



## Trends Paving the Way for an Influx of Biosimilar Development

**Promising broader patient access to critical medicines, biosimilars offer a more cost-effective alternative therapeutic option compared with originator products. With many patents for "blockbuster" commercial biologics set to expire in the next few years, biopharma developers have become increasingly drawn to the biosimilars market.**

**Understanding the benefits of having more readily available cutting-edge treatment options available for patients, a number of government and regulatory body-backed incentives are being introduced to streamline the biosimilar development process. In this article, Jim McNally, Chief Scientific Officer and Lynn Kamen, the company's Scientific Officer, explore the incentives, regulations, and other trends pushing biopharma companies down the biosimilar development route.**

### A Drive Towards Biosimilars

At the onset of 2010, the biopharmaceutical industry witnessed an unprecedented wave of top-selling drugs reaching their patent expirations. Drug developers reacted quickly, recognising the potential for new biosimilar products when entering a market previously dominated by one player and acting to further establish the biosimilars market. With a total of 26 blockbuster molecule patents set to expire between 2022 and 2026, it can be expected that more developers in biotherapeutics will turn their hand to the biosimilars market.<sup>1</sup>

The potential to benefit financially from new exposure in the market is not the only driving force toward biosimilars. Lower development costs and more competitive product pricing quickly result in broader patient access to critical medicines. Innovator products that may have previously been too costly to distribute to patients in developing countries widely must make way for these often more affordable alternatives.

With the many advantages that can come from entering the biosimilars market as soon as possible after patent expiration, time is of the essence in what can be expected to be a competitive race to market. If timelines to critical milestones in biosimilar development cannot be accelerated, there is a risk that one of the many competitors will overtake, gaining the market share.

### Expanding Biosimilar Availability

Moving towards an era with a continually steady stream of blockbuster therapeutic molecules coming off patent, biosimilar developers must carefully consider all areas where opportunities for increased speed lie - from process development to bioanalytical assessment. However, the biopharma industry is not alone in the push for more biosimilars to enter the market. Several noticeable trends have begun to emerge, driven by the desire of drug developers as well as government and regulatory

changes to provide a wider patient population access to vital therapeutics.

### Policy Changes in the US

One notable trend in the market is the promotion of biosimilar use over innovators through policy changes. An example of this can be seen in the US, where policies have been introduced to provide favourable reimbursement for biosimilars.

In 1992, the US federal government introduced the 340B drug pricing program. The aim of 340B was to facilitate outpatient drug access to uninsured and/or low-income patients by allowing hospitals, clinics, and outpatient facilities to purchase these therapeutics from manufacturers at discounted prices. However, in 2018, the Centres for Medicare and Medicaid Services (CMS) significantly reduced drug reimbursement for therapeutics purchased through the 340B drug pricing program. These Medicare cuts severely impacted sales of both innovators and biosimilars, discouraging developers from entering the market.

In 2021, policy changes in the US awarded biosimilars a "pass-through status". This means that for 340B-designated hospitals (those recognised by Section 340B of the Public Health Service Act to care for many uninsured and low-income patients), biosimilars are now reimbursed at a higher rate than before. Now, biosimilars are reimbursed at a rate of average sales price (ASP) plus 6%, as opposed to the previous rate of ASP minus 22.5% which still applies to the innovator products.<sup>2</sup>

This policy revision has completely changed the face of the biosimilars market, incentivising 340B-designated hospitals to prescribe biosimilars over innovator products. However, there has been some backlash from developers of originator products claiming that biosimilars should not be awarded pass-through status as they are highly similar to existing products rather than being "innovative". Despite this, these policy changes are likely to be retained and continue to help patients access critical therapeutics.

### Streamlining Approvals

Improved patient access to biological drugs is not only being facilitated in the US but is now predicted to be seen globally through more streamlined methods of biosimilar approval. The World Health Organization (WHO) is revising its 2009 guidelines for developing biosimilars following scientists highlighting the need for policies to effectively make biosimilars less costly to attain.

The 2009 guidelines were introduced as a "living" document, providing scientific principles and a stepwise approach to demonstrate the similarity between a biosimilar and the originator. The WHO Committee recommended a revision of the guidance in 2020 to evaluate new developments and identify areas where guidance could improve flexibility without compromising its basic principles.



The revisions propose that if biosimilarity can be inferred from other parts of the comparability exercise, an "adequately powered" comparative efficacy trial may not be necessary.<sup>3</sup> This means that the large and often expensive Phase III trials previously required to demonstrate confirmatory efficacy could be forgone with suitable alternatives, effectively reducing development and manufacturing costs.

