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Research

# The Biologics Revolution

## Navigating the Global Landscape of Biosimilars, BPCIA, and the Patent Dance

February 2026

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# Contents

# List of Abbreviations

| Abbreviation | Description |
|---|---|
| **BPCIA** | Biologics Price Competition and Innovation Act of 2009 |
| **mAb** | Monoclonal Antibodies |
| **API** | Active Pharmaceutical Ingredients |
| **ADC** | Antibody-Drug Conjugates |
| **IPR** | Intellectual Property Rights |
| **RP/RPS** | Reference Product/Reference Product sponsor |
| **FDA** | Food and Drug Administration |
| **EMA** | European Medicines Agency |
| **R&D** | Research and Development |
| **HTS** | High Throughput Screening |
| **DEL** | DNA Encoded Library |
| **CQA** | Critical Quality Attribute |
| **QTPP** | Quality Target Product Profile |
| **ICH** | International Council for Harmonisation |
| **AE** | Adverse Events |
| **PSURs** | Periodic Safety Update Reports |
| **RMP** | Risk Management Plans |
| **PMC** | Post-Marketing Commitments |
| **PK/PD** | Pharmacokinetics/Pharmacodynamics |
| **CDSCO** | Central Drugs Standard Control Organization |
| **DCGI** | Drugs Controller General of India |
| **DBT** | Department of Biotechnology |
| **RCGM** | Review Committee on Genetic Manipulation |
| **RBP** | Reference Biologic Product |
| **NDS** | New Drug Submission |
| **CRBD** | Canadian Reference Biologic Drug |
| **BLA** | Biologics License Application |

## List of Abbreviations

| Abbreviation | Description |
|---|---|
| **aBLA** | Abbreviated Biologic License Application |
| **NDA** | New Drug Application |
| **NMPA** | National Medical Products Administration |
| **TGA** | Therapeutic Good Administration |
| **ABN** | Australian Biological Name |
| **PBS** | Pharmaceutical Benefits Scheme |
| **PMDA** | Pharmaceuticals and Medical Devices Agency |
| **MHLW** | Ministry of Health, Labour and Welfare (Japan) |
| **MFDS** | Ministry of Food and Drug Safety (South Korea) |
| **ANVISA** | Agência Nacional de Vigilância Sanitária(Brazil) |
| **USPTO** | United States Patent and Trademark Office |
| **EPO** | European Patent Office |
| **IPR** | Inter-Partes Review |
| **PGR** | Post Grant Review |
| **AIA** | Americal Invents Act |
| **EHR** | Electronic Health Record |
| **WAC** | Wholesale Acquisition Costs |
| **PBM** | Pharmacy Benefit Managers |
| **IRA** | Inflation Reduction Act |
| **CMS** | Centers for Medicare & Medicaid Services |
| **MFP** | Maximum Fair Price |
| **ASP** | Average Sales Price |
| **CDMO** | contract development and manufacturing organizations |
| **CEE** | Central and Eastern Europe |

# Executive Summary

The global pharmaceutical landscape is undergoing a structural transformation driven by the rapid expansion of biologics and the accelerating entry of biosimilars. This research paper provides a focused analysis of the core regulatory, intellectual property (IP) and market dynamics shaping the global biologics (Reference Product Sponsor) and biosimilar market. It particularly focuses on the evolving regulatory frameworks across major jurisdictions, the strategic deployment of biologics patent portfolios, and the unique litigation architecture established under the U.S. Biologics Price Competition and Innovation Act (BPCIA). Together, these forces define market access, competition timelines, pricing outcomes, and patient availability.

Biologics being complex therapeutics derived from living systems have revolutionized modern medicine by enabling highly targeted treatments for oncology, autoimmune diseases, and rare disorders. Their market share has expanded rapidly, accounting for over 40% of global pharmaceutical revenues and projected to surpass small-molecule drugs by 2027[1]. However, they remain among the most expensive therapies, creating systemic affordability challenges. Biosimilars, which are highly similar follow-on products with no clinically meaningful differences from reference biologics, offer a critical pathway for enhancing competition, improving patient access, and reducing healthcare expenditures. Despite regulatory advances, biosimilar uptake remains uneven, particularly in the United States, due largely to complex patent landscapes and litigation barriers

Prior to the BPCIA, there was not a pathway for approval of biosimilars in the US, while the EU established the pathway in 2005. Now there are nearly 70 FDA approved biosimilars for 19 different reference products, since the first FDA approval of a biosimilar in 2015[2]. Regulatory policy is shifting to enhance access to affordable medicine. In Sep 2025, the FDA announced a first-ever regulatory change, allowing the waiver of clinical efficacy studies for certain biosimilar monoclonal antibodies[3]. The FDA's draft guidelines, published on Oct 29, 2025, propose to reduce "unnecessary clinical testing" of biosimilars, allowing manufacturers to use analytical testing instead[4].

A detailed comparative review of global regulatory frameworks reveals increasing convergence around the principles of stepwise comparability, totality-of-evidence, and extrapolation of indications. The European Union continues to serve as the global benchmark, while the U.S. FDA's unique "interchangeability" designation introduces pharmacy-level substitution, significantly affecting market dynamics. Emerging markets such as India, China, Brazil, South Korea, and Japan have developed robust biosimilar pathways, though regulatory fragmentation, local reference product requirements, and divergent clinical standards continue to hinder global harmonization and increase development costs.

At the core of market entry challenges lies the biologics patent landscape. Innovator companies systematically construct dense patent thickets comprising formulation, manufacturing, and method-of-use claims, extending effective market exclusivity far beyond primary patent expiry. Case studies of Humira and Enbrel demonstrate how layered patent strategies combined with aggressive litigation can delay U.S. biosimilar entry by up to a decade compared to Europe, resulting in massive revenue retention for originators. These practices reflect a broader shift from molecule-centric to lifecycle-centric patenting, emphasizing substitution, uncertainty, and strategic portfolio expansion.

1 Global Pharma Industry Outlook: The Ups and Downs & Projections Near Term, DCAT Value Chain Insights (May 30, 2024).

2 https://www.fda.gov/drugs/cder-conversations/commemorating-15th-anniversary-biologics-price-competition-and-innovation-act.

3 https://www.pharmacytimes.com/view/fda-to-waive-clinical-efficacy-studies-for-monoclonal-antibody-biosimilars.

4 https://www.fda.gov/media/189366/download.

The paper provides an in-depth analysis of the BPCIA framework, which governs biosimilar approvals and patent litigation in the U.S. The statutory "patent dance" and the 180-day Notice of Commercial Marketing have created a complex litigation choreography that significantly influences launch timing and settlement strategies. Landmark judicial decisions, including Sandoz v. Amgen, have reshaped litigation tactics, granting biosimilar developers greater procedural flexibility while preserving innovators' ability to leverage extensive patent portfolios. As a result, biosimilar companies pursue three primary market entry pathways: structured litigation, at-risk launches, or negotiated settlements-each involving substantial financial and legal trade-offs.

Market data analysis reveals strong growth trajectories for both biologics and biosimilars but also identifies a persistent "biosimilar void," wherein only approximately 10% of biologics losing patent protection have biosimilars actively in development. Factors contributing to this gap include high development costs, regulatory fragmentation, manufacturing complexity, and litigation risk. Strategic alliances, licensing structures, and geographic carve-outs have therefore emerged as critical tools for managing regulatory heterogeneity and optimizing global commercialization strategies.

In conclusion, the biologics and biosimilars sector stands at a critical inflection point. Regulatory agencies are increasingly embracing science-based efficiency, while innovators continue to deploy sophisticated IP strategies to extend exclusivity. The interplay between regulatory reform, patent law evolution, and market competition will ultimately determine whether biosimilars can fulfill their promise of improving access, reducing costs, and sustaining innovation. Policymakers, regulators, industry participants, and healthcare stakeholders must collaboratively address systemic barriers to unlock the full societal and economic potential of biosimilars in the coming decade.

# Introduction – The Era of Biologics and Biosimilars

The pharmaceutical industry is currently defined by the era of biologics, representing a major advance in medicine. Biologics are complex, large-molecule drugs like vaccines, therapeutic proteins, and gene therapies and derived from living organisms. Unlike simple small-molecule drugs, biologics are highly heterogeneous and are uniquely produced by living systems.

Biologics revolutionized healthcare starting around the 2000's by offering highly targeted therapies for previously untreatable, unmanageable diseases. Their market presence has surged, growing from 31% of the global pharmaceutical market in 2017 to 42% by 2023[1], and are projected to surpass small molecules in market share by 2027[2]. This shift is leading toward precision medicine, offering treatments tailored to a patient's genetic makeup for better outcomes and fewer side effects.

The high cost of originator biologics necessitates competition, which is provided by biosimilars, i.e., follow-on products confirmed to be highly similar to the approved Reference Product Sponsor (RPS) with no clinically meaningful difference in safety or potency[3]. Biosimilars are crucial because, upon approval, they introduce market competition, affordability and patient access to life-saving treatments, thus promoting sustainable healthcare systems. The US's BPCIA pathway for litigation landscape provides key insights and strategies used by both the RPS and the biosimilar companies in launching their products and keeping competition off the shelf.

Navigating this field requires a careful regulatory balance: IP laws both patents and data exclusivity are essential to incentivize the massive R&D investment by originator companies. Simultaneously, scientifically rigorous approval pathways for biosimilars are vital. By providing a clear, accelerated route for equivalents, regulators foster the competition needed to drive down costs and ensure affordability. This paper aims to analyze how global regulatory pathways intersect with IP, BPCIA litigation, and market strategies to maintain this balance.

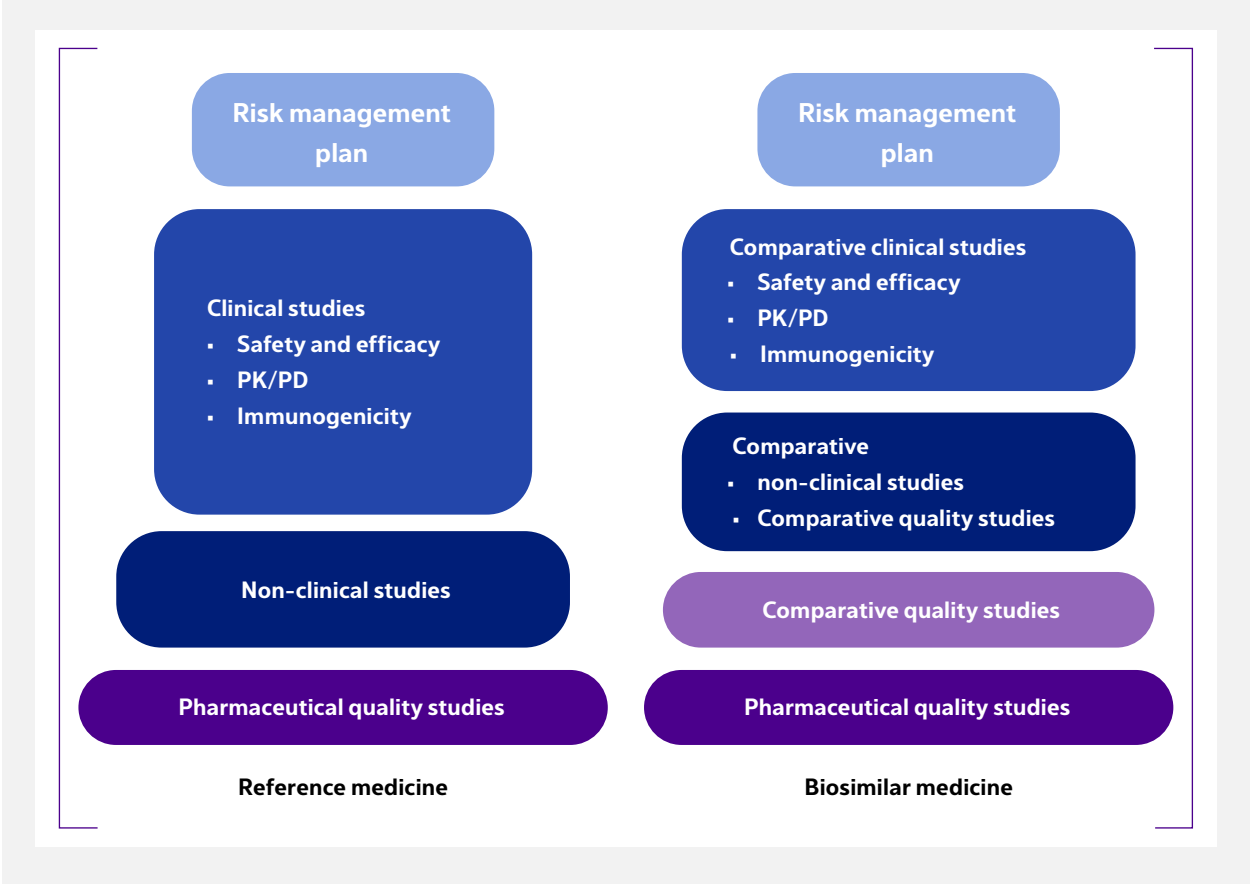
1 Global Pharma Industry Outlook: The Ups and Downs & Projections Near Term, DCAT Value Chain Insights (May 30, 2024),: https://www.dcatvci.org/features/global-pharma-industry-outlook-the-ups-and-downs-projections-near-term/.

2 id

3 Biologics Price Competition and Innovation Act of 2009, Pub. L. No. 111-148, § 7001, 124 Stat. 119, 804 (2010).

# The Developmental Cycle for Biologics and Biosimilars

Manufacturing biologics is complex, starting with the synthesis of the DNA sequence for the desired protein, which is then engineered into a living host cell line. This cell line acts as a factory, producing the protein, which is later harvested, purified, and prepared as the final drug. For a follow-on drug to be classified as a biosimilar, its active protein must have the exact same amino acid sequence and 3D folding as the originator. Since living cells are inherently variable, minor structural changes can occur. Therefore, strict regulatory standards demand that any such variability must be maintained within a narrow, acceptable window to guarantee the biosimilar's efficacy and patient safety.




*Comparison of data requirements for approval of a biosimilar versus reference medicine as published by the EMA*

**Development & Lead Identification Phase:** The R&D strategy for a pharmaceutical company varies significantly between RPS and biosimilars. The discovery process for a new biologic is focused on innovation; it begins with target identification and requires extensive research to find a novel molecule. This involves techniques like high-throughput screening (HTS) and in-silico methods to identify promising "lead" molecules, which are then refined for optimal potency and stability.

Conversely, biosimilar development is a reverse engineering effort. The primary goal is not discovery, but precise replication. This phase requires rigorous characterization of the reference biologic and the subsequent creation of an expression system capable of producing a copy that is "highly similar," ensuring low toxicity and high stability

**Preclinical Requirements (Non- clinical):** The pre-clinical requirements for an original biologic and a biosimilar differ significantly due to their distinct development goals. A new biologic must establish its safety, purity, and potency from the ground up, necessitating an extensive non-clinical program that includes comprehensive mechanistic, pharmacology, and toxicology studies before human trials begin.

In contrast, the pre-clinical phase for a biosimilar is fundamentally comparative and abbreviated. Its goal is simply to demonstrate that it is highly similar to the approved reference product, with no clinically meaningful differences. This is achieved through a stepwise process involving rigorous analytical characterization to prove functional and physicochemical similarity.

Achieving a high degree of analytical similarity is key, as it allows for a reduced scope of subsequent non-clinical and clinical testing, often permitting animal toxicity studies to be significantly reduced or entirely waived[1].

**Clinical Trials Phase I, II, & III:** Phase I, II, and III clinical studies are mandatory to guarantee the safety and efficacy of the new biologic. On the contrary, biosimilars optionally skip Phase II clinical trials, as dosage to be same as the reference product and therefore may not need to be tested extensively[2]. These differences help biosimilars save ~3-4 years in the development cycle and approx. 10-20% of the total cost[3].

