pathways such as priority review and accelerated assessment for CGT development. Many countries are introducing initiatives that are designed to support the efficient development of promising therapies:

- The US FDA, for example, prioritises CGTs for paediatric rare diseases that are difficult to study with randomised or placebo-controlled trials.
- EMA's voluntary PRIME programme enhances support for the development of medicines that target an unmet medical need.
- Japan's PMDA offers the Sakigake designation to accelerate innovative therapies addressing serious unmet medical needs, offering shorter lead times for regulatory consultation and faster new drug application reviews.

Ensuring patient accessibility

Innovation deserves recognition, for the substantial investments and risks that biopharmaceutical manufacturers take to develop groundbreaking treatments. By fostering innovation, agility, and collaboration, manufacturers can strengthen their commitment to improving the lives of patients with rare diseases and accelerating the development of life-improving therapies. The essential goal is to ensure that the benefits of these new treatments are accessible to patients.

Number of orphan drugs approved by the EMA available to patients in Europe as of 2024, by country

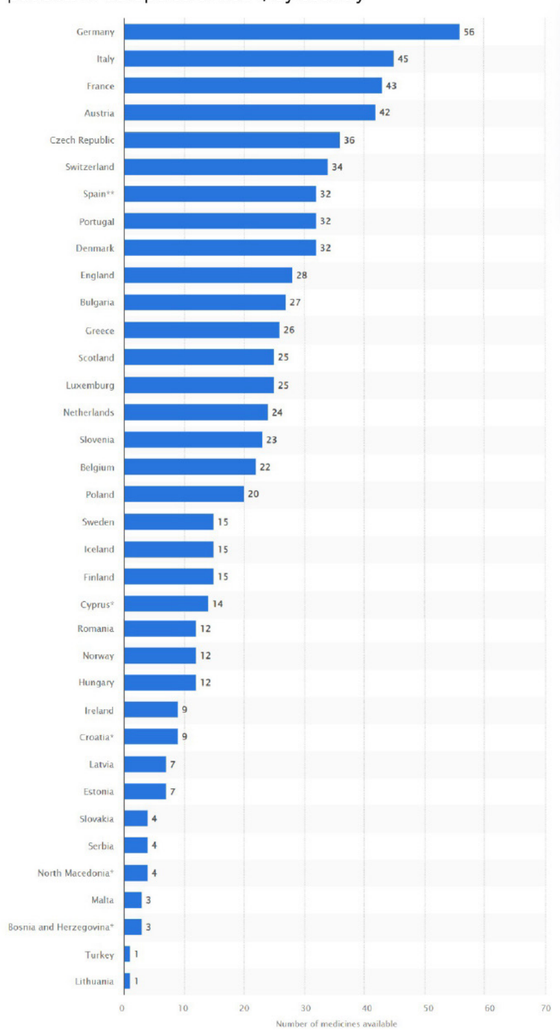


IMAGE: Source: STATISTA, 2024

https://www.statista.com/statistics/1248698/rate-of-orphan-drugs-availability-europe-by-country/

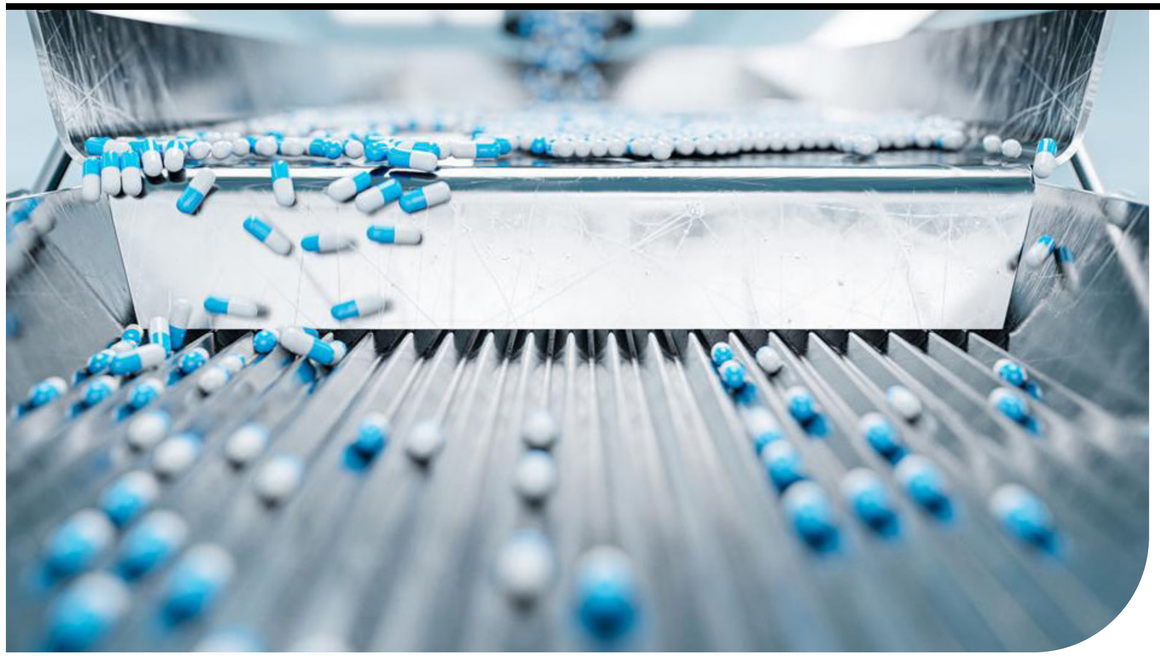
NOTE: Availability equates to reimbursement, with a few exceptions