The WHO has highlighted that the decision to revise these guidelines is to reflect the anticipated increase in biosimilar availability, leading to increased competition and decreased pricing, which should improve access to biosimilar products.

## Outsourcing to Australia

With WHO guideline revisions remaining on the horizon, for now, some developers are aiming to outsource to Australia, where clinical trials can be conducted under a streamlined timeframe and at a lower cost.

Currently, Australia offers developers increasingly attractive tax incentives that aim to enable innovation and growth by offsetting some of the costs of certain R&D activities. This means that some biopharma companies are eligible to receive a tax rebate of up to 43.5% on clinical trial-related R&D expenses.<sup>4</sup>

Relief of the biosimilar clinical trial burden is further supported by the flexibility of the Australian clinical trial process, which offers increased speed while achieving comparable quality to data sourced from US clinical trials. In a market where accelerated timelines to market can make or break gaining a market share, it is not surprising that more than 50% of global clinical trials have treatment sites in the Asia-Pacific region.

## Accelerated Biosimilar Development Requires Accelerated Bioanalytical Support

With these incentives and benefits set to drive developers towards an increasingly cost-effective biosimilars market, those taking on the challenge will need to carefully consider options that can minimise delays and compress timelines. If not, there will be a risk of missing out due to growing competition.

Speed to market requires development programs that can operate under compressed timelines while minimising delay risks. A key element that must be considered to achieve this is the need for thorough and complete assay development and validation of bioanalytical assays that support biosimilar programs.

Initial assay development and validation of bioanalytical assays supporting a biosimilar program must also be thorough and complete. This will involve incorporating all necessary evaluations to assess critical program characteristics, ultimately allowing for meaningful interpretation of necessary comparability study data.

As process development and analytical method development typically go hand in hand, appropriately designed and robust assays will be required promptly to avoid bottlenecks and process hold-ups. However, analytical development and validation take time, especially if platforms or basic methods do not already exist. Relying on support from those with analytical

expertise and experience in development and validation could prevent a product from being delayed on its journey to market and potentially missing the opportunity for success.

## A Look to the Future

As the patents for approved blockbuster drugs naturally come to an end, the desire for increased patient accessibility is being further facilitated by regulatory revisions, policy changes, and reduction in development costs. Offering attractive prospects for financial gain, the biosimilar market will likely continue to swell, with competition translating into a reduced cost burden for patients.

However, being first to the post in the race to market is no simple feat. Biosimilar developers will need to contemplate how processes can be accelerated without detrimentally impacting safety and efficacy. One important area that cannot be overlooked is bioanalytical development, where the results of the assays performed will influence the determination of whether the drug is "highly similar" enough to be considered a biosimilar.

## REFERENCES

1. <https://www.statista.com/statistics/1247142/expiring-patents-blockbuster-small-molecule-drugs-worldwide/>
2. <https://www.ropesgray.com/en/newsroom/alerts/2022/06/Supreme-Court-Overturms-Reduction-in-Reimbursement-for-Outpatient-Drugs-Purchased-by-Hospitals>
3. [https://cdn.who.int/media/docs/default-source/biologicals/who-guidelines-on-evaluation-of-biosimilars---4-nov-2021.pdf?sfvrsn=f17799ae\\_5](https://cdn.who.int/media/docs/default-source/biologicals/who-guidelines-on-evaluation-of-biosimilars---4-nov-2021.pdf?sfvrsn=f17799ae_5)
4. <https://www.svb.com/industry-insights/healthcare-life-science/the-advantage-of-oz-offshore-tax-rebates-for-lshc-rd-in-australia#:~:text=Key%20Takeaways,and%20accelerate%20time%20to%20market.>



## Jim McNally

Jim McNally, Ph.D., Chief Scientific Officer has an extensive background in bioanalytical assay development and program leadership spanning nearly 20 years working in the pharmaceutical and biotechnology industry.



## Lynn Kamen

Lynn Kamen is a Scientific Officer at BioAgilytix. She earned her Ph.D. in Immunology at the University of Michigan and completed a postdoctoral fellowship in immunology at the University of California San Francisco. Lynn has over a decade of experience working in drug development, from early target discovery through clinical development for both large and small molecules at several companies including Portola Pharmaceuticals, and Alektor. More recently, Lynn was a principal scientist at Genentech where she supported the in vitro biological characterization of large molecules and lead the development of immunogenicity assays including ADA, NAb and immunogenicity risk ranking assays. She is co-lead of the AAPS NAb working group and member of the AAPS NAb drug tolerance sub-team.