**Table 1: Comparative requirements in clinical trial phase I, II, & III between biologics and biosimilars**

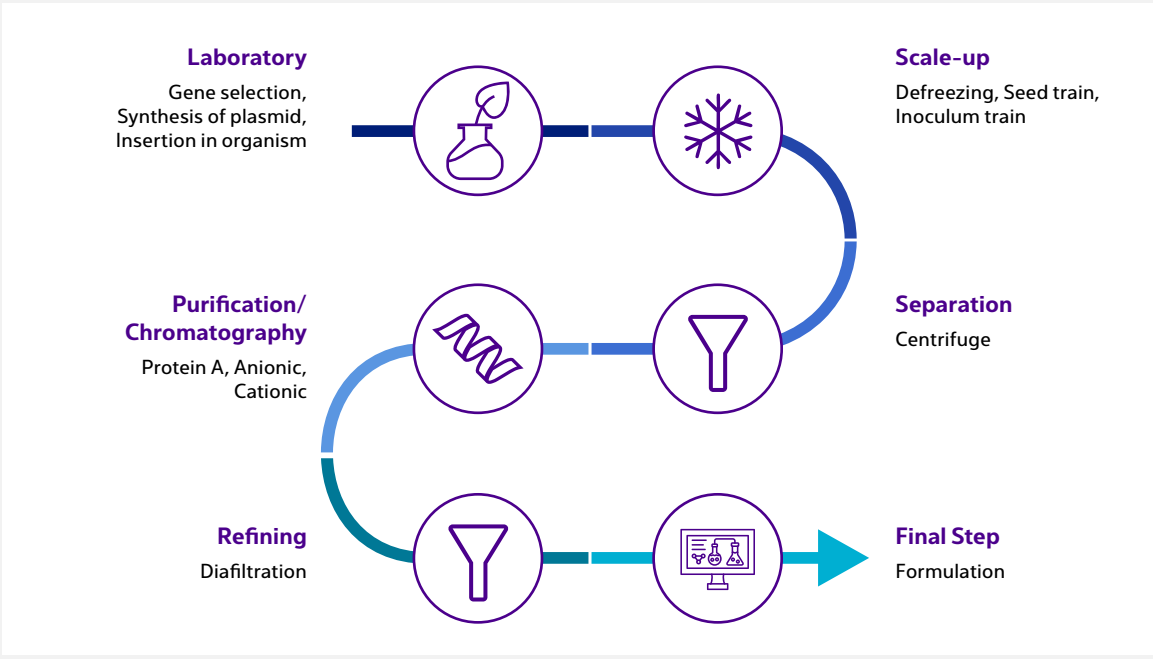
| Phase | Biologics (Reference Product) | Biosimilars (Comparative Product) |
|---|---|---|
| **Phase -I** | **Goal:** Assess safety, dose-limiting toxicity (DLT), and initial PK and PD in a small group.<br>**Study Design:** Single Ascending Dose (SAD) and Multiple Ascending Dose (MAD) are usually in healthy volunteers (where ethically appropriate) or patients.<br>**Focus:** Identifying the Maximum Tolerated Dose (MTD) and understanding how the drug behaves in the body. | **Goal:** Demonstrate PK and PD similarity to the reference product. Safety and immunogenicity are also monitored.<br>**Study Design:** Comparative PK/PD study, often a crossover design (or parallel for long half-lives) in healthy volunteers (preferred for sensitivity).<br>**Focus:** Statistically proving that the biosimilar's concentration (PK) and biological effect (PD) are within a tight pre-defined equivalence margin to the reference product. |
| **Phase II** | **Goal:** Determine optimal dose regimen and initial efficacy in the target patient population. | **Often Waived or Omitted.** The dosing regimen is already established by the reference product, removing the need for dedicated dose-finding trials. |
| **Phase III** | Goal: Conduct large, randomized, controlled trials (RCTs) to confirm efficacy and safety in a diverse patient population and provide substantial evidence for approval. | Goal: Comparative Clinical Efficacy Study (CCS). The trial is an Equivalence Study, not a superiority or non-inferiority study. The aim is to confirm that the biosimilar and reference product have equivalent clinical outcomes in one highly sensitive indication of the reference product. |
| **Immunogenicity** | Assessed throughout all phases, with focus on identifying the rate of anti-drug antibodies (ADAs). | Required & Critical. Comparative immunogenicity data (ADA incidence and titer) is collected in the comparative clinical study to ensure no meaningful difference exists that could impact safety or efficacy. |

1 U.S. Food & Drug Admin., Development of Therapeutic Protein Biosimilars: Comparative Analytical Assessment and Other Quality-Related Considerations, Draft Guidance for Industry (May 2019)

2 Chirag, A. G., and E. W. Stolk. The Global Biosimilar Market: Development, Regulatory, and Commercial Considerations. Pharmaceut Reg Affairs 4 (2015): 1000140.

3 Filipa Mascarenhas-Melo et al., An Overview of Biosimilars—Development, Quality, Regulatory Issues, and Management in Healthcare, 17 Pharmaceuticals 235 (2024),

### Biomanufacturing Process




**Manufacturing Process:** A biologic's quality is intrinsically tied to its proprietary (often patented) manufacturing process. Since each manufacturer utilizes a unique host cell bank and resulting cell line, biosimilar developers must create their own distinct processes, involving *E. coli*, yeast, or mammalian cell lines (CHO, HEK) and media. This means the resulting biosimilar will inevitably possess minor structural differences from the original reference product. Consequently, regulators require biosimilars to provide rigorous proof that they are equivalent to the reference product in terms of safety, efficacy, and quality, while also maintaining the same dosing and administration route (posology).

The manufacturing process is guided by understanding the Critical Quality Attributes (CQA) and the Quality Target Product Profile (QTPP) of the reference biologic. Biosimilar makers use advanced laboratory techniques to meticulously characterize the reference product's structure (primary and higher order), post-translational modifications, size, aggregation, binding, and biological activity. This knowledge then informs the upstream process (cell line creation and production) and the downstream process (isolation and purification).

**Formulations:** The formulation of a biosimilar is a critical and strategic step in the approval process, as manufacturers can deliberately choose a new formulation (liquid, frozen, or lyophilized) that differs from the original. Regardless of the form, the final medicine requires the precise addition of components like stabilizers and surfactants to shield the protein structure from stress, aggregation, and damage during preservation. Also, the manufacturing process is so vital, it must be efficient and consistent. Following ICH Q5E guidelines[4], any time a manufacturer changes the process, they must thoroughly study the product's Critical Quality Attributes both before and after the change to ensure quality remains uncompromised.

4 ICH, Comparability of Biotechnological/Biological Products Subject to Changes in Their Manufacturing Process (Q5E Guideline) 1 (June 2005),

**Post Marketing Studies:** Post-marketing surveillance or pharmacovigilance is a critical component of the regulatory process for all medicines, but it holds a uniquely enhanced role for complex biological products. As biologics are prone to manufacturing variability leading to the risk of immune response, regulatory agencies require robust, long-term monitoring for both originator biologics and their follow-on biosimilars. While the pre-approval phase for a biosimilar is abbreviated, the post-marketing requirements largely converge with those of the originator biologic, with specific added emphasis on tracing and immunogenicity.

For both originator biologic and biosimilars, standard pharmacovigilance including post-marketing surveillance activities are mandatory. Adverse Event (AE) Reporting, Periodic Safety Update Reports (PSURs) and Risk Management Plans (RMPs) with a unique focus on immunogenicity are required. Originators may require Post-Marketing Commitments (PMCs) for long-term safety studies or registries to study specific safety signals. Traceability is the key for biosimilars with unique tracking being Mandatory. Healthcare providers are strongly encouraged (and in some jurisdictions required) to record the specific brand name and batch number in the patient's record to ensure a safety signal is correctly linked back to the biosimilar manufacturer responsible[5].

**Extrapolation of Therapeutic Indications:** If the biosimilar successfully demonstrates analytical, PK, PD, and clinical similarity in one sensitive indication (e.g., rheumatoid arthritis for an antibody), regulatory bodies like the FDA[6] and EMA allow the manufacturer to extrapolate the clinical findings to the other approved indications of the reference product. This eliminates the need for expensive, time-consuming efficacy trials for every single indication

5 Eur. Med. Agency, guideline on good pharmacovigilance practices (GVP): product- or population-specific considerations ii: biological medicinal products 4 (sept. 2017).

6 FDA, Guidance for Industry: Scientific Considerations in Demonstrating Biosimilarity to a Reference Product 17–19 (2019).

# The Regulatory Framework for Biosimilar Approvals

## 1. European Union: The Pioneer

The EU leads the world in establishing a clear, scientifically rigorous process for approving biosimilars. This pioneering effort stems from a crucial understanding that biological medicines as complex, large-molecule products derived from living systems do not allow for exact, identical generic copies. Consequently, they developed a specialized pathway that focuses on confirming that the biosimilar is effectively the same as the original drug, exhibiting no clinically meaningful differences.

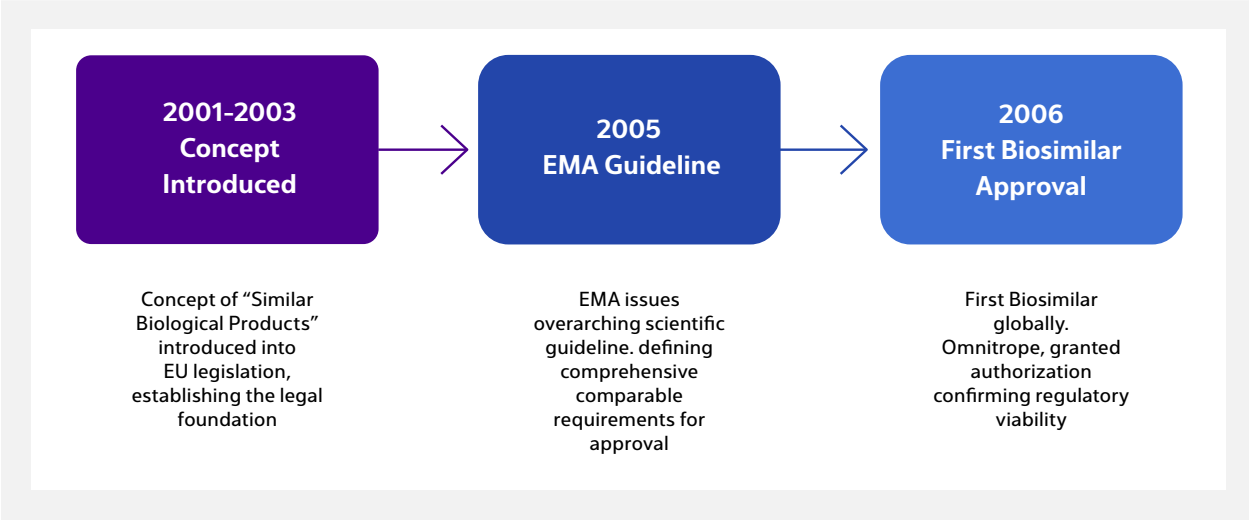



*Fig: Key milestones spearheaded by the European Medicines Agency (EMA)*

A stepwise comparability approach requires manufacturers to demonstrate similarity through rigorous analytical and functional head-to-head testing. This data is then supplemented by focused clinical trials to confirm equivalent safety and efficacy.

A major benefit of the EU concept, validated by the European Medicines Agency (EMA), is the extrapolation of indications. When a biosimilar proves its similarity in one key use, the existing safety and efficacy data can be scientifically extended to cover all other reference product indications, significantly speeding up development and eliminating unnecessary studies.

The EU's long-standing clinical experience has proven that biosimilars are safe and effective. Their science-led framework has been critical not only for fostering market competition and improving patient access within Europe but also for establishing the global standard that regulatory bodies, like the FDA, have since adopted. The EU is an undisputed pioneer in the field and is evident in the comparative list of biosimilar adoption.

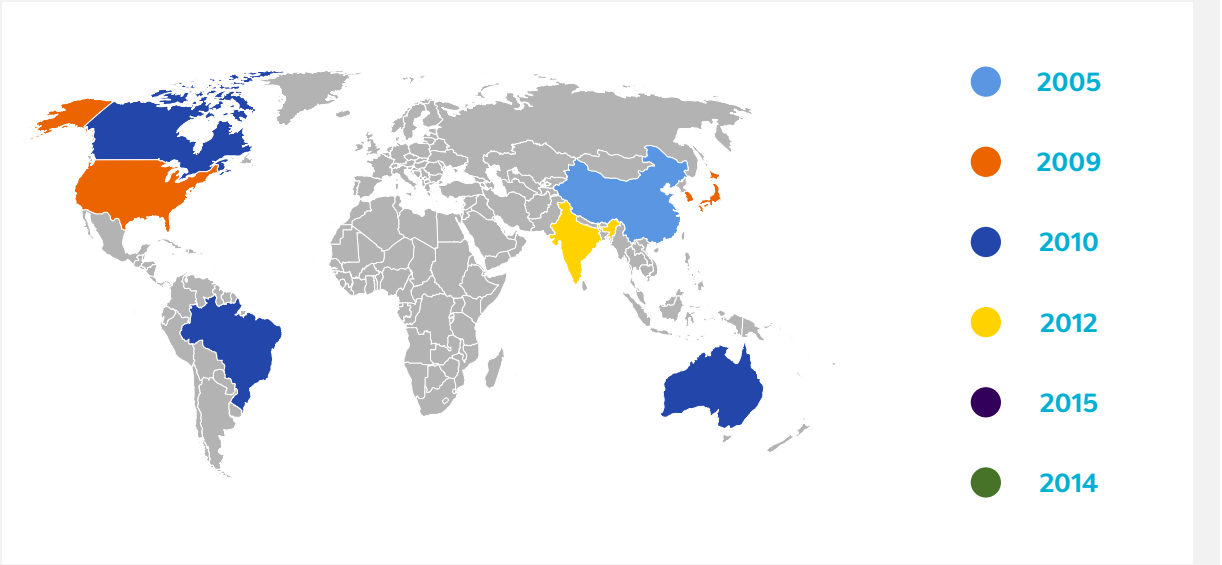
# 2. The US FDA's Interchangeability

The US FDA licenses biosimilar products through the abbreviated 351(k) Biologics License Application (BLA) pathway, established by the BPCIA of 2009.

351(K) Pathway was designed to reduce the time and cost of development by allowing manufacturers to rely, in part, on the FDA's prior finding of safety and effectiveness for an approved reference product. The core requirement of this pathway is proving, through a "totality-of-the-evidence" approach, that the proposed biosimilar is "highly similar" to the reference product (allowing only minor differences in inactive components) and has "no clinically meaningful differences" in safety, purity, or potency. This proof begins with extensive comparative analytical studies and is supported by comparative non-clinical and clinical data, including studies on pharmacokinetics, pharmacodynamics, and immunogenicity.

**US FDA's distinctive Role of Interchangeability:** A key aspect of the agency's' framework, and where it has acted as a pioneer, is the designation of "Interchangeable Biosimilar." The interchangeable biosimilar designation, a subset of FDA-approved biosimilars, requires manufacturers to meet additional statutory requirements. A biosimilar can be deemed interchangeable if the manufacturer provides data demonstrating that firstly it is expected to produce the same clinical result as the reference product in any given patient[1]. Secondly, for a product administered more than once, the risk of alternating or switching between the biosimilar and the reference product is no greater than the risk of using the reference product without such alternation or switch (known as "switching study")[2]. This designation is critical because, subject to state pharmacy laws, it allows an interchangeable biosimilar to be substituted for the reference product at the pharmacy level without the need for the prescriber's intervention, similar to how generic small-molecule drugs are substituted for their brand-name counterparts.

### Timeline for Regulatory Pathway Established for Biosimilars




1 Public Health Service Act (PHS Act), 42 U.S.C. § 262(k)(4)(A), 2018.

2 Id.

A pivotal distinction between the two regulatory bodies is the FDA's formal authorization of pharmacy-level substitution. While EMA scientifically supports the interchangeability of biosimilars, it lacks a federal designation, leaving the authority to permit substitution up to the individual national governments in the EU. The FDA's interchangeability status, a pioneering concept, provides a unified, federal mechanism in the U.S. designed to rapidly boost market access and use of these lower-cost biologic alternatives.

## 3. India – "Similar Biologics"

India has positioned itself as a global leader in the production and supply of affordable biological medicines. The regulatory framework for these products, officially termed "Similar Biologics," is robust, science-based, and continuously evolving to align with international standards.

Unlike the single-agency approach in many western nations, the approval of "Similar Biologics" in India involves two key governmental bodies, which ensures scrutiny from both clinical/marketing and genetic/manufacturing safety perspectives:

i. **Central Drugs Standard Control Organization (CDSCO):** Headed by the Drugs Controller General of India (DCGI), is the apex body responsible for granting final approval for the marketing and manufacturing of the Similar Biologic, as per the *Drugs and Cosmetics Act, 1940*. It also approves the clinical trial protocols.

ii. **Department of Biotechnology (DBT):** Operating through the Review Committee on Genetic Manipulation (RCGM), is responsible for overseeing the R&D, and preclinical evaluation of all recombinant DNA-derived products, including Similar Biologics.

**The Stepwise Comparability Approach:** The Indian guidelines, most recently updated in 2016 (and with further revisions proposed in draft form), mandate a stepwise comparability exercise to demonstrate that the "Similar Biologic" is highly similar to the approved Reference Biological Product (RBP), which must be either an innovator product licensed in India or one from an International Council for Harmonization (ICH) country.

**Table 2: Analysis of the data requirements which are abbreviated compared to a novel biologic in India**

| Phase | Assessment Focus | Key Requirement |
|---|---|---|
| **Quality** | Comprehensive analytical comparison (the foundation) | Detailed head-to-head comparison of structural, physicochemical, and biological properties. High analytical similarity is mandatory. |
| **Non-Clinical** | Pharmacodynamics (PD) and Toxicology | In vitro assays are strongly preferred to animal studies. Animal studies are waived unless residual uncertainty remains or if the in vitro assays are deemed insufficient. |
| **Clinical** | Pharmacokinetics (PK), Pharmacodynamics (PD), and Immunogenicity | Comparative PK/PD studies are the next critical step. Confirmatory Phase III clinical efficacy trials may be waived if robust analytical, non-clinical, and PK/PD data confirm a high degree of similarity, as per newer draft guidelines. |
| **Immunogenicity** | Potential for unwanted immune response | Assessed comparatively across all clinical studies. |

**Extrapolation of Indications:** A similar biologic that gains approval based on clinical trial data from a single, sensitive indication can have its approval extrapolated to all other approved uses of the RBP. This is only permissible provided that the mechanism of action, receptor target, and patient population are consistent across every indication, and the product's safety and immunogenicity profile is thoroughly documented and characterized[3].