The social impact of these medicines is palpable: patients stay in the workforce, contribute to society and have a better quality of life. Prior to the availability of these curative treatments, these lifestyle improvements would not be possible. Patients may have been unable to work because treatment was geared towards symptom management only, resulting in heavy utilisation of hospital emergency departments and in-patient care.

Looking ahead, global information sharing is crucial for accelerating drug development and deepening understanding of many rare diseases. Advancing the regulatory science needed to evaluate treatments for rare disease drugs will necessitate stronger collaboration between the FDA, EMA, and other leading agencies. Such global collaboration will expedite the development and approval of drugs targeting rare conditions, alleviating burdens on patients and caregivers while enhancing the quality of life for some of the world's most vulnerable populations.

About the author

Gillian Molloy serves as VP of market access, EU/UK, at AscellaHealth. Molloy brings almost 20 years of experience in the life sciences industry to her role, in both the European and US markets. She has held commercial and market access leadership positions at Baxter, Novartis Oncology, and AstraZeneca, as well as trade relations and formulary strategy leadership roles at UnitedHealth Group. At AscellaHealth, Molloy provides strategic innovation and consultative market access support to pharmaceutical manufacturers and healthcare organisations. Prior to moving into the life sciences industry, Molloy held a chief pharmacist position in the Mater Misericordiae University Hospital, Dublin. She holds a BSc in Pharmacy and an MSc in Hospital Pharmacy from the University of Dublin, Trinity College, as well as an MBA from University College Dublin Michael Smurfit Graduate Business School. Molloy also has a Diploma in Health Economics from the National University of Ireland Whitaker School of Government and Management.



Innovation in generics: Increased efficiency through peptide API synthesis expertise

With the healthcare landscape continually evolving, the generic medicines industry guarantees widespread access to affordable medications for millions of patients worldwide. Generics play a pivotal role in meeting the diverse needs of today, ensuring the consistent availability of medications.

However, amidst the competitive and logistical hurdles the pharmaceutical industry faces, generics manufacturers must continually assess and fortify their resilience and adaptability strategies, in order to remain at the forefront of healthcare innovation in a changing global market.

In pharmaceutical manufacturing, API (Active Pharmaceutical Ingredients) production expertise is vital to achieve process efficiency and affordability. Industry leaders in generic drugs will incorporate technological and methodological synergies in the production of different APIs, with a collective responsibility to improve production processes to support the goals of the generic drug industry.

Among the different families of APIs, peptides represent a growing class, with challenges revolving around accessibility and affordability. One example of generic peptides that offer potential for improvement in the manufacturing process are Gonadotropin-releasing hormone (GnRH) analogues – Goserelin, Leuprorelin, and Triptorelin. Improving manufacturing not only improves affordability, but also brings about reliable and replicable quality, a resilient supply chain, and accelerated product innovation.

Peptide API synthesis – a uniquely challenging process

The production process of peptide APIs is not without obstacles. Peptides are a short chain of monomers called amino-acids and linked together in a certain order called a sequence, which is responsible for their biological properties. The nature of this class of molecules makes them complex and requires specialist expertise to synthesise them efficiently.

Peptide APIs are manufactured via a series of chemical reactions assembling a chain from monomeric components. The most common synthesis routes consist of either solid-phase peptide synthesis (SPPS) or liquid-phase peptide synthesis (such as GnRH analogues).