**Post-Marketing Surveillance (PMS):** Due to the abbreviated pre-market data, the Indian guidelines place a significant emphasis on post-approval monitoring. A Risk Management Plan (RMP) and a formal Phase IV study (long-term safety and immunogenicity) are mandatory to ensure the continued safety and efficacy of the Similar Biologic in a real-world setting[4]. In essence, India's regulatory framework balances the need for scientific rigor and patient safety with the national imperative of increasing patient access to cost-effective biological therapies.

## 4. Canada: "High Degree of Similarity"

The regulatory pathways for biosimilar approval in Canada and the United States, while sharing the common goal of ensuring safety and efficacy based on similarity to a reference product, have key differences, particularly regarding the formal process and the concept of "interchangeability." There is no Federal designation of "interchangeability" in Canada. Automatic substitution is a matter of provincial/territorial jurisdiction. Provinces implement their own policies (e.g., mandatory switching).

The New Drug Submission (NDS) application uses the designating term "Biosimilar Biologic Drug". Further, Canada requires demonstration of "High Degree of Similarity" to the Canadian Reference Biologic Drug (CRBD)[5]. Historically it required a comparative Phase III trial in most cases. However, Health Canada has been moving toward *removing this requirement* in updated guidance, focusing instead on analytical and comparative PK/PD data, mirroring global trends[6].

## 5. China: "Totality of Evidence" Approach

In China, biosimilars are formally reviewed under the same New Drug Application (NDA) or Biologics License Application (BLA) pathway as novel biologics. The regulatory review adopts a "totality of evidence" approach, requiring a comprehensive data package with a strong emphasis on analytical characterization and quality attributes to prove similarity. Like global standards, the process requires comparative quality, non-clinical, and clinical studies, all aiming to show that any minor differences from the reference product are not clinically meaningful.

A key, distinctive element of the National Medical Products Administration (NMPA) framework is its requirement for Reference Product Sourcing. The NMPA typically requires that the RP used in comparative clinical studies be sourced from the China-approved version; however, recent reforms permit using non-Chi-

3 Central Drugs Standard Control Org. & Dep't of Biotechnology, Guidelines on Similar Biologics: Regulatory Requirements for Marketing Authorization in India (2016),

4 id.

5 Can. Dep't of Health, Guidance Document: Information and Submission Requirements for Biosimilar Biologic Drugs (2016).

6 Health Can., Draft Guidance Document: Information and Submission Requirements for Biosimilar Biologic Drugs (June 10, 2025).

na-sourced RP if scientific comparability can be demonstrated [7]. Furthermore, the NMPA allows extrapolation of indication [8] on a case-by-case basis, provided a scientific rationale is supplied. Finally, the framework mandates unique proprietary names for each biosimilar to ensure distinguishability in naming for pharmacovigilance purposes.

## 6. Australia: Australian Biological Name

Australia's biosimilar approval pathway was effectively established in August 2008, when the Therapeutic Goods Administration (TGA) adopted key guidelines from the EU on similar biological medicinal products. Later, TGA published its own specific guidance on the evaluation of biosimilars effective July 2013.

The key distinction primarily lies in its naming convention and the policies around substitution and extrapolation, compared to some other major regulatory bodies.

- **Australian Biological Name (ABN):** Biosimilars use ABN without a specific biosimilar identifier or suffix, unlike the FDA. This aims to avoid distinguishing between the biosimilar and the reference product at the active ingredient level, promoting biosimilar adoption.
- **Interchangeability:** The TGA assesses and approves the biosimilar, but the decision regarding interchangeability (*automatic substitution*) is primarily managed by the Government through the **Pharmaceutical Benefits Scheme** (PBS), under the Department of Health. If an approved biosimilar is listed on the PBS as 'a-flagged', it allows for automatic substitution.

## 7. Other Major Markets – Japan, Korea and Brazil

The regulatory pathways for biosimilars in Japan, South Korea, and Brazil are well-established and generally follow the "comparability" principle set by the WHO, focusing on demonstrating high similarity to an approved reference product to justify an abbreviated development program.

- **Japan (Pharmaceuticals and Medical Devices Agency - PMDA):** Japan was an early adopter of biosimilar guidelines, which were first issued by the Ministry of Health, Labour and Welfare (MHLW) in 2009 [9].
- **South Korea (Ministry of Food and Drug Safety - MFDS):** South Korea is a major global player in biosimilar development and manufacturing and was one of the first countries, after the EU, to establish a detailed regulatory framework in 2009 [10].
- **Brazil (National Health Surveillance Agency - ANVISA):** Brazil's regulations, established in 2010 (RDC 55/2010), offer a unique model that provides two primary avenues for follow-on biologics [11].

7 id.

8 C. for Drug Evaluation, Guideline for Similarity Evaluation and Indication Extrapolation of Biosimilars, (2021).

9 Min. of Health, Labour & Welfare, Guideline for the Quality, Safety, and Efficacy Assurance of Follow-on Biologics, PFSB/ELD Notification No. 0304007 (Mar. 4, 2009).

10 Min. of Food & Drug Safety, Guideline on Evaluation of Biosimilar Products (July 2009).

11 Agência Nacional de Vigilância Sanitária, , Resolução da Diretoria Colegiada No. 55, de 16 de Dezembro de 2010, Diário Oficial da União, Dec. 17, 2010 (Braz.)

**Table 3: Comparative Regulatory pathway, requirements and nomenclature for Biosimilars in Japan, Korea and Brazil.**

| Feature | Japan | Korea | Brazil |
|---|---|---|---|
| **Pathway Principle** | Follows an abbreviated path based on a stepwise demonstration of comparability to the reference product.<br>The goal is to show that the biosimilar is highly similar and has no clinically meaningful differences. | Structured as a three-tiered system (Act, Notification, and Guideline) that requires a full comparability data package.<br>The pathway is abbreviated from the new biological product pathway. | ANVISA uses the term "Follow-on Biological Products" and offers two pathways:<br>1. **Comparability Pathway (True Biosimilar):** This is the globally recognized pathway where a complete comparative dossier must be submitted to demonstrate high similarity in quality, safety, and efficacy to the comparator product.<br>2. **Individual Development Pathway (Stand-Alone):** This pathway is more permissive, allowing for a reduced dossier with non-comparative or non-parallel clinical trials, which may result in a product that does not meet the strict 'biosimilar' definition but is a 'copy' or 'non-biosimilar' biological product. |
| **Data Requirements** | Emphasizes comprehensive comparative analytical assessments (structural, physicochemical, and biological activities) as the foundation. Clinical data requirements are then tailored based on the level of analytical similarity, often including:<br>▪ Comparative Pharmacokinetic (PK) and Pharmacodynamic (PD) studies.<br>▪ A comparative confirmatory clinical trial (though PK/PD alone may suffice in some cases). | Highly science-driven, focusing on a head-to-head comparison with the reference product:<br>▪ Extensive analytical, functional, and biological characterization.<br>▪ Immunogenicity studies are essential.<br>▪ Comparative PK/PD studies.<br>▪ Comparative clinical studies to assess safety and efficacy (equivalence or non-inferiority). | For the Comparability Pathway, requirements are similar to other major agencies: a stepwise approach starting with extensive analytical comparison, followed by comparative non-clinical and clinical data. |
| **Extrapolation** | Permitted to other indications of the reference product, provided scientific justification, such as the same mechanism of action, receptor involvement, and sufficient safety and immunogenicity characterization, is provided. | Actively permitted. Once biosimilarity is established in one sensitive indication, it can be extrapolated to other approved indications of the reference product with scientific justification. | Permitted for the Comparability Pathway if scientific justification is provided, including identical mechanism of action, same receptors, and adequate safety/immunogenicity data.<br>Unlike the US FDA, Brazil does not have a formal "interchangeable" designation, and automatic substitution at the pharmacy level is generally not regulated at the federal level, though new regulations (like RDC 875/2024) continue to modernize the framework. |
| **Nomenclature** | Uses a distinct naming convention to identify biosimilars (e.g., 'BS' suffix in the non-proprietary name, like 'somatropin BS'). | biosimilars are identified by a unique, market-specific brand name and the internationally recognized INN of the active substance | ▪ Maintains the same INN of the innovator biological medicine in authorized biological medicines – Does not use the term 'biosimilar' |

# 8. Global (ICH) Harmonization of Biosimilar Approval

There exists a need for a single, globally harmonized development program for biosimilars to reduce costs, speed up development, and increase patient access worldwide. However, the existing regulatory framework has difference that pose a greater hurdle towards this goal[12].

## Key Hurdles to Global Harmonization

- **Local Reference Product Requirement:** Many countries (including the EU, U.S., China, Japan, and South Korea) require a biosimilar to be compared against a locally sourced batch of the reference product, forcing developers to conduct additional analytical or clinical bridging studies instead of relying on a single "global comparator".
- **Comparative Animal Toxicology Studies:** Despite a scientific trend away from these tests, at least eight countries (e.g., Brazil, Argentina, China, Iran) still mandate comparative animal toxicology, which the which may provide little value beyond what in-vitro assays offer and contradicts efforts to minimize animal testing.
- **Divergent Clinical Study Designs:** Different health authorities request varying designs for the pivotal clinical study, with some requiring traditional Phase III efficacy trials and others accepting or preferring pharmacodynamic (PD) surrogate biomarkers.
- **Local Clinical Data Requirement:** Some jurisdictions, such as China, Japan, and Taiwan, require additional clinical data to be generated specifically within their local patient populations.
- **Hybrid Product Labels:** While the EMA, FDA, and many other major markets use a generic-style label based solely on the reference product's data, some countries (e.g., Australia, Brazil, China, Japan, Singapore) require a "hybrid label" that includes data from the biosimilar's clinical studies.

Not accepting a global comparator product, requiring mandatory animal toxicology studies and demanding duplicative local clinical data unnecessarily complicate and delay biosimilar development, which ultimately limits patient access and slows financial relief for healthcare systems. This fragmentation explains why biosimilar developers adopt geographic carve-outs (Section 7.6), letting regional partners navigate divergent requirements while the licensor controls IP and development.

12 Global Harmonization of Biosimilar Development by Overcoming Existing Differences in Regional Regulatory Requirements - Outcomes of a Descriptive Review.

# The Biologics Patent Landscape

The biologics patent landscape differs fundamentally from small molecules in one critical way: biosimilar makers cannot simply wait for patent expiration. Unlike generic applicants who face only a foundational patent and a use patent, biosimilar developers must contend with a multi-layered 'patent thicket' constructed by innovators to extend exclusivity well beyond the original patent term.

This patent thicket strategy works because innovators systematically file secondary patents covering formulations, manufacturing processes, and therapeutic indications (methods of use). The foundational product patent, filed early in development, is succeeded by a cascade of protective patents, each extending exclusivity by 6–7 years on average.

This represents a shift from a **'molecule-centric' model** (one dominant patent protecting one molecule) to a **'lifecycle-centric' model** (multiple patents protecting one molecule across its commercial lifespan). Top-selling U.S. biologics now carry ~70 granted patents, each contributing to this thicket. Formulation patents extend exclusivity by ~6.5 years; method-of-use patents by ~7.4 years[1].

Notably, pharmaceutical companies adopt a tiered filing strategy: conservative early patenting during high-risk development phases (broad but risky claims), followed by aggressive, targeted patents later when the drug's value and safety profile are proven. This allows companies to generate specific data and file more defensible applications protecting formulations and indications, the true drivers of market life extension.

**Patent Value Creation – Substitution Patenting & Uncertainty:** The industry tactic of "substitution patenting" involves filing patents on minor improvements, like new formulations or indications, to extend a drug's effective market life (biologics and API's). While patenting DNA sequences may not be a primary focus for therapeutic biologics, companies aim for diversification by filing formulation and preparation patents later in the drug's lifecycle.

However, timing is a major hurdle, a patent filed after the drug's public launch risks being invalidated due to a lack of novelty (prior disclosure). Therefore, formulation patents are only effective if they represent a significant improvement and are filed before regulatory disclosure. This crucial constraint raises questions about patent strategies relying solely on late-stage formulation patents, leading many companies to shift focus to manufacturing or platform technology as an alternative.

Ultimately, companies engage in creating competitor uncertainty by filing continuous, overlapping patents throughout the drug's lifecycle, a strategy that requires complex portfolio management. Further, patenting mAb's is particularly crucial as unlike small molecules, biologics can be characterized by both the process used to make them and the product itself, requiring careful comparison against existing antibodies.

**Patent Value Creation - Drug Repositioning:** Strategies that focus on developing next-generation recombinant proteins offer significant financial returns when they include meaningful improvements. A prime example is Amgen's second-generation erythropoietin, Aranesp, which achieved sales of $4.1 billion in 2006, surpassing

1 Amy Kapczynski, Chan Park \& Bhaven Sampat, Polymorphs and Prodrugs and Salts (Oh My!): An Empirical Analysis of "Secondary" Pharmaceutical Patents, 7 PLoS One e49470, at e49470,tbl.4(2012).

the $2.5 billion of its predecessor, Epogen[2]. This success stemmed from a key improvement: an approximate three-fold increase in biological half-life, which reduced the dosing frequency from three times to just once per week[3].

Such advancements in the protein structure and formulation necessitate precise claim drafting and careful timing for patent filings. In a study of 180 new pharmaceutical formulations approved by the FDA, the formulations related patents were found to significantly extend product lifecycles[4]. These drug repositioning efforts are more effective amongst smaller biotech companies, due to their lower cost, reduced risk, and shorter development cycles. This strategic patenting for repositioning is likely accelerating the growth of biotech patent applications, potentially at a faster rate than the discovery of genuinely new, breakthrough drugs.

**Early-stage defensive strategy:** Early defensive strategy is designed to set the stage for later offensive filings. This strategy involves initially filing a few broad patents to carve out a protected space, enabling more extensive and specific offensive patenting later in the lifecycle. This strategy targets the later stages of the lifecycle, focusing on 'Uncertainty' and 'Substitution'. However, this broad early patenting is risky as it might encourage competitors to file narrow, challenging patents. Furthermore, late stage 'Substitution' patenting can be difficult, often resulting in granted patents with significantly narrow scopes. Overall, maintaining a large patent portfolio, especially later on, serves a dual purpose, one it decreases the risk of damaging exclusivity litigations and second, can be actively used as a mechanism to avoid lawsuits altogether.

**Humira: Formulation Patent Thicket in the US** AbbVie's defense of Humira exemplifies how a patent thicket with around 70+ Patents in the US was strategically deployed to suppress competition well after the active ingredient patent expired in 2016[5]. This is in comparison to only 8 patents in the European Union around the same time[6]. Shortly after the active ingredient (adalimumab) patent expired in 2016, Boehringer obtained FDA approval in the US for its Humira biosimilar, Cyltezo. However, Abbvie brought suit alleging infringement of 74 Humira patents. The case eventually settled without Cyltezo entering the US market only in 2023. In the interim, Humira earned $114 billion[7] which is far different in the EU where the biosimilar version of Humira was available in 2018[8].

The disparity in patent scope for formulation claims, which are central to building drug patent thickets, stems from different patent examination standards. The USPTO allowed for broad claims covering many ingredients, even if the patent application only provided a "laundry list" of prophetic examples without supporting data. In contrast, the European Patent Office (EPO) enforced a stricter requirement, restricting claims to only the "essential features" of the invention. This practical difference meant the EPO only granted narrowly tailored claims that corresponded specifically to the excipients found in the patent's working examples (i.e., *those with test results*).

2 Amgen Inc., Amgen's Fourth Quarter 2006 Revenue Increased 17% to $3.8 Billion; Full Year 2006 Revenue Increased 15% to $14.3 Billion (Press Release, Jan. 25, 2007).

3 Peter Sandner & Karl Ziegelbauer, Second-Generation Erythropoietin-Stimulating Agents: The Evolution of Drug Innovation, 7 Drug Discovery Today 518, 519 (2008).

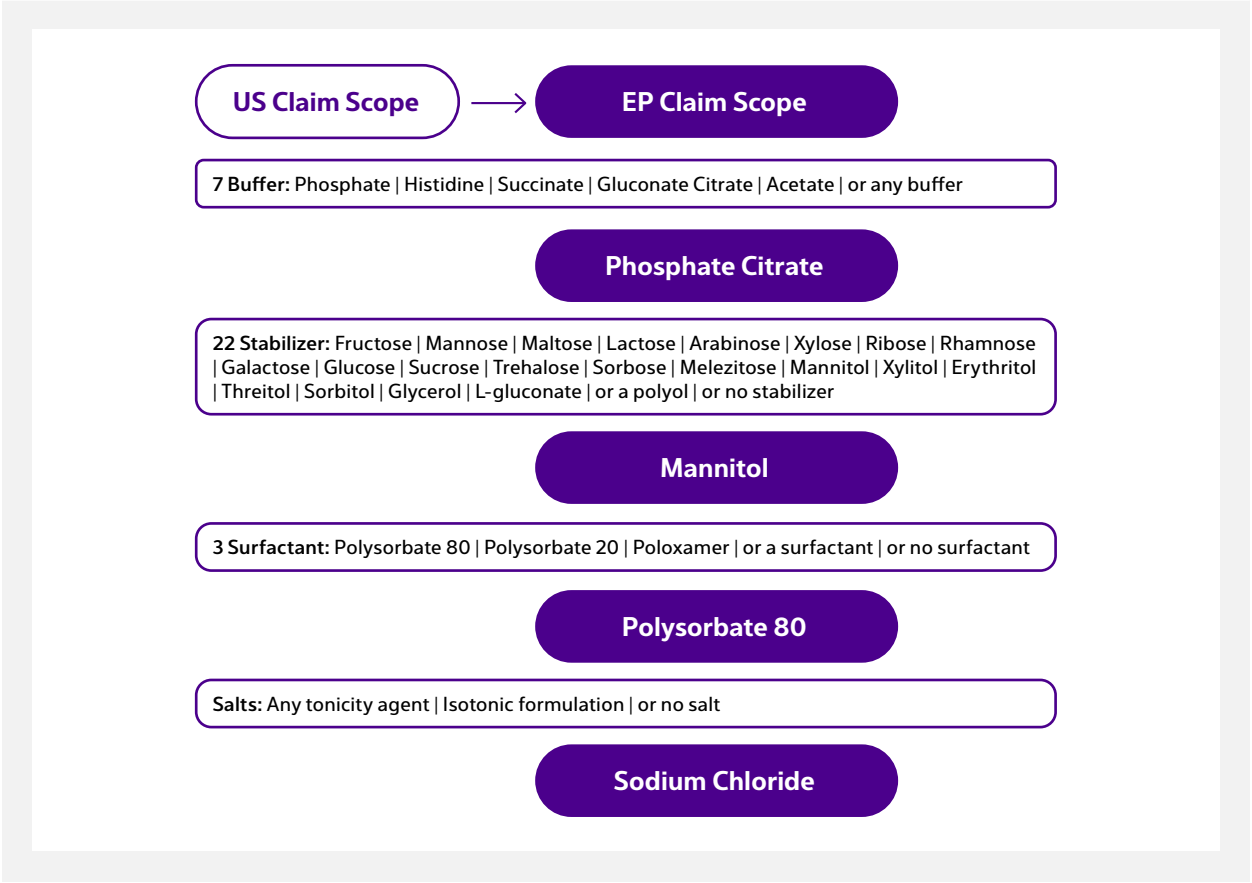
4 Kengo Daidoji, Satoshi Yasukawa & Shingo Kano, Analysis of the Life Cycle Extension Period of New Formulation Pharmaceuticals Utilizing the Orange Book Data, 18 Drug Discovery Today 782, 783 (2013).

5 Bernard H. Chao, USPTO's Lax Policy Leads to Humira Formulation Thicket, 52 J. L., Med. & Ethics 429 (2024).

6 Rachel Goode & Bernard Chao, Biological patent thickets and delayed access to biosimilars, an American problem, 9 J.L. & Biosci. lsac022 (2022).

7 id.

8 Ned Pagliarulo, Humira Biosimilars Launch in Europe, Testing AbbVie, BioPharma Dive (Oct. 17, 2018).




*US and EU claim scope comparison for the Adalimumab formulation patents*

The second key difference between the USPTO and the EPO lies in how each office handled functional claims (claims that define an invention by its result rather than its structure). The USPTO often allowed these functional definitions, leading to extremely broad U.S. patents that could cover a wide range of known and unknown compounds that satisfy the defined function. In sharp contrast, the EPO objected to functional claim language, stating it "lacks clarity" under Art.84 of EPC as it describes a result to be achieved, not the technical means[9]. While this difference undeniably resulted in broader U.S. patents, the EPO's overarching "essential features" requirement was ultimately the larger factor limiting claim scope in Europe. This resulted in 22 US formulation patents vs. 2 EU formulation patents impacting the same biosimilar market in two geographies.

**Offensive strategy with early uncertainty:** Offensive strategy is centered on generating early-stage 'Uncertainty' in their patent portfolios. This involves filing broad patent applications that cover multiple fields, which is intended to increase the private value of the portfolio by preventing competitors from patenting and delaying their market entry. This approach often leads to high levels of patent opposition and litigation.

9 Bernard H. Chao, USPTO's Lax Policy Leads to Humira Formulation Thicket, 52 J. L., Med. & Ethics 429 (2024).

The success of creating 'Uncertainty' is most pronounced when a valid patent is maintained for 5 to 10 years after the expiration of the original patent. However, increasing 'Uncertainty' later in the drug lifecycle may be less effective. The strategy then shifts focus on generating private value through selective product 'Substitution' (incremental improvements) later on.

The ability to build this "internal patent thicket" through 'Uncertainty' and 'Substitution' may be facilitated by a perceived weakness in patentability requirements and the ease of patenting particularly regarding obviousness. Since the patent system does not distinguish between breakthrough and incremental improvements, it has inadvertently incentivized these strategic behaviors, leading to a high volume of patents that are often low in commercial or technical value. This ambiguity creates significant competition due to the high costs associated with litigation or competitor market entry.

**Enbrel: Amgen's 30 Years Patent Thicket Monopoly** Amgen strategy successfully building a "patent thicket" around its blockbuster drug, Enbrel (etanercept), to extend its U.S. monopoly and block biosimilar competition until 2029 is a classic case study. The original patent for Enbrel (first sought in 1992) would have expired much earlier (around 2010), but Amgen's IP strategy is expected to keep biosimilars off the U.S. market until 2029, resulting in an approximately 37 years of total exclusivity and cumulative sales potentially approaching $100 billion[10].

Amgen created a "patent thicket" around their product after acquiring Immunex in 2002 by aggressively filing dozens of new patents covering manufacturing, formulation, and methods of use. This defense was bolstered by the most crucial patents, which Immunex had licensed from Hoffmann-La Roche in 1999[11]. Due to a quirk related to pre-TRIPS filing dates, these key patents were granted a 17-year term upon issuance in 2011/2012, effectively extending market protection until 2028 or 2029[12]. These patents, related to a fusion protein and a DNA encoding it, were filed in the early 1990s.

A combination of patent strategy with aggressive litigation strategy successfully kept biosimilar away from the market. Amgen successfully defended these key patents in court against biosimilar applicants like Sandoz (Erelzi) and Samsung Bioepis (Eticovo). The Federal Circuit affirmed the validity of the patents, and the Supreme Court declined to hear the appeal, resulting in an effective total market blockade for these biosimilars approved by FDA since 2016[13]. In contrast to the U.S. blockade, Enbrel biosimilars launched in Europe in 2016 and quickly took a significant market share, driving prices down substantially[14].

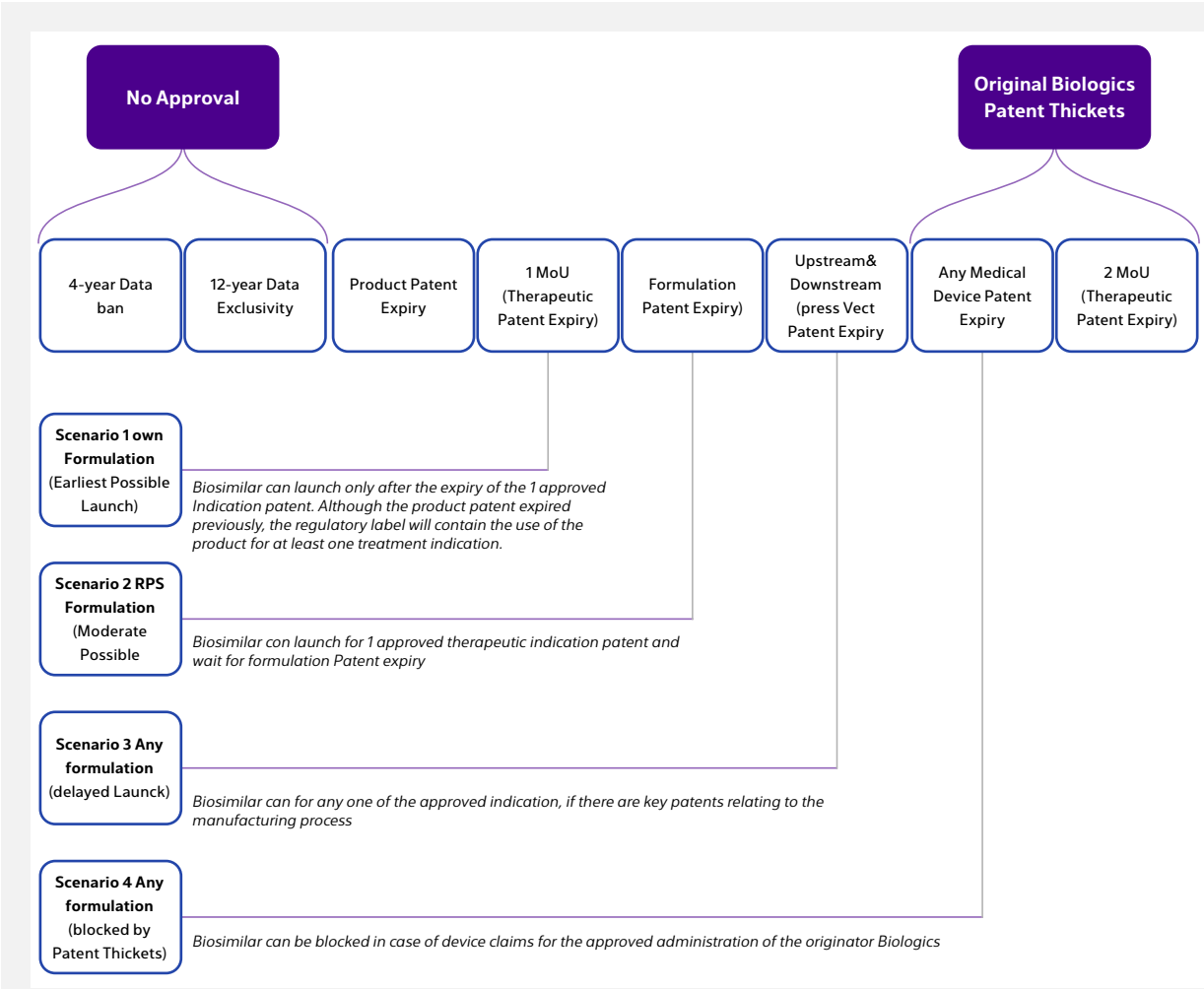
10 Jonathan Gardner, A three-decade monopoly: How Amgen built a patent thicket around its top-selling drug, BioPharma Dive (Nov. 1, 2021),

11 The Pharmaceutical Patent Playbook: Forging Competitive Dominance from Discovery to Market and Beyond, DrugPatentWatch (Oct. 17, 2024),

12 id

13 Sandoz Reviewing Options After Federal Circuit Upholds Lower Court Ruling in Biosimilar Erelzi Case, Novartis (July 2, 2020).

14 Initiative For Meds., Access & Knowledge (I-Mak), Over patented, overpriced: How Amgen Stretched Its Enbrel Monopoly for Decades (Oct. 6, 2020)




*An exemplary Biosimilar Strategy mapping launch date with regulatory and Patent Expiry timelines*

### Product vs. Process Patent Strategies in Biologics

In nearly all patent strategies, product patents and formulations are filed much more frequently than process patents. This preference exists because product patents are viewed as more effective tools for the strategic goals of creating 'Uncertainty' and facilitating 'Substitution' throughout the drug's lifecycle management. For instance, an improved formulation patent (product-focused) is more defensible in court than a process claim limited to 'a bioreactor operated at pH 6.8,' which competitors can easily design around.

This focus on the product aligns with the fact that trade secrecy is often a better protection mechanism for complex manufacturing processes than it is for the final product. Since a drug's composition must be made public for regulatory approval, it's easier to secure the product with patents, while the intricate, proprietary manufacturing steps can often be kept confidential as a trade secret, a practice more common among large, resourceful companies.

Although process patents may sometimes be filed early suggesting an initial strategy shared with chemical drugs, their limited use later in the lifecycle indicates they are generally less effective at boosting drug lifecycle value due to difficulties in enforcement.

Furthermore, the prevalence of product-oriented patenting is supported by the increasing trend of drug repurposing i.e., finding new uses for existing drugs, as these efforts typically result in new product claims rather than process-related claims. While blocking patents (broad subject matter like gene sequences) have historically been used, patenting gene sequences is now less frequent, likely due to recent restrictions likely due to the Supreme Court's interpretation in *Amgen Inc. v. Sanofi* (2023), which tightened enablement requirements under 35 U.S.C. § 112(a) for biotechnological sequences.

Ultimately, while the findings show a strategic similarity in the use of formulations and peptides across patent strategies, a detailed technical analysis of the claims within the context of biologics is necessary to fully understand the strategic attributes of patenting around each drug class.

# Understanding BPCIA -15 Years and Still Going on!

## 1. The Biologics Price Competition and Innovation Act (BPCIA)

The BPCIA, enacted in 2010 as part of the Patient Protection and Affordable Care Act, fundamentally transformed the landscape for biologic medicines in the United States. The FDA states that the goals of the BPICA are "to provide more treatment options, increase access to lifesaving medications, and potentially lower health care costs through competition."[1]

The BPCIA achieves this through two interconnected mechanisms: (1) a 12-year data and market exclusivity period protecting the innovator's reference product, and (2) a structured patent dispute process (the 'Patent Dance') governing how biosimilar applicants and innovators negotiate IP disputes before market launch.

## 2. Data Exclusivity

**Phae I:** 4-Year Data Protection (Submission Ban): For the first four years after the reference product is first licensed by the FDA, a manufacturer of a biosimilar product is prohibited from submitting a 351(k) abbreviated Biologics License Application (aBLA) that relies on the reference product's data.

**Phase II:** 12-Year Market Exclusivity (Approval Ban): The FDA is prohibited from making the approval of a 351(k) application effective until 12 years after the date the reference product was first licensed. This is often referred to as market exclusivity, as it effectively blocks market entry of the biosimilar, even if the application was accepted for review after year four. Pediatric exclusivity, like with small-molecule drugs, if the innovator conducts pediatric studies requested by the FDA, an additional 6 months of exclusivity can be added to the 12-year period.

**"First Licensure" is Key:** The clock starts on the date the specific reference product was first licensed under 351(a) BLA. Say, if Biologic X was licensed on January 15, 2010, the 12-year exclusivity clock runs until January 15, 2022, regardless of subsequent approvals for new dosage forms or indications of the same molecule. Hence, this regulatory exclusivity is separate from and runs concurrently with any patent protection. The market entry of a biosimilar is ultimately determined by the *later* of the exclusivity expiration date or the resolution of all relevant patent litigation.

## 3. The 'Patent Dance'

The landscape of biosimilar patent litigation in the United States is primarily governed by the Biologics Price Competition and Innovation Act (BPCIA) of 2009. A unique feature of this framework is a pre-litigation process popularly known as the "patent dance". This structured information exchange aims to govern how patent disputes between an innovator (RPS) and a biosimilar applicant are managed and litigated before a biosimilar product is launched. The "patent dance" is typically triggered when the biosimilar firm submits its aBLA to the FDA.

1 The Biosimilars Pathway, U.S. FOOD & DRUG ADMIN. (last updated Sept. 12, 2024).

The "patent dance" involves several key steps:

1. **Initiation by Applicant:** Within 20 days of the FDA accepting the aBLA for review, the biosimilar applicant is statutorily required to provide the RPS with a copy of the application and other manufacturing information. Only a Biosimilar applicant can initiate this "Patent Dance".
2. **RPS Patent List Exchange:** The RPS then has 60 days to provide the biosimilar applicant with a list of patents Section 42 U.S.C. 262(l)(3) it reasonably believes could be infringed and indicating willingness to license any of them.
3. **Applicant's Response to Claims:** Within another 60 days, the biosimilar applicant must provide a detailed, claim-by-claim statement outlining the factual and legal bases for any assertions of invalidity, unenforceability, or non-infringement, or whether it would accept a license.
4. **RPS Rebuttal:** Within another 60 days, the RPS provides a reciprocal statement defending its position on infringement and validity.
5. **Negotiation and First Wave Litigation:** After the RPS responds, the parties engage in a 15-day good-faith negotiation period to agree on a list of patents for immediate litigation (the "first wave"). If no agreement is reached, both parties exchange lists for court action. During the 'first wave,' the biosimilar applicant first discloses how many patents it will list, and the parties simultaneously exchange patent lists within 5 days after the disclosure. The RPS may not list more patents than the biosimilar application except, if the biosimilar applicant lists none, the RPS can list one Patent. The RPS then has 30 days to file a patent infringement complaint asserting the patents listed by both parties. If the RPS does not file a complaint within 30 days, it faces certain ramifications such as limiting its damages recovery to only a reasonable royalty.
6. **Second Wave Litigation:** A "second wave" of litigation can be triggered by the biosimilar's 180-day notice of commercial marketing, which can be provided before or after FDA approval. During this phase, the RPS can assert any remaining patents not included in the first wave and may seek a preliminary injunction to prevent the biosimilar from launching.