In SPPS, the peptide chain is built one amino acid at a time on a solid support, with each amino acid added one after another until the desired sequence is achieved. Meanwhile, liquid-phase peptide synthesis (LPPS) involves the coupling of amino acids in solution, resulting in greater flexibility in sequence. With SPPS being a purely linear approach, LPPS offers more convergence in the synthesis in comparison.

Such synthesis methods are effective in producing a variety of peptides, however, the process must be optimised in order to keep up with increasing customer demand and authorities' requirements. Thus, it is vital to increase process efficiency and quality when multiple peptides are synthesised at the same time and on a similarly-scaled production floor – as adding more reactor capacity might not be possible. With this in mind, peptides sharing a constant segment of amino acids, such as the GnRH analogues, offer potential efficiency improvements using synergies in the manufacturing of various peptide APIs.

The “constant segment” shared among different analogues results in a more uniform production process, ensuring more product meets stringent quality checks.

What is converging LPPS? Achieving efficiency through commonalities

Liquid-phase peptide synthesis (LPPS) is a particularly important synthesis method in the manufacturing of GnRH analogues, hosting numerous benefits.

Each of the GnRH analogue sequences have a “constant segment”, where they share the same amino acids. This common segment between different APIs confers numerous advantages when optimising manufacturing efficiency. The

general synthesis of these GnRH analogues is done through LPPS, which facilitates a convergent approach. The constant segments are synthesised individually and then used in all subsequent steps.

The customer then benefits from these synergies, through process efficiency, consistency in production quality, a more secure supply chain, accelerated development of new processes, and a faster time to market.

Converging LPPS provides significant advantages for synthesis of multiple peptides

1. Process efficiency

Through the convergent approach, greater efficiency is achieved by utilising common steps to produce multiple analogues, thus streamlining processes. These improvements, encompassing raw materials, labour, and overall production costs - which can have an impact on the price of the finished drug product for patients - are realised by customers through more attractive prices. This widens access to these life-saving medications, making them more available to a broader patient population.

2. Consistent quality

This approach also results in consistent quality in the manufacturing process. The “constant segment” shared among different analogues results in a more uniform production process, ensuring more product meets stringent quality checks. This in turn reduces production time, ensuring on-time supply of medications to patients.

3. More resilient supply chain

Through synthesis of multiple analogues via a common process, manufacturers reduce risk of shortages or disruptions in the supply chain. This is particularly important in making sure patients who depend on regular supply have reliable access to their medication, which is made possible by the continuous and consistent flow of APIs produced.

4. Faster development of new products

The convergent synthesis approach is able to accelerate the development of new GnRH analogues or new processes – in turn providing patients in need of urgent care with the medication they require more promptly and efficiently. Experienced manufacturers can navigate the complexities of convergent synthesis with assurance, resulting in a faster time to market.

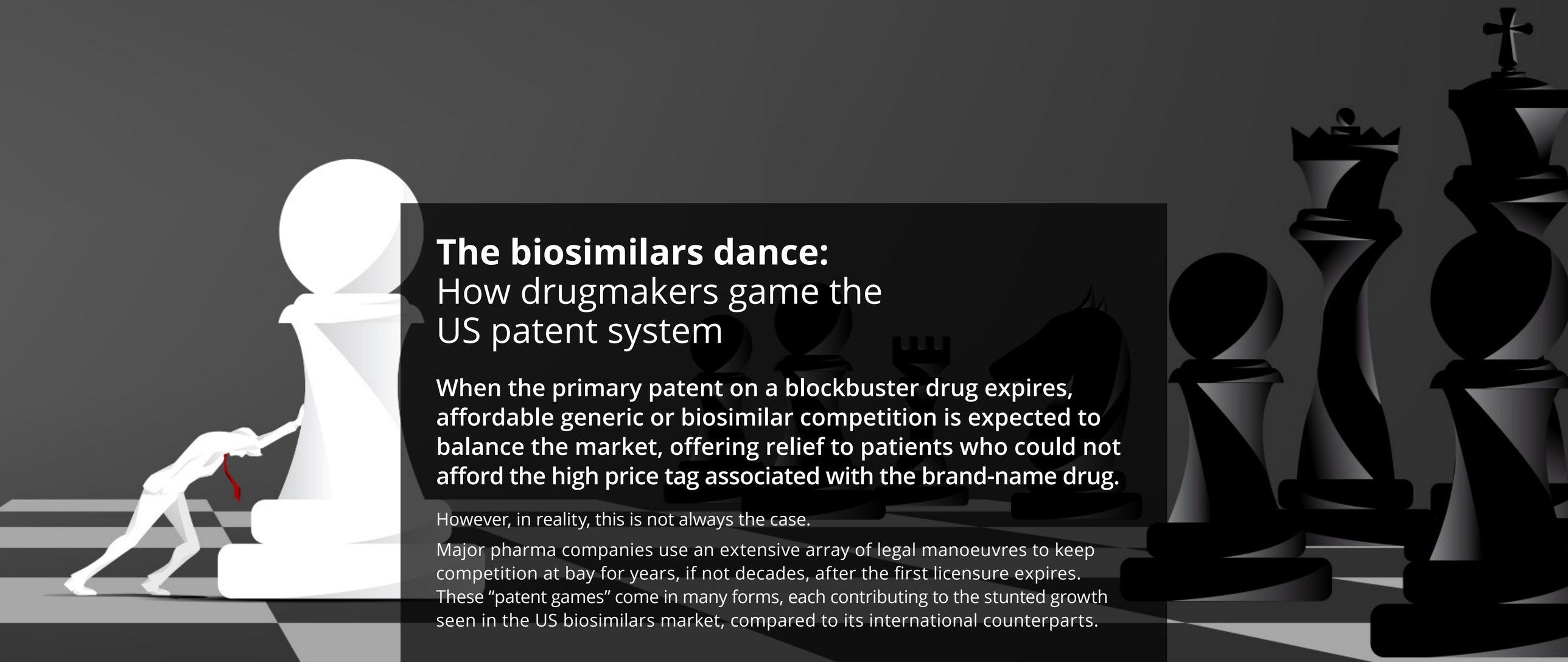
Unlocking improved API development

When synthesising GnRH analogues, specialist production knowledge and experience is key in promoting efficiency and realising a multitude of benefits. From process efficiencies and reliable quality at scale to a flexible supply chain, the convergent approach through LPPS is a huge step forward in the improvement of pharmaceutical manufacturing.

As demand for generics medications grows, the ensured supply of APIs becomes increasingly important – along with ensuring such demand is responded to with affordable and accessible prices.

About the author

Elodie Decuypere is a product manager for generic APIs at Bachem. Before her current role, she worked as a scientific writer for global marketing within the company. Decuypere graduated in Organic Chemistry from the University of Montpellier in 2013 and obtained her PhD from the French Atomic Commission in 2016. Prior to her position at Bachem, she also worked as a postdoctoral fellow, focusing on oligonucleotide synthesis at ETH Zurich and Roche.



The biosimilars dance: How drugmakers game the US patent system

When the primary patent on a blockbuster drug expires, affordable generic or biosimilar competition is expected to balance the market, offering relief to patients who could not afford the high price tag associated with the brand-name drug.

However, in reality, this is not always the case.

Major pharma companies use an extensive array of legal manoeuvres to keep competition at bay for years, if not decades, after the first licensure expires. These “patent games” come in many forms, each contributing to the stunted growth seen in the US biosimilars market, compared to its international counterparts.

Generics vs biosimilars

When the first biosimilar therapeutic launched in the US back in 2015, the news was heralded as the start of a tectonic shift in pharma. Albeit the decision came almost a decade after the European Medicines Agency approved the first biosimilar in Europe, the news of a "generic" copy of Amgen's cancer drug Neupogen (filgrastim) paved the way for an entire class of costly drugs to enter the US market.

According to The Initiative for Medicines, Access & Knowledge (I-MAK), three drugs – Humira, Eliquis, and Enbrel – launched in Europe an average of 7.7 years before their belated US entries, costing American patients an estimated $167 billion during that competition gap.

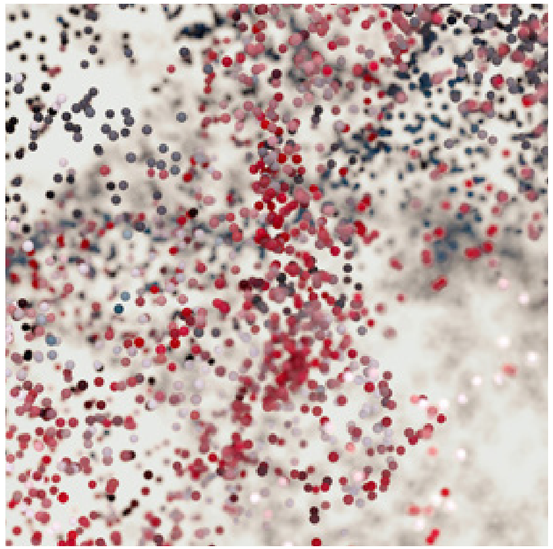
While generics manufacturers are well prepared to navigate the challenges involved in getting copycat drugs from approval to patients, in the growing biologics space, the path to market is far more complicated for biosimilars.