If the biosimilar applicant initiated the patent dance, neither party may bring a declaratory judgment action on patents that were not included in first-wave litigation until the biosimilar applicant provides 180-day notice of commercial marketing. If, after initiating the patent dance, the biosimilar applicant skips parts of the dance, the biosimilar applicant may face ramifications. For example, the RPS, but not the biosimilar applicant, may bring a declaratory judgment action of infringement, validity, and enforceability on patents if the biosimilar applicant "failed to complete an action".

180 day notice of commercial marketing (NCM): At least 180 days before the biosimilar is first marketed, the biosimilar applicant must give notice to the RPS. Upon receipt of the 180-day NCM, the RPS can immediately initiate 'the second wave' litigation, seeking a preliminary injunction to prevent the biosimilar's commercial launch. During this litigation, RPS can enforce any patents from the initial list (Section 262(l)(3) patent lists). If the RPS does not bring a preliminary injunction action, or if the court refuses to grant a preliminary injunction, the biosimilar may be launched while litigation proceeds.

The "patent dance" creates a legal time-trap for biosimilar developers. They are forced to invest years (~4 years, on average) in costly Phase 3 trials, reach FDA approval readiness, and meet the 20-day aBLA disclosure deadline before initiating patent disputes. Consequently, when litigation finally begins, the RPS's primary patent already be near or past expiration, limiting the innovator's leverage. This delay is reinforced by the judicial "ripeness" doctrine and due to this, biosimilar developers face an extreme financial hazard and

launching "at risk" could expose them to hundreds of millions of dollars in damages if they lose the pending patent infringement lawsuit. The "patent dance" is best summarized as a high-stakes legal and business negotiation that often overrides the formal litigation process intended by the BPCIA.

## 4. Interchangeability

An aBLA approval standard that there are no clinically meaningful differences between itself and the reference product in terms of safety, purity, and potency assures prescribers and patients that the biosimilar is just as safe and effective as the originator. However, a "biosimilar" designation alone does not permit automatic substitution at the pharmacy level. A pharmacist must generally obtain a new prescription or authorization from the prescriber to dispense a non-interchangeable biosimilar in place of the reference product.

The designation of "interchangeable biosimilar" represents a higher regulatory bar and is the BPCIA's equivalent to the automatic substitution afforded to traditional generic drugs. An interchangeable product must first meet all the stringent requirements of a biosimilar, but then must satisfy two additional legal criteria, namely Same Clinical Result & switching risk. The manufacturer must demonstrate that the product is expected to produce the same clinical result as the reference product in any given patient. This ensures a consistent treatment outcome regardless of which product is used. For a product that is administered more than once, the manufacturer must show that the risk of alternating or switching between the interchangeable product and the reference product is no greater than the risk of simply using the reference product continuously. To satisfy this, applicants often conduct "switching studies," which involve administering the originator product, switching patients to the proposed interchangeable product, and then switching them back to the originator to monitor for any adverse effects or loss of efficacy.

**The Impact of Interchangeability: Automatic Substitution:**

The true significance of the interchangeable designation lies in its market access implications i.e., pharmacy-level substitution. Unlike a standard biosimilar, an interchangeable biosimilar may be substituted for the reference product without the intervention of the healthcare provider who prescribed the reference product. This automatic substitution, subject to state pharmacy laws is the most potent driver of market uptake and competition, as it streamlines the process for patients and providers, quickly translating to lower costs in the healthcare system. The first interchangeable biosimilar, Semglee (insulin glargine-yfgn), was approved in July 2021, marking a major milestone in the evolution of the U.S. biosimilar market.

While the BPCIA has successfully fostered the approval of dozens of biosimilars, the path to interchangeability remains complex and costly. The need for additional clinical switching studies can significantly delay market entry and add tens of millions of dollars to development costs, leading many manufacturers to initially pursue the standard biosimilar designation.

Nevertheless, the interchangeable designation is vital. It represents the ultimate fulfillment of the BPCIA's promise i.e., to bring robust, competition-driven price relief to the biologics market by establishing a level of confidence and administrative ease equivalent to that of generic drugs. As more manufacturers invest in the necessary data, the presence of interchangeable biosimilars is expected to accelerate patient access, increase market competition, and drive down the cost of life-saving biologics across the United States.

# Landmark BPCIA Patent Cases & Litigation Strategies

Landmark cases interpreting the BPCIA have fundamentally shaped the landscape for patent litigation and biosimilar market entry not just within the US. Although litigated publicly, patent litigation strategies employed by innovators and biosimilar manufacturers reveal consistent patterns that have evolved over the past decade.

## 1. Landmark BPCIA Patent Cases

### A. The Precedent Setter: Sandoz v. Amgen (Neupogen/Zarxio)

A landmark Supreme Court ruling in Sandoz v. Amgen (2017) significantly impacted the "patent dance". This was the first BPCIA case to reach the Supreme Court and dealt with the biosimilar for Amgen's Neupogen (filgrastim). This decision gave biosimilar applicants more strategic flexibility regarding patent litigation. The Court clarified two critical BPCIA provisions:

- **Information Exchange ("Patent Dance"):** This landmark 2017 Supreme Court decision gave biosimilar developers significant flexibility. The Court held that a biosimilar applicant is not required by federal law to provide its aBLA and manufacturing information to the RPS to initiate the "patent dance" (42 U.S.C. § 262(l)(2)(A)). The exclusive federal remedy for failing to comply with this disclosure is an immediate patent infringement action by the RPS.
- **Notice of Commercial Marketing (NCM):** The Court ruled that the 180-day NCM, which triggers the second wave of litigation, may be provided either before or after the biosimilar receives FDA licensure. This reversed the Federal Circuit's requirement that the notice could only be given after approval.

### B. Amgen v. Sandoz (2020)

Following the 2017 Supreme Court decision in Sandoz Inc. v. Amgen Inc., the Federal Circuit, on remand, addressed whether state law remedies like unfair competition could be used by Amgen to enforce the BPCIA disclosure requirement against Sandoz. The Federal Circuit ultimately held that the BPCIA preempted state law claims, thereby cementing that the remedies detailed within the federal statute's "patent dance" framework are the exclusive mechanism for resolving disputes over a biosimilar applicant's failure to comply with the information disclosure provision.

### C. Janssen Biotech v. Celltrion Healthcare (2017)

The Janssen Biotech v. Celltrion Healthcare (2017) case involved Celltrion's biosimilar of Remicade (infliximab) and established critical consequences for biosimilar applicants who initiate the BPCIA's "patent dance." The court ruled that a biosimilar applicant who initiates the patent dance but then refuses to participate in the required good faith negotiation steps can forfeit the statutory damages limitation, meaning the applicant

may be liable for the reference product sponsor's lost profits instead of being limited to a reasonable royalty. This decision underscored the mandatory and consequential nature of the BPCIA's negotiation phase for any applicant who chooses to participate in the information exchange and wishes to secure the most favorable limits on potential patent infringement damages.

### D. Ongoing Litigation Trends

Recent and ongoing BPCIA litigation continues to shape the biologics market, often concerning high-value reference products:

- **Regeneron v. Celltrion, Samsung Bioepis, et al.:** Regeneron (aflibercept) has successfully used the **U.S. Patent No. 11,084,865** (the '865 patent) covering drug formulations to secure preliminary injunctions against most applicants (Celltrion, Samsung Bioepis, Formycon). The court's decision to deny an injunction against Amgen allowed its biosimilar (Pavblu) to launch while its rivals remained blocked. This creates a temporary first-mover advantage for one biosimilar competitor over others.
- **Amgen v. Celltrion, Samsung Bioepis, et al.:** Several cases related to biosimilars for Amgen's **Prolia/ Xgeva** (denosumab), which have largely resulted in settlements (Sandoz, Celltrion & Fresenius Kabi) often allowing the biosimilar to launch (Sandoz launched in June 2025 and Celltrion & Fresenius Kabi in July 2025. Amgen still has pending BPCIA litigations including Biocon.

These cases are vital in establishing the bounds of the BPCIA, refining the legal strategies available to both innovator and biosimilar companies, and ultimately affecting the timeline for biosimilar market entry and consumer access to lower-cost therapies.

## 2. Litigation and Patent Thickets

The BPCIA established a pathway for biosimilar drugs, aiming to increase competition and lower costs. Studies establish that original biologics have increasingly leveraged BPCIA's patent provisions to deploy extensive patent thickets, successfully delaying market entry.

Analysis of the BPCIA litigation landscape by Big Molecule watch[1] filed since 2014 shows a clear and significant trend that RPSs are asserting a rapidly increasing number of patents against biosimilar challengers. Early litigation phase from 2014 to 2019 showed an average of 13 patents asserted each BPCIA litigation. On the contrary, current litigation trends from 2020-2024 show that an average of 24 patents is asserted in each BPCIA litigation. Only two of the 15 complaints filed in 2023–2024 asserted fewer than 20 patents, demonstrating that a large patent portfolio is now the norm.

This trend is driven by RPS proactively investing in large, diverse patent portfolios to gain leverage in settlement negotiations and to avoid the BPCIA's complicated second-wave litigation process. By asserting as many patents as possible upfront, RPS narrow the pathway to success for biosimilar manufacturers.

1 https://www.bigmoleculewatch.com/2024/12/31/are-reference-product-sponsors-asserting-more-patents-in-bpcia-litigation/.

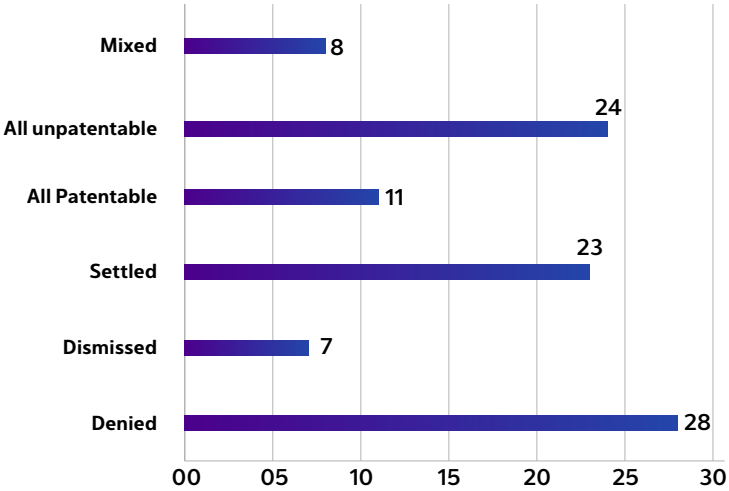
# 3. IPR/PGR – AIA Patent Challenges

An increasingly utilized strategy for biosimilar manufacturers involves challenging RPS patents outside of litigation through USPTO administrative procedures, such as Inter Partes Review (IPR) and Post-Grant Review (PGR). These options were established by the Leahy-Smith America Invents Act (AIA) of 2011 as a more rapid and cost-effective mechanism to invalidate potentially erroneous patents across all industries.

A study published in *Nature Biotechnology* in March 2024[2] provided a comprehensive analysis of the impact of these AIA (America Invents Act) administrative procedures. The methodology examined all public records of FDA-approved biologics and their associated patent filings to identify challenge rates. The study found they are an effective way to correct erroneously granted biologic patents, which could help promote timely drug competition and benefit the US healthcare system.

In this analysis a total of 102 Patents were challenged covering 34 FDA approved biologics of which Forty-three patents (42%) were associated with 87 AIA institutions (84 IPRs, 3 PGRs). The study found that 24 of 43 patents (56%) had all the claims found to be unpatentable, of which 67% (8 of 12) of primary biologic patents and 68% (21 of 31) of secondary patents were invalidated. This suggests that biosimilar developers can challenge primary patents with a ~67% success rate, a notably higher invalidation rate than for small-molecule generic drug patents, indicating that biologic patents may have broader, less defensible claims. Also, the most common and successful ground for challenging a patent was obviousness (35 USC 103), which was the main ground for 100% of patents where claims were found unpatentable.

### AIA Proceeding outcome for all 102 patents




It should also be noted that of the 87 instituted challenges, biologic drug manufacturers filed 51% followed by biosimilar manufacturers 48% which goes to show that these procedures play an equal tool for both RPS and biosimilar manufacturers. The study also observed that for the total of 33 AIA administrative judgments out of 87 (38%) were appealed to the Court of Appeals for the Federal Circuit, leading to 23 affirmations, with the other 10 either procedurally dismissed or settled.

2 Biologic patent challenges under the America Invents Act.

Since AIA challenges have targeted patents associated with a wide variety of biologic drugs, leading to invalidation of all claims about half the time, these results show that AIA challenges work well to invalidate improperly granted patents on biologic drugs. Biosimilar firms may be using these AIA proceedings more frequently and more successfully than their generic small-molecule counterparts. This strategy works well strategically, as these proceedings often are concluded within one year after the decision to institute the AIA challenge.

## 4. Biologics & Biosimilar Litigation Tactics and Market Strategy

An analysis of the U.S biosimilar patent litigation landscape (Appendix) revels the evolving landscape of U.S. biosimilar market entry under the BPCIA. The overwhelming trend is a shift from protracted legal battles to controlled, negotiated market entry via settlement, though key procedural and patent disputes have defined the framework.

**The Dominance of Settlement and Controlled Entry:** The litigation data presented in the Appendix shows that for the majority of reference biologics, including RITUXAN (Rituximab), HERCEPTIN (Trastuzumab), and STELARA (Ustekinumab), the BPCIA lawsuits ended in a stipulation of dismissal based on a settlement agreement.

- **Predictable Outcome:** The high frequency of settlements indicates that both innovators and biosimilar makers prioritize predictability over the risks of trial. Innovators secure a defined launch date, often significantly delayed (e.g., HERCEPTIN biosimilars launching 11-15 months post-approval), while biosimilar makers gain certainty for their investment.
- **Pre-Approval Agreements:** Settlements often occur before FDA approval (e.g., STELARA's ABP 654), suggesting that the market entry date is a key commercial term negotiated well in advance of regulatory approval.

**Landmark Procedural Rulings Define the Litigation Floor:** While most cases settle, the framework for litigation was set by a few high-stakes legal outcomes. The Amgen v. Sandoz ruling set the stage for "patent dance" being not mandatory and the timing of NCM. This decision effectively prevented innovators from relying on a mandatory 6-month delay post approval. The Amgen v. Apotex (Neulasta) established the innovator's right to an injunction requiring the NCM to occur at least 180 days before launch, ensuring a statutory launch lock-out period even if the biosimilar manufacturer opts out of the full patent dance.

**Patent Merits exhibit a Mixed and Inconsistent Picture:** The cases that reached a judgment on patent validity or infringement show that innovator patents are not universally robust:

- **Innovator Loss:** In NEULASTA (Peg-filgrastim) litigation, Amgen lost multiple litigations with courts granting summary judgment of non-infringement to biosimilar makers (Sandoz, Apotex) and outright dismissal (Coherus). Similarly, Janssen lost its patents against the INFLECTRA (Infliximab) biosimilar. These judicial decisions significantly weakened the innovator's position, leading to rapid subsequent launches for those products.
- **Innovator Victory:** Conversely, Immunex (Amgen) achieved complete victories against two ENBREL (Etanercept) biosimilars, successfully defending key patents in court and on appeal, resulting in a total blockade of both approved products years after their FDA clearance. Erelzi by Sandoz was approved in 2016 and Eticovo by Samsung Bioepis in 2019 by the FDA.

### Launch Timing: Settlement Leads to Delay & Permanent Injunction Denial Leads to Speed:

The time lag between FDA approval and US launch is highly dependent on the legal outcome:

| Outcome Type | Example Product | Lag (Approval to Launch) | Market Implication |
|---|---|---|---|
| **Settlement** | HERCEPTIN, TRAZIMERA | 11-15 months | Negotiated delay to protect innovator revenue. |
| **PI Success** | Eylea (aflibercept) Opuviz/SB15 | Blocked | The **District** and **Federal Circuit** affirmed PI grants against three biosimilars (Celltrion, Samsung Bioepis, Formycon), |
| **PI Denied** | KANJINTI (HERCEPTIN) | ~ 1 month | Launch proceeds quickly when injunction fails. |
| **Innovator Victory** | ERELZI, ETICOVO (ENBREL) | Blocked | Market access was denied until patent expiration. |
| **Innovator Loss** | INFLECTRA (REMICADE) | ~ 7.5 months | Patent defeat leads to relatively rapid entry. |

### Innovator (RPS) Focus:

- **Prioritizing a Win on the PI Motion:** Failure to secure a PI (as in EYLEA v. Amgen) results in an immediate loss of market control. The focus must be on patents likely to be found both valid and infringed at the preliminary stage.
- **Proactive, Centralized Filing:** Filing lawsuits against all applicants' pre-approval in a preferred venue to encourage MDL (Multi-district Litigation) consolidation likely pressure uniform settlement terms.