As more blockbuster biologics start facing patent expirations, Pharma's efforts to protect their exclusive pricing power are coming under heightened scrutiny.

Yet, despite being touted as cost-effective alternatives to biologic drugs, biosimilars have faced significant challenges in gaining market share in subsequent years. According to Goldberg Distinguished Professor of Law, and Director of the Center for Innovation at the UC Law San Francisco, Professor Robin Feldman, a decade after the Biosimilars Act, only 18 biosimilars corresponding to seven biologic drugs had entered the US market as of 2020. Even by 2023, just 27 biosimilars for 11 biologics had launched.

UK leader of Pharma and Life Sciences at PwC, Stephen Aherne, highlights that biologics, including advanced therapies like cell and gene therapies, now make up nearly 50% of the drug development pipeline. In fact, many of today's blockbuster drugs, including Merck's Keytruda and BMS' Opdivo, are biologics. However, whereas generic drugs for small molecule therapeutics are a ubiquitous part of the industry, for biologics, the emergence of non-brand name options has been dramatically slower.

There are many reasons for this disparity. Primarily, there are stringent regulatory requirements for biosimilars. Unlike small molecules, which are clinically like-for-like replicas of a brand-name drug, biosimilars (once known as bio-generics) cannot be exact replicas due to their large, intricate molecular structure and manufacturing variations. "They are never exactly the same," explains Aherne.



Consequently, biosimilars must demonstrate that their product is "highly similar without meaningful clinical differences," says Feldman; however this requires clinical trials and development, which, according to Pfizer, "may take five to nine years and cost more than $100 million, not including regulatory fees." Compare these numbers to generics, which take approximately two years to develop and cost between $1-2 million, and you begin to see the problem.

Further complicating biosimilar adoption is the "interchangeable" subcategory requiring switching studies to prove alternating use doesn't diminish efficacy or increase risk.

"With US generics, the pharmacist can substitute for a prescription that has the brand without

contacting the doctor," explains Feldman. "With biosimilars, the pharmacist can only substitute without contacting the doctor for the subcategory of interchangeables. Even then, only if there's a state law permitting it."

At the time of writing, only seven US biosimilars have achieved this holy grail of interchangeable status.

Ultimately, Feldman laments the "deeply disappointing" market penetration and price reductions for biosimilars, describing it as "more of a trickle than a waterfall."

The biologics patent dance

In the US, biologics are granted a 12-year period of exclusivity from the date of first licensure. On paper, that sounds like a long time. This exclusivity is crucial, as it compensates for the extensive costs and risks associated with the development of biologics; however, when you account for the time needed to develop the drug after the initial discovery, which can be upwards of 10 years, by the time the product reaches patients, the exclusivity period can be nearing its end.

But as many pharma companies have discovered, there are ways to game the system to extend exclusivity beyond a product's initial protection term. Key strategies include "evergreening", which Feldman defines as "artificially extending the period of monopoly from the core patent rights", and "patent thicketing", which involves accumulating secondary patents to artificially extend the monopoly period of time on aspects such as dosage forms, manufacturing methods, or minor molecular modifications, elements that can make a big difference in biologics.

In the biologics space, companies have been known to file for hundreds of patents on a biologic drug, with large swathes of such patents filed after the drug has been approved. I-MAK argued in a 2023 report titled "Overpatented, Overpriced", that patenting activity today "extends well beyond the time-limited monopoly intended by the Constitution", with drugmakers filing more than 140 patent applications on average per drug.

"Patent thickets can also serve to deter potential competitors from even developing a competing version of a patent product if they feel the patent barriers are too difficult to navigate. In both cases, competition is affected and consumers end up paying higher prices for longer during the branded drugmaker's extended market monopoly," explains I-MAK founder and CEO, Tahir Amin.

Even if a company can afford the costs and resources needed to develop and market a biosimilar, it first must navigate a minefield of dispute resolution in a process known as the patent dance.

"At the heart of the biosimilar entry process is the patent dance," says Feldman. "With the patent dance, the brand and the biosimilar follow an intricate structured set of steps to exchange information about patent rights that the brand could assert against the biosimilar.

"If a biosimilar company wants to enter the market, it has to answer four simple questions. What's the drug? How do you make it? What patents apply? When do those patents expire?" Feldman explains. "These should be relatively simple to answer under the current system. They're not."

The challenge is that the brand does not have to publish patent information until after a biosimilar has requested approval, and it doesn't have to submit information unless the parties reach certain stages in the processes. As a result, Feldman explains, companies face an information desert where, "the biosimilar company has to enter in the dark, in terms of patent rights."

Cushioning the fall

From a business perspective, it makes a lot of sense for pharma companies to employ aggressive legal tactics to extend exclusivity for as long as possible, as they ultimately face significant revenue declines once biosimilar competition enters the market. AbbVie, maker of the blockbuster biologic Humira and infamous patent chaser, provides a stark example. Although Humira sales reached $20.6 billion in 2021, its revenue dropped by 36.2% in Q3 2023 as its exclusivity erosion accelerated.

Industry analysts expect company-wide revenue to decline for at least a year due to Humira biosimilar competition. Executives have even walked back earlier predictions of growth returning in 2024, indicating sales may remain sluggish. As Aherne explains, "Typically, whether it's a patent expiry date, or the data exclusivity, or the market exclusivity period, it allows for competition in the space…the more competitors… it's going to typically drive the price down."

The impact of biosimilar entry can be severe but more gradual compared to small molecule generics. Take Pfizer's cholesterol-lowering drug Lipitor, for example. Once heralded as the pinnacle example of a blockbuster drug, Lipitor held the top-selling drug spot for many years. That was until 2012 when Pfizers' revenue fell from $68 billion to $59 billion after generics launched for the statin. In contrast, AbbVie is forecasted to retain over one-third of its 2022 US Humira sales in 2024 and over $2 billion through 2030, according to Evaluate Pharma.

This underscores why branded firms vigorously pursue patenting tactics to delay competition. As I-MAK states, "Humira's patent thicket fostered a legal environment perfect for pay-for-delay" settlements with biosimilar makers. Despite its primary Humira patent expiring in 2016, AbbVie continued aggressive patenting, accumulating a thicket of at least 166 granted patents, according to Amin.

"Notably, two-thirds of AbbVie's total US revenue earned on Humira since the drug was approved, was made in the additional seven years of monopoly after its main patent expired," he explains.

While financially rewarding for AbbVie, garnering an estimated $100 billion post-patent expiry, such practices directly oppose societal interests of affordable access that Feldman highlights.

"This is certainly manipulation of the existing systems. However, pharmaceutical companies are profit-making," she says." If a CEO of a pharmaceutical company were to stand before the board and say, 'I'm going to lower prices, because it's the right thing to do,' one would see a new CEO shortly."

As patent cliffs loom, all eyes on Big Pharma

With blockbusters such as Keytruda and Opdivo facing patent expirations before 2030, scrutiny on pharma's exclusivity games will likely intensify, particularly in the run up to the US presidential election in November. But how can we begin to unravel the tangled web created by the current system to encourage innovation in biosimilars?

"Markets thrive on information," says Feldman. "For a robust biosimilar market, brand companies have to put their rights into a public data set and update changes over time."

Acknowledging that this would likely be rejected by brand companies due to the sheer number of patents in existence, Feldman offers an alternative, which would require designating a restricted patent list for biosimilar challenges at approval. This "one-and-done" approach would enhance transparency, she says.

Ultimately, she argues that regulatory reforms are essential to balance innovation incentives with affordable access. "It's society's job, it's government's job to make sure company incentives align with ours," Feldman states. "If not, the result is skyrocketing prices and difficulty accessing medications."

In recent years, attempts to curb the costly and time-consuming switching study requirements for biosimilars to achieve interchangeability have tried, and failed, to make an impact. Most notably Republican Senator Mike Lee's proposed original (and subsequently amended) Red Tape Elimination Act, which did not pass Congress. However under the combined spotlight of a presidential election and a rapidly approaching patent cliff, we are likely to see further proposals to change the system in the near future.

Whatever the outcome, the decisions made over the coming years will set a precedent for the future of biosimilars. And for the millions of patients priced out of potentially life-saving treatments by patenting gambits, the stakes are very high.

About the author

Eloise McLennan is the editor for pharmaphorum's Deep Dive magazine. She has been a journalist and editor in the healthcare field for more than five years and has worked at several leading publications in the UK.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