### Biosimilar Applicant Strategy:

1. **Exploit Claim Construction:** Biosimilar developers are aggressively litigating non-infringement arguments based on technical claim language (e.g., Amgen's argument that its EYLEA biosimilar did not infringe the patent due to lacking a separate "buffer" component).
2. **Accelerate Approval:** Obtain FDA approval as quickly as possible. If the PI is denied, the biosimilar is then positioned to launch at risk and establish market share while the full patent litigation plays out.
3. **Challenge Personal Jurisdiction:** Foreign manufacturers like Celltrion and Samsung Bioepis continue to challenge personal jurisdiction in the chosen U.S. district courts, though the Federal Circuit has consistently affirmed jurisdiction based on the nationwide commercial intent indicated by the aBLA filing.
4. **Extended use of IPR/PGR:** An important strategic distinction for biologics: Unlike small-molecule generics, biosimilar developers filing IPR/PGR do not trigger the 180-day automatic stay on competitive entry that exists under the Hatch-Waxman Act. Consequently, biosimilar firms increasingly use IPR/PGR as parallel strategies to litigation, aiming for patent invalidation without losing time to procedural stays.

BPCIA litigation primarily functions as a negotiation tool for settlement, allowing innovators to secure a controlled, multi-month or year-long launch delay. However, the legal landscape is not monolithic; patent strength remains product-specific, leading to outcomes ranging from total market blockade to rapid, contested entry. Post grant IP challenges on obviousness and devising unique strategy for each drug based underscores the approval and launch of biosimilars. The primary driver of biosimilar market entry is now the confidential settlement date, not the public FDA approval date.

# Biologics & Biosimilar Market Analysis and Strategies

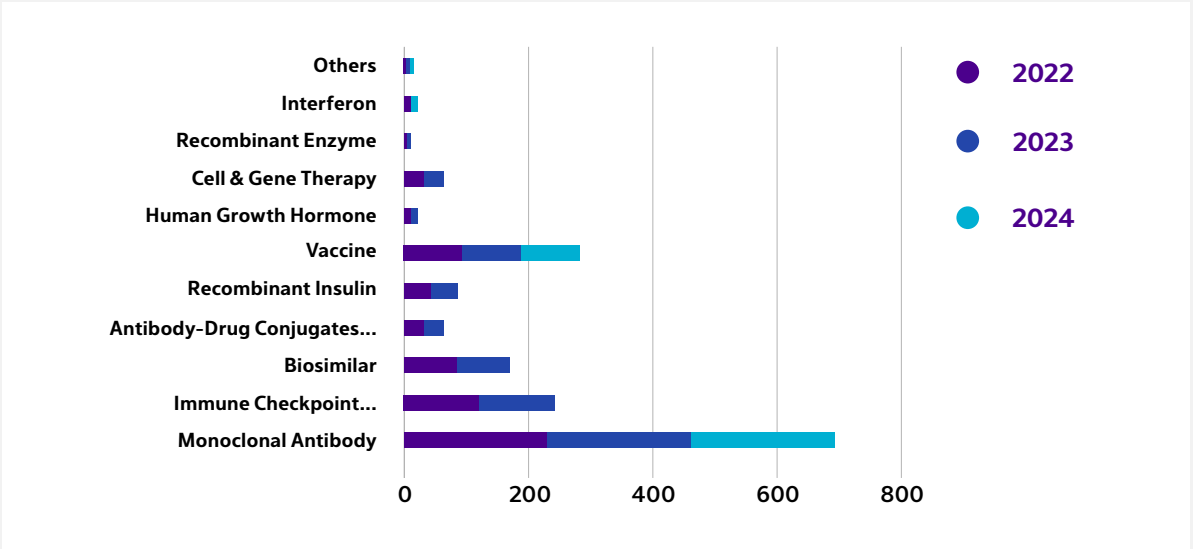
The biologics & biosimilars market is booming, driven by patent expirations of blockbuster drugs, increasing chronic diseases, and demand for cost-effective treatments. The market size, by revenue and forecasts offer key insights to embrace and prepare for opportunities and challenges.

## 1. Biologics Market Revenue Trends (2022-2024)

### A. Biologics Market Revenue Trends by Product (2022-2024)

The Biologics market consistently grew across all product categories between 2022 and 2024. Monoclonal Antibodies (mAbs) remained the dominant revenue driver, expanding from $211 to $251 billion. Immune Checkpoint Inhibitors were the second-largest category, rising from $116 to $138 billion. The Biosimilar segment also saw steady growth (from $71.9 to $86.8 billion). Furthermore, Cell & Gene Therapy and Antibody-Drug Conjugates (ADCs) exhibited strong, high-growth expansion[1].

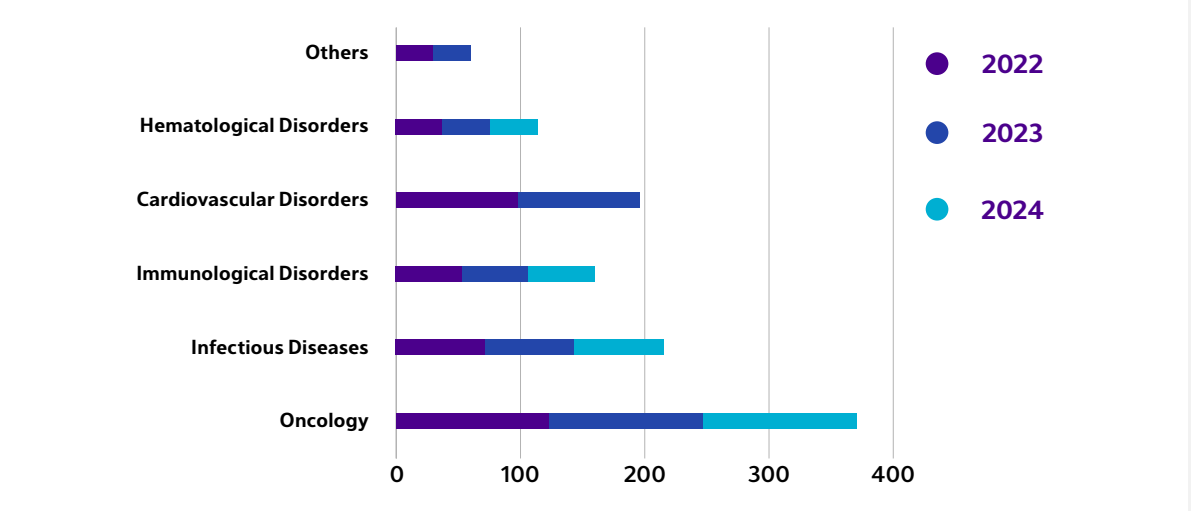
**Biologics Market Revenue, By Product, 2022-2024 (USD Billion)**




*Source Data: Precedenceresearch*

1 Precedence Research. (2024). Biologics Market Size, Share, and Trends Analysis Report By Source (Microbial, Mammalian, Others), By Product, By Disease, By Region, and Segment Forecasts, 2023-2032.

**Biologics Market Revenue, By Disease, 2022-2024 (USD Billion)**

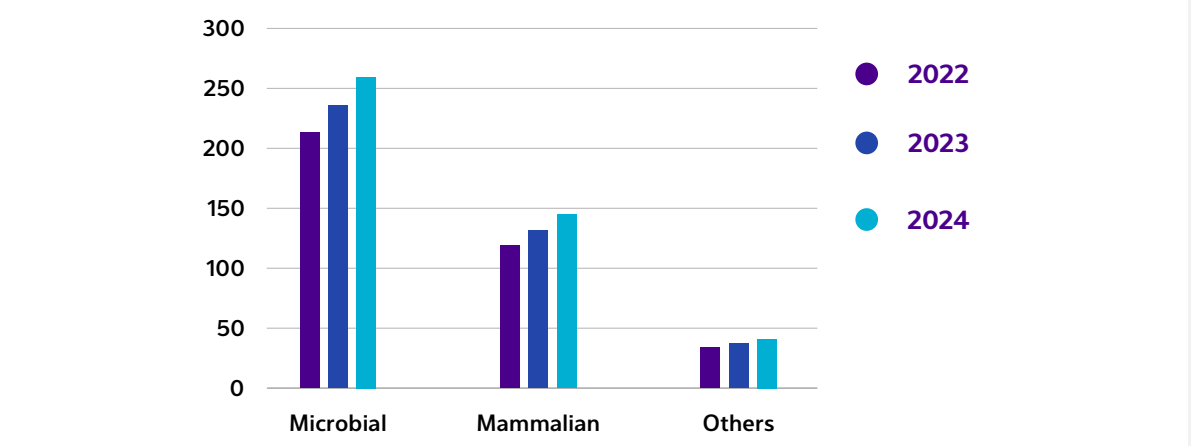



*Source Data: Precedenceresearch*

## B. Biologics Market Revenue by Disease (2022-2024)

Revenue data shows that the biologics market experienced widespread growth across all therapeutic areas, underscoring the vital role these products play in treating major diseases. Oncology leads the market as the largest therapeutic indication for biologics, with revenue climbing from $111 billion in 2022 to $135 billion in 2024. Other areas represent substantial markets as well. In 2024, Cardiovascular Disorders and Infectious Diseases recorded the next highest revenues at $106 billion and $74.5 billion, respectively. Furthermore, Immunological Disorders remains a key and expanding segment, contributing $57 billion to the overall market revenue in 2024[2].

**Biologics Market Revenue, By Source, 2022-2024 (USD Billion)**




*Source Data: Precedenceresearch*

2 id.

### C. Revenue by Source (2022-2024)

The data on revenue by source highlights the dominance of Microbial-sourced biologics sources (*E. coli* and yeast) generated the highest revenue, growing from $221.1 billion in 2022 to $261.2 billion in 2024. Mammalian sources represent the second-largest revenue segment, expanding from $119.3 billion to $143.8 billion over the same period[3].

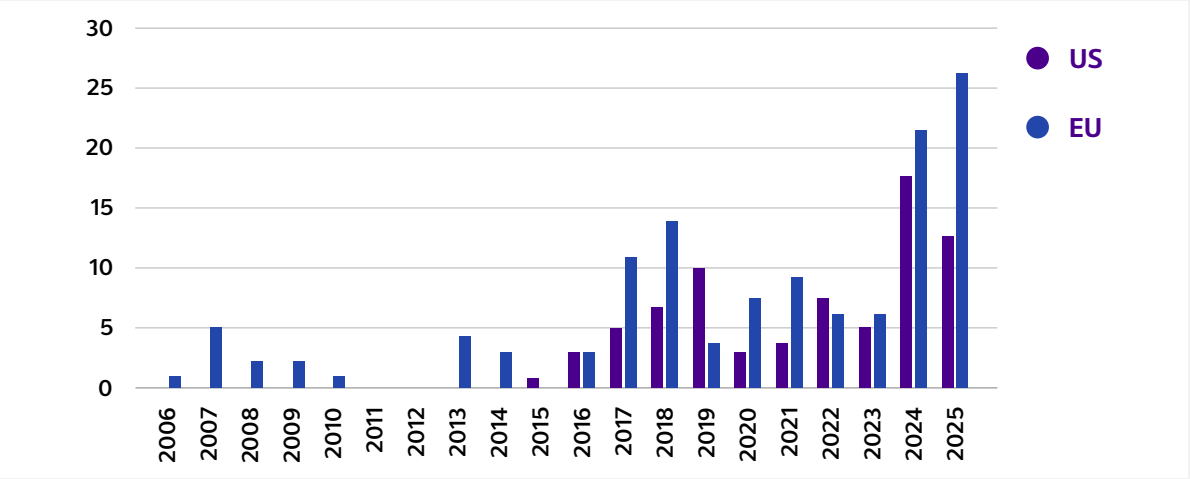
#### Market Segmentation

| Product | Application | Manufacturing Type |
|---|---|---|
| ▪ Monoclonal Antibodies | ▪ Oncology | ▪ In-house Manufacturing |
| ▪ Insulin | ▪ Autoimmune | ▪ Contract manufacturing |
| ▪ G-CSF | ▪ Diabetes | |
| ▪ Erythropoietin | ▪ Blood Disorders | |
| ▪ Human Growth Factor | ▪ Growth Hormone deficiency | |
| ▪ Interferons | ▪ Infectious Diseases | |
| ▪ Others | ▪ Others | |

## 2. Biosimilar Approval Trends (2015-2024)

Comparing the annual number of biosimilar product authorizations in the US and EU from 2006 to 2025 indicates a trend of increasing authorization activity in both regions, though with significant differences in timing and scale driven by oncology and immunology products and increasingly streamlined requirements.

#### Biosimilar Product Authorisation




3 id.

The US FDA approved its first biosimilar, Sandoz's Zarxio (filgrastimsndz), in March 2015 under the 351(k) pathway created by the BPCIA. By late 2024, cumulative US biosimilar approvals had risen to roughly 70–75 products across about 18 reference biologics, including filgrastim, infliximab, etanercept, adalimumab, trastuzumab, bevacizumab, ranibizumab, aflibercept, insulin glargine, insulin aspart, pegfilgrastim, denosumab and others.

Annual approval numbers remained modest through 2018, then climbed as more applications reached maturity and FDA experience increased. This surge reflects both a maturing pipeline and FDA's willingness to accept more targeted clinical packages when PK/PD and analytical data are strong.

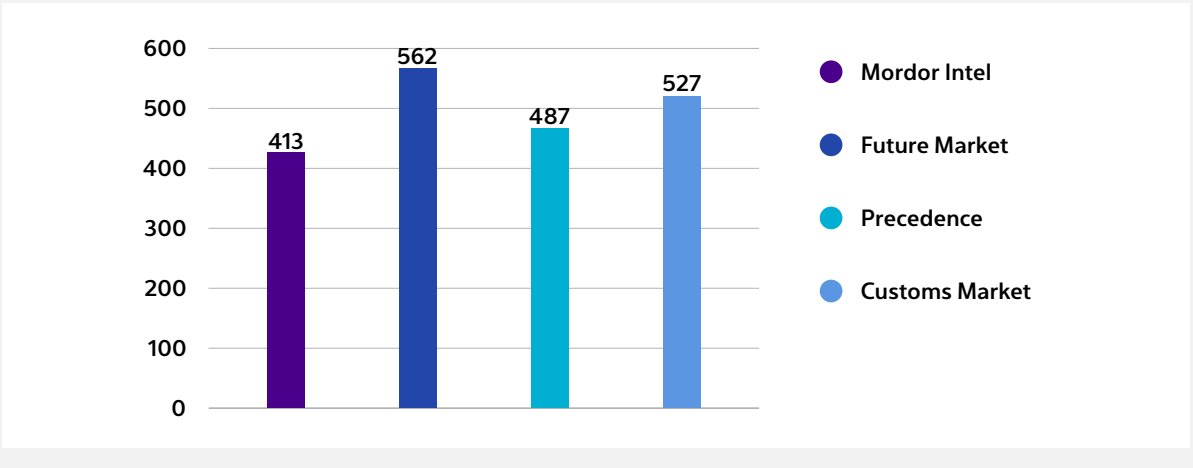
The EMA had nearly a decade's head start, with the first EU biosimilar (Omnitrope, somatropin) authorized in 2006, so 2015–2024 represents a consolidation and acceleration phase. By the end of 2024, the EMA had authorized more biosimilars than any other regulator, with multiple products in key classes (epoetin, filgrastim, infliximab, adalimumab, trastuzumab, bevacizumab, insulin glargine, etanercept, rituximab, ranibizumab, aflibercept, denosumab, ustekinumab and others). By the end of December 2024, a total of 17 biosimilars have been withdrawn after approval[4].

While annual numbers fluctuate, both markets are experiencing record or near-record levels of new product authorizations in the recent years, indicating strong and growing activity in the global biosimilar landscape.

## 3. Future Outlook for Biosimilars

The biologics market valued between USD 400-562 billion in 2025 by various estimates is projected to exceed USD 1 trillion by 2035 according to various reports[5].

**Biologics Market 2025 Multiple Estimates**




*Research Firms*

4 GaBI, EMA Approved a Record 28 Biosimilars in 2024, GaBI Online (Mar. 28, 2025).

5 Future Market Insights, Biosimilars and Follow-on Biologics Market : https://www.futuremarketinsights.com/reports/biosimilars-and-follow-on-biologics-market.

Biosimilars represent the fastest-growing segment with delivering substantial cost savings estimated and increasing access to affordable medicines. However, the global market is divided by inherent Regulatory differences for each jurisdiction which further complicate launch strategies of biosimilars based on pricing, interchangeability and approvals.

## A. Biosimilar Approval Dynamics Across Continents

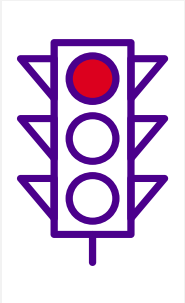
The geographic structure of the biosimilar market is unchanged, but regulatory momentum has shifted. According to the IGBA's November 2024 report, Singapore is the new leader in total biosimilar approvals (146), ahead of India (128) and the European Union (110). Other key approval markets include Brazil (65), Canada (64), the U.S. (60), Egypt (56), and South Africa (31)[6].

Despite this global diffusion of approvals, Europe remains the engine of biosimilar adoption, accounting for over 50% of global utilization. The region's consistent use has led to 5.8 billion patient treatment days since 2006 and significant economic value, totaling 50 billion in cumulative savings through 2023, including €10 billion in savings just in 2023. By 2028, biosimilars are projected to represent more than half of Europe's off-patent drug competition[7].

### Factors influencing Biologics/Biosimilars Market Growth

**Drivers**

- Advancements in Biosimilar and Biologic Production
- Rising prevalence of chronic diseases & need for effective, affordable treatments
- Increasing acceptance of biosimilars due to their cost-effectiveness



**Limitations**

- Regulatory Complexities & automatic Substitution
- High development costs
- Supply chain issues

## B. Psychological Barrier to Biosimilar Adoption

One of the core challenges for biosimilar adoption stems from the fundamental distinction that they are mandated to be "highly similar, not identical," to the originator biologic. While this "totality of the evidence" standard is scientifically rigorous and proves no clinically meaningful difference, it creates a persistent "confidence gap" among physicians and patients. Adoption is further complicated by practical issues, including misaligned reimbursement policies that don't always incentivize biosimilar use, and the need for updated Electronic Health Record (EHR) systems and pharmacy protocols to clearly distinguish and track biosimilar products.

6 Joseph Pategou, The Alchemy of Biosimilars: The Dawn of a New Epoch, Bioanalysis Zone (Apr. 7, 2025).

7 id.

This psychological barrier, fueled by questions about safety and efficacy, particularly regarding patient switching cannot be overcome by a strategy designed only around pricing. This forces the biosimilar manufacturers to invest heavily in medical education and real-world evidence to translate regulatory approval into clinical trust and accelerate market uptake.

## C. Interchangeability Affecting Market Landscape

The regulatory approach by EMA, where "approved means interchangeable" for biosimilars fosters deep clinical confidence for prescribers. This confidence empowers national health systems to rapidly drive adoption through competitive tendering, making price the main determinant and leading to deep biosimilar penetration. In contrast, the US required until recently extensive switching studies to be approved as an "interchangeable". This approach resulted in viewing the interchangeable product as a "lesser" option, slowing adoption, a barrier the EU had avoided.

### PESTEL Analysis of the Global Biologics & Biosimilar Market

### D. Biosimilar Development Cost and Supply Chain Issues

The supply chain resilience for biosimilars is critical due to the inherent fragility of biologics. This sensitivity requires precise, unbroken cold chain management from production to patient. Adding to this complexity is the globalized structure of the biosimilar industry, with raw materials sourced from multiple emerging economies and manufacturing concentrated in regions like the US and EU.

This global dispersion introduces significant logistical hurdles, including varied regulations, and geopolitical risks. Consequently, any disruptions like a pandemic can compromise product efficacy, cause major economic losses, and dangerously lead to patient drug shortages. This means biosimilars must strategically invest in buffer inventories, diversifying sourcing, and building flexible manufacturing capacity ensuring continuous patient access, and safeguarding long-term market presence.

## 4. Biologics & Biosimilar Pricings: Divergent Impact on Adoption

The distinct healthcare and regulatory frameworks in the EU and the US have resulted in fundamentally different pricing strategies and adoption trajectories for biosimilars.

### A. European Union is Price-driven Adoption and High Savings

Europe features a mature biosimilar market characterized by centralized procurement and aggressive national price negotiations, which have ensured high uptake and significant cost savings.

The European market for biosimilars is largely defined by competitive tendering and direct price negotiation, especially for drugs administered in hospitals, where the lowest-priced bid often secures the contract. This system demands deep, immediate price cuts, often leading to biosimilar launches with discounts ranging from 15% to 30% (with confidential rebates pushing net prices even lower), and subsequent market entrants continue to push prices down further.

This aggressive pricing environment has resulted in significant overall price reductions for molecule classes, sometimes 25% or more[8]. Crucially, the EMA's scientific stance on interchangeability for the prescriber facilitates high-volume, rapid adoption across national health systems. This combination of competitive pricing and regulatory clarity has consistently resulted in faster and higher adoption rates than in the US, yielding cumulative savings for European health systems.

### B. US is Rebate-Driven Barriers and the IRA's Intervention

The US market has historically been constrained by a fragmented, rebate-centric payment system that has severely hampered biosimilar adoption.

8 Price controls, competition and tendering for biosimilars, Generics & Biosimilars Initiative (Feb. 26, 2021).

Although biosimilars launch with Wholesale Acquisition Costs (WAC) 15% to 40% below originators, the true price advantage is often obscured by complex rebate contracts. Originator manufacturers employ large rebates to secure preferred formulary placement with Payers and Pharmacy Benefit Managers (PBMs).

This "Rebate Trap" creates a perverse incentive structure that favors the higher-list-price originator product over the lower-list-price biosimilar, forcing biosimilar developers to offer aggressive net pricing just to gain market access. Systemic factors, like the 340B Drug Pricing Program, further skew financial incentives toward using higher-cost reference biologics, thereby slowing market penetration[9].

### Impact of the Inflation Reduction Act (IRA) on Biosimilars

The IRA[10], enacted in 2022 to lower healthcare costs, introduces two major mechanisms directly affecting the biosimilar landscape.

#### I. Medicare Drug Price Negotiation (The "Special Rule")

The IRA directs Medicare to "negotiate" prices for high-expenditure, single-source biologics (eligible after 11 years of licensure). While this price control process primarily targets originators, it includes a crucial provision, the "Special Rule," which allows the Centers for Medicare & Medicaid Services (CMS) to defer negotiation for two years if a biosimilar is highly likely to enter the market. This aims to shift the dominant originator strategy from blocking market entry to a coexisting strategy, using the negotiation delay as an incentive to foster biosimilar competition and catalyze the industry.

- **Unintended Consequence:** A key challenge is that a successfully negotiated, low Maximum Fair Price (MFP) for a reference biologic could undercut the potential profitability of an *upcoming* biosimilar. Since the decision to invest in a biosimilar occurs years before the IRA price-setting takes effect, this uncertainty regarding future market value could preempt investment, potentially leading to a biosimilar void (a lack of biosimilar development for certain products.

#### II. Temporary Reimbursement Boost

To immediately incentivize biosimilar utilization, the IRA temporarily increases the Medicare Part B add-on payment for qualifying biosimilars from the standard 6% to 8% of the reference product's Average Sales Price (ASP). This five-year boost, applicable only to qualifying biosimilars with an ASP equal to or less than the reference product, encourages providers to use the lower-cost biosimilar by increasing their reimbursement

Despite the initial slow adoption due to market barriers, biosimilar savings in the US are currently driven by the intense downward pressure on the originator's net price. Market uptake is expected to accelerate rapidly as competition increases and as the effects of the IRA's negotiated pricing are to be observed post-2026.

9 Nicole Longo, The 340B Program Is Interfering with the U.S. Biosimilars Market and Impacting Patient Costs, PhRMA (Nov. 21, 2022).

10 Inflation Reduction Act of 2022, Pub. L. No. 117-169, 136 Stat. 1818 (2022)..

# 5. The Biosimilar Void

The 'biosimilar void' represents a critical market failure, the gap between the number of biologic drugs losing patent protection and the number of biosimilars presently in development to compete with them. While 118 originator biologics are projected to lose patent exclusivity between 2025-2035 (representing ~$234 billion in potential market opportunity), fewer than 12 of these molecules currently have biosimilars in development[11]. This void threatens the economic sustainability of the entire biosimilar industry and limits cost-savings realization for healthcare systems globally.

**THE BIOSIMILAR VOID AT A GLANCE**

| | |
|---|---|
| **Today (2024/2025)** | 62 off-patent biologics<br>▪ Only 14 have biosimilars (23%)<br>▪ 48 have ZERO pipeline |
| **Next Decade** | 118 will lose patent protection<br>▪ Only ~12 in development (10%)<br>▪ $180+ billion savings gap |

## A. Foundational Phase (until 2024)

The Foundational Phase[12] has been characterized by three key features with increasing market adoption to biosimilars, industry adoption with manufacturing capabilities and expanding CDMO's integration.

| Market Establishment | Technology Focus | Operational Dynamics |
|---|---|---|
| ▪ building robust infrastructure<br>▪ credibility for complex molecule manufacturing<br>▪ increasing adoption of Mabs & biosimilars<br>▪ expanded capacity by Global CDMOs (Samsung Biologics, and WuXi Biologics)<br>▪ GMP compliance and regulatory transparency | ▪ Manufacturing relied on stainless-steel bioreactors and batch-fed processes<br>▪ Priority to meet global FDA EMA Standards<br>▪ Early integration of single use bioreactors reducing contamination risks | ▪ Increased outsourcing for small biotech firms<br>▪ Increased demand in North America and Western Europe.<br>▪ APAC participation in fill-finish and analytical services<br>▪ Partnership was framed by cost effectiveness and reliability |

According to the IQVIA report, as of 2024, around 62 originator biologics have no patent blockages (Patent expired) of which only 14 of them have approved biosimilars in the market. This leaves over $22 billion in sales exposure without competition. With the remaining 48 originator biologics only 11 of them have pre-expiry sales of over $500M and only 2 of these have last biosimilars in their stage drug development. The remaining 48 biologics have no biosimilar pipeline as of 2024.

11 Skylar Jeremias, The Biosimilar Void: 90% of Biologics Coming Off Patent Will Lack Biosimilars, Ctr. for Biosimilars (Feb. 5, 2025).

12 Future market Insights Report on Biosimilar Market - Global Industry Analysis (2020-2024) & Opportunity Assessment (2025-2035).

## B. Acceleration Phase (2025 - 2030)

The acceleration Phase[13] is characterized by four features majorly the biosimilar pipeline for near expiring (Patent term) originator biologics. They would exhibit increasing biosimilar adoption and easing of the formalizing biosimilar approval pathways beginning to show relaxation such as the recent FDA revised guidelines.

| Process Diversification | Strategic Consolidation | Regulatory Advancement | Regional Expansion |
|---|---|---|---|
| ▪ continuous and modular biomanufacturing platforms<br>▪ Adaptive manufacturing by CDMO's<br>▪ PAT (Process Analytical<br>▪ Technology), and AI-driven analytics | ▪ strategic alliances with innovators for production suites<br>▪ Increased M&A activity with service portfolios for upstream and downstream process. | ▪ Regulators (FDA, EMA, PMDA) begin formalizing guidance accelerating tech-transfer efficiency and reducing approval timelines | ▪ APAC (South Korea, Singapore, and China)<br>▪ emerge as key biomanufacturing hubs, supported by<br>▪ domestic biosimilar pipelines |

## C. Transformational Phase (2030 - 2035)

The transformational Phase[14] is characterized by four features majorly the integration of the digital ecosystem and enabling biomanufacturing as a service and co-development of CDMO's.

| Digital Ecosystem Integration | Sustainable Manufacturing | Collaborative Innovation | Global Decentralization |
|---|---|---|---|
| ▪ AI-Driven Production<br>▪ Predictive QA<br>▪ Autonomous Control<br>▪ Digital Twin for Optimization | ▪ Sustainability Priority<br>▪ Eco-efficient biologics manufacturing<br>▪ low-carbon facilities<br>▪ aligned with ESG mandates | ▪ Co-development CDMOs, biotech, and tech firms to redefine biologics R&D | ▪ reduced logistics dependency, localized modular facilities.<br>▪ biomanufacturing-as-a-service may be an enabler |

The acceleration and transformation phase (2025-2035) according to the IQVIA reports 118 originator biologics with patent expiry in the next decade. Of this only 10% of biologics have biosimilars in its development phase. While analyzing both sales and timing of expiry for the 118 biologics, it is observed that biosimilar development is concentrated in high-sales biologics where near term patent perishes in the next five years (acceleration phase). The figure below with data from IQVIA reports establish that sales and expiry timing are not the only factors influencing biosimilar developer decision-making.

13 Future market Insights Report on Biosimilar Market - Global Industry Analysis (2020-2024) & Opportunity Assessment (2025-2035).

14 Future market Insights Report on Biosimilar Market - Global Industry Analysis (2020-2024) & Opportunity Assessment (2025-2035).

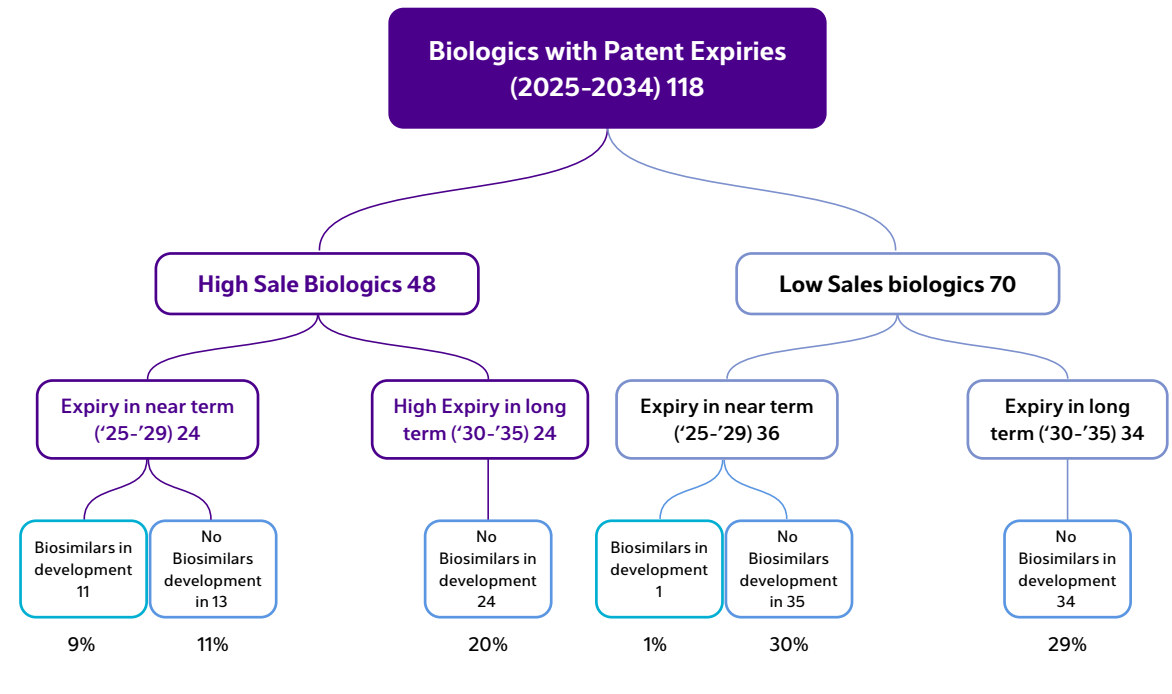



*Fig - Cluster of Patents expiries and biosimilars under development*

The biosimilar market presently faces multiple hurdles, including complex regulatory burdens, slow patient and physician adoption, high investment costs, and lingering confusion over interchangeability and reimbursement policies. To better understand the biosimilar void, other complexities must be evaluated and addressed.

## 6. Strategic Alliances and Licensing in Biosimilars: Structures & CarveOuts

The global biologics and biosimilar industry rely on strategic alliances and licensing agreements as the primary model for growth. These collaborations pool development resources, reduce financial risk, and accelerate market access across diverse regulatory environments. They are highly complex, often involving geographic carve-outs, tailored revenue sharing, and staged launches.

### A. Strategic Alliances in Biosimilars

Strategic alliances in biosimilars typically combine a development-focused partner with a commercialization-focused partner, or pair originators with regional specialists to maximize market penetration. Alliances often cover co-development, manufacturing, and co-promotion, while leaving regional pricing, market access, and medical affairs to the partner with stronger local presence.

Notable examples include global partnerships such as Biocon–Viatris (Formerly Mylan), and Samsung Bioepis–Biogen, where one partner leads largescale biologics development and manufacturing, and the other brings payer access, field forces, and regulatory experience in key markets like the US and EU.

In newer alliances, contract development and manufacturing organizations (CDMOs) like Chime Biologics partner with biosimilar developers (e.g., Polpharma Biologics)[15] to provide flexible capacity and speed to market while the partner focuses on pipeline and commercialization.

## B. Licensing Models and Deal Structures

Licensing remains the primary mechanism for achieving cross-border expansion in the biosimilar market, particularly when a developer seeks rapid entry into regions outside their home base. Under this common structure, the biosimilar developer (licensor) grants a licensee the rights to develop, register, and/or commercialize the product within specific territories.

In return, the licensor receives a combination of upfront fees, milestone payments, and ongoing royalties on sales. Royalty rates are typically tiered, often ranging from a single digit to a high percentage of net sales, with rates skewing higher in emerging markets due to smaller initial payments and greater risk.

Most agreements employ a hybrid payment structure, combining an initial license fee, various milestone payments tied to development and regulatory success (like Phase III completion or FDA/EMA approval), and commercial milestones linked to launch or sales targets. This comprehensive approach aligns incentives by rewarding timely approvals and strong commercialization while sharing downside risk from regulatory delays, pricing pressure, or loss in competitive tender.

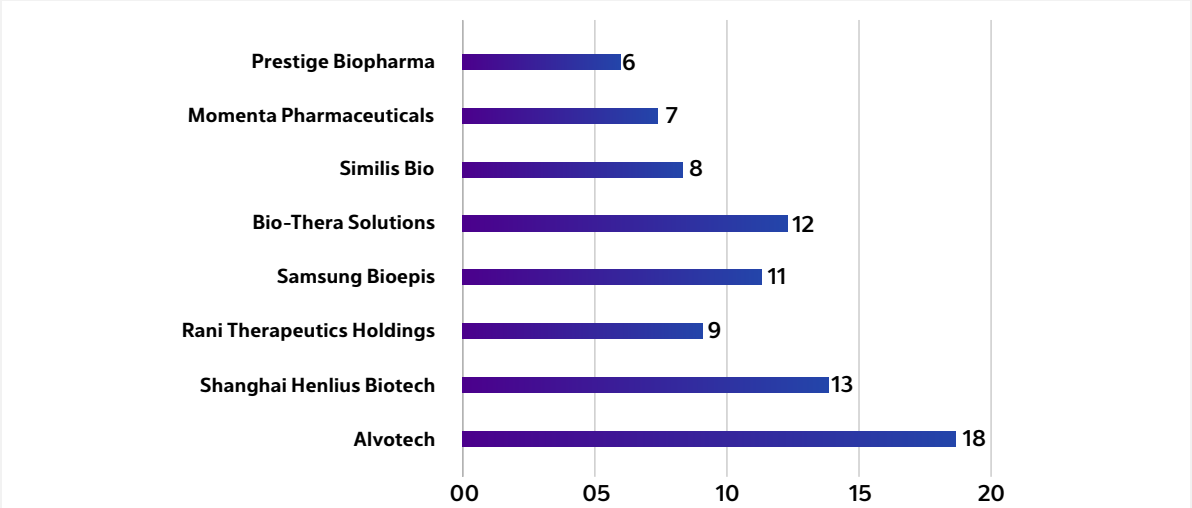
## C. Biosimilar Deal Landscape

The M&A, Licensing Trends, and Market-Shaping Partnerships report by Alira health[16] provides deep insights into the strategic partnership activities significantly shaping the biosimilar industry. Since 2015 there has been a steady flow of biosimilar partnering and M&A, with dealmaking peaking around 2021–2022 at roughly 23 licensing deals and 8 acquisitions per year, underscoring that licensing clearly dominates over acquisitions.

15 Chime Biologics, Chime Biologics Partners Polpharma Biologics to Advance Global Biosimilar Development (Apr. 16, 2025).

16 Biosimilar Deal Landscape: M&A, Licensing Trends, and Market-Shaping Partnerships, Alira Health (2025).

**Top Licensors by Number of Deals, 2015-2024**




Among licensors, the top companies by deals frequently structure deals with regional or global carve outs, using upfront fees, milestones, and royalties tied to sales in specific geographies to fund continued R&D.

The report also suggested the rise of generics companies in the biosimilar market as licensees. The growing share of earlierstage molecules[17] (clinical) in these deals highlight a maturing market in which alliances are shifting from latestage "inlicensing for launch" towards earlier platformstyle partnerships that anticipate multiregion carveouts and longterm portfolio growth.

## D. Some of the Successful Licensing Deals

Several biosimilar licensing deals illustrate how these structures work in practice and how they are adapted to regional opportunities.

- **Lupin and Valorum Biologics** exclusive licensing agreement announced on December 4, 2025, with for peg filgrastim (Armlupeg)[18] in the US gives Lupin manufacturing responsibility while Valorum leads commercialization, with an upfront fee and royalties structured[19] to reflect the competitive US GCSF market and the value of a differentiated pegfilgrastim biosimilar.
- **mAbxience and Intas Pharmaceuticals** a significant example of a regional licensing deal used to achieve broad global commercialization for a biosimilar candidate. In 2023, they entered into multiple regional licensing deals, for an etanercept biosimilar covering over 150 countries, where mAbxience leads development and manufacturing and Intas manages registration and commercialization across its global footprint[20].

17 id.

18 EP News Bureau, Lupin Signs Exclusive Licensing Agreement with Valorum Biologics for Armlupeg in the U.S., Express Pharma (Dec. 4, 2025).

19 id.

20 mAbxience, mAbxience Announces Licensing Agreement with Intas Pharmaceuticals Ltd. for Etanercept Biosimilar Targeting Autoimmune Diseases in more than 150 Countries, including Europe and the United States of America (Dec. 20, 2023).

- **mAbxience and Teva Pharmaceuticals** entered into an agreement in 2024 covering a biosimilar candidate currently in development for the treatment of multiple oncology indications using anti-PD-1 biosimilar candidate[21]. This partnership allows Teva to expand its biosimilar pipeline and commercial presence in oncology by leveraging mAbxience's development and production expertise, aligning with the common model of specialization in the industry.
- **mAbxience and Egis** agreed a strategic license in 2024 covering multiple Central and Eastern European (CEE) countries, with mAbxience holding marketing authorizations and Egis running commercial operations, tailored to Egis' strong presence in CEE markets[22]. The agreements covered two biosimilar candidates, Rituximab and Trastuzumab.

## E. Some of the Landmark Acquisition Deals

- **Pfizer and Hospira:** Pfizer's 2015 acquisition of Hospira[23] significantly boosted its biosimilars presence, creating a leading global sterile injectables and biosimilars business by combining Hospira's existing portfolio (like the infliximab biosimilar) and pipeline with Pfizer's own development efforts. This help positioning them to capitalize on major biologics losing patent protection, though the deal also brought integration challenges and some internal restructuring, including potential cuts to certain pipeline candidates[24].
- **Biocon Biologics and Viatris** created a broad, multiasset biosimilar partnership (licensing) in 2009 spanning insulin glargine, trastuzumab, bevacizumab, and others, later culminating in Biocon acquiring Viatris' biosimilar business and associated rights[25]. The licensing deal led to the acquisition of Viatris' Global by Biocon Biologics in 2022 to consolidate global rights while leveraging Viatris' historical market access and distribution to scale revenues in the US and Europe[26].
- **Fresenius Kabi and Merck** acquisition of Merck KGaA's (Merck Group) entire biosimilars pipeline, including development assets, an experienced team, and ongoing projects (like an adalimumab biosimilar), for 170 million upfront plus potential milestones up to 500 million and royalties, by Fresenius Kabi aiming to bolster its biosimilar portfolio, especially in oncology and autoimmune diseases, as Merck shifted focus[27]. This strategic move allowed Fresenius Kabi to significantly expand its presence in the growing biosimilar market, while Merck exited the business.
- **Fresenius Kabi and mAbxience** Fresenius Kabi acquired a majority stake (55%) in mAbxience in a deal that closed in August 2022, significantly expanding its presence in the high-growth biosimilars market. The acquisition was a key part of Fresenius Kabi's "Vision 2026" growth strategy[28]. The deal enabled Fresenius Kabi's entry into the high-growth Contract Development and Manufacturing Organization (CDMO) market for biologics[29].

21 mAbxience, Teva and mAbxience Expand Strategic Partnership to include an additional Oncology Biosimilar Candidate (Oct. 3, 2024).

22 mAbxience, mAbxience and Egis Enter Strategic License Agreement for Biosimilar Candidates in Key Central and Eastern European Markets (Nov. 12, 2024).

23 Pfizer, Inc., Pfizer Completes Acquisition of Hospira, Press Release (Sept. 3, 2015).

24 RBSA Advisors, M & A Deal Analysis: Pfizer Acquisition of Hospira Inc. (Apr. 2015).

25 Mylan Inc., Mylan Announces Strategic Collaboration with Biocon to Enter the Global Generic Biologics Market (June 29, 2009).

26 Biocon Biologics, Biocon Biologics Completes Acquisition of Viatris' Global Biosimilars Business, BIOCON (Nov. 29, 2022).

27 Fresenius Kabi, Fresenius Kabi completes acquisition of Merck KGaA's biosimilars business, Press Release (Sept. 1, 2017).

28 mAbxience, Fresenius Kabi completes majority stake acquisition of mAbxience Holding S.L., significantly enhancing presence in high-growth biopharmaceuticals market, Press Release (Aug. 1, 2022).

29 Fresenius Kabi, Next Generation Patient Care: Fresenius Kabi Buys a Majority Stake in mAbxience and Acquires Ivenix.

- **Formycon and ATHOS:** The key component of the 2022 acquisition of biosimilar assets (ranibizumab and ustekinumab) from ATHOS KG was asset consolidation and operational integration[30]. This deal and subsequent product launches marked Formycon's transition to a commercial-stage company, generating revenue from product commercialization.

## F. Partnership Ecosystem: Key Players and Strategy

The biosimilar partnership landscape is defined by two primary types of active players: large commercial leaders that seek portfolio expansion and smaller, specialized R&D-focused licensors that generate value through deals. This activity fuels a global strategy focused on integrated portfolios and coordinated, multi-regional launches.

**Big commercial market leaders:** These global pharmaceutical and biotech companies lead the market in revenue and portfolio size, often relying on in-licensing & acquisitions to build their assets

| Company | Key Strategy & Portfolio |
|---|---|
| **Sandoz** | Global revenue leader. Portfolio of 11+ marketed and 20+ pipeline biosimilars, often built through in-licensing (e.g., trastuzumab, bevacizumab) and committing over $1 billion to manufacturing expansion. |
| **Amgen** | One of the top three players (~$3.7B biosimilar revenue in 2024). Position largely built on its early 2011 co-development alliance (Watson/Viatris) for key oncology & immunology agents. |
| **Samsung Bioepis** | Highly active partnership platform, consistently out-licensing its portfolio (adalimumab, etanercept) to regional partners globally. |
| **Biocon Biologics** | Driven by global alliances, including the full acquisition of Viatris' biosimilar business, alongside numerous regional licensing deals for insulins and monoclonal antibodies (mAbs). |
| **Celltrion** | Aggressively uses co-marketing and regional licensing (e.g., with Pfizer in some territories) for its immunology (infliximab) and oncology biosimilars, while retaining direct sales in other regions. |

### Most active R&Dfocused licensors:

These companies specialize in the development and clinical stage, using licensing deals as their core business model to monetize their pipeline assets across different regions[31].

| Licensor | Deal Volume & Focus |
|---|---|
| **Alvotech** | 18 deals since 2015, frequently carving out territories and partnering with major generics firms (Teva, Stada) for commercial rights. |
| **Shanghai Henlius Biotech** | 13 deals, primarily out-licensing its mAb biosimilars to regional and global partners. |
| **Bio-Thera Solutions** | 12 deals, focused on oncology and immunology biosimilars licensed into major markets. |
| **Samsung Bioepis** | 11 deals acting as the licensor (licensing to originator and generics companies across Europe, US, and Asia). |
| **Mid-Tier (Rani Therapeutics, Similis Bio, etc.)** | 6–9 deals each, licensing pipeline and early-stage assets to larger pharmaceutical or regional champions. |

30 Formycon AG, Formycon and ATHOS KG merge development activities through the acquisition of biosimilar assets in a long-term strategic partnership, Press Release (Mar. 29, 2022),

31 Biosimilar Deal Landscape: M&A, Licensing Trends, and Market-Shaping Partnerships, Alira Health (2025)

Taken together, this means Sandoz, Amgen, Samsung Bioepis, Biocon, Celltrion, and Alvotech are among the most consistently active companies in biosimilar partnerships globally, with a long tail of specialized R&D firms and regional generics players driving a dense licensing network. Also, regional companies in India, Korea, and Central/Eastern Europe (for example, Viatris, Stada, Intas, Egis) are frequently on the licensee side, taking territorial rights from Alvotech, mAbxience, Samsung Bioepis, and others to build regional portfolios.

## G. Geographic Carve-Outs: Strategy, Timeline and Deal Structure

Geographic carve-outs are a core strategic element in biosimilar commercialization, defining which partner controls the rights to specific countries or regions. A carve-out grants one partner exclusive or co-exclusive commercialization rights to a defined territory, while the original licensor retains or licenses the remaining global rights to others. This structure is favored because it allows companies:

- **Tailor Strategies:** Develop market-specific pricing, regulatory, and tender strategies that reflect the varying healthcare systems across the globe.
- **Mitigate Risk:** Manage risks efficiently, such as navigating dense patent landscapes (e.g., the U.S.) versus capitalizing on more accessible markets (e.g., the E.U.) and
- **Leverage Local Expertise:** Efficiently utilizes a licensee's commercial strength, especially in complex, hospital-tender-driven markets.

The market entry sequence for Humira (adalimumab) biosimilars provides a key example. While EU launches occurred in 2018, the U.S. launches were delayed until 2023 due to patent settlements. This created a de facto carve-out, directing early investment and resources toward EU and ex-U.S. markets. Consequently, many biosimilar products are seen being commercialized through multi-partner networks, with distinct partners holding rights for the EU, the U.S., Japan, and emerging markets.

**Influence on Launch Timings:** Carve-outs are critical determinants of launch sequencing, allowing sponsors to prioritize commercially "easier" or less legally encumbered regions first. In Europe and other ex-U.S. markets where patent barriers often expire sooner, biosimilars typically launch rapidly following EMA approval, gaining quick market share through national tenders and price competition.

In contrast, U.S. market entry often faces substantial delays between regulatory approval and commercial launch due to protracted patent disputes or settlement terms, with lags measured in years for some major biologics. This disparity means a partner may launch successfully in their carved-out European territory years before a U.S. launch, using the early revenues to fund subsequent indications, life-cycle studies, or U.S. market preparation.

**Label Carve-Outs for Market Staging:** In addition to geography, sponsors may employ label carve-outs (or "skinny labels") to stage market entry. This involves seeking FDA approval for only a subset of the reference product's indications to avoid infringing "use patents" still in force for specific therapeutic uses. The strategy enables an earlier approval and launch in patent-clear therapeutic areas, with the broader indications added later as patents expire.

In certain cases, regional and label carve-outs interact, allowing for broader labels to be pursued first in patent-clear ex-U.S. regions while a narrower, safer label is launched in the legally complex U.S. market.

**Revenue Sharing and Financial structure:** Revenue sharing in geographic carve-outs is structure to reflect both the economics of the region and the relative contributions of licensor and licensee. Deals commonly combine:

- Upfront payments for the transfer of territorial rights.
- Milestone payments linked to regional development, regulatory, & launch achievements and
- Ongoing royalties on net sales, often tiered by volume..

Royalty ranges generally fall from mid-single-digit to high-teens percentages of net sales, with higher royalties often seen when the licensee bears substantial commercial risk or where the licensor has limited existing market presence. Alternatively, some joint ventures utilize pre-agreed profit-share splits. To manage the volatility of tender markets, agreements may include flexibility, such as royalty scales that decrease as competitor entry intensifies or as initial launch investments are recovered.

## H. Global Expansion Strategy (2026 Outlook)

Biosimilar companies are achieving global expansion not through unilateral efforts, but via an integrated strategy that connects US/EU commercial leadership with Asia-Pacific manufacturing strength and emerging-market tender opportunities.

**US and EU as primary growth engines:** These markets account for over 80% of global biosimilar sales. Companies are prioritizing building broad portfolios (via in-licensing) and leveraging favorable policies (US interchangeability, EU tenders) for rapid volume share gain

**Partnershipled regional expansion:** Deals are used to enter or deepen presence in regions where direct infrastructure is lacking. Example: Celltrion granting Hikma exclusive rights in MENA, allowing for a faster, cheaper route to regional scale.

**Asia Pacific as a manufacturing and demand hub:** Asia-Pacific serves as both a low-cost production base and a fast-growing demand center. Companies use US and EU approvals as “quality badges” to facilitate registrations and sales across Latin America, the Middle East, and Africa

**Indian companies pivoting to the US:** Firms are re-orienting pipelines (especially high value mAbs) toward the projected $90 billion US market (by 2034). This involves partnering with US/EU firms for commercialization while retaining cost-efficient manufacturing in India.

**Broader access via policy and multiregional launches:** Regulatory bodies (including the WHO) are promoting biosimilars for wider access, leading sponsors to design development programs for simultaneous or near-simultaneous launches in the US, EU, and emerging markets, using shared data packages.

## I. Strategic Implications for Biosimilar Sponsors

For companies planning biosimilar strategies, the experience of licensing deals and acquisition suggests several lessons:

- Geographic carve-outs should align with patent strategy, regulatory sequence, and payer dynamics, not just sales potential, prioritizing early-entry regions to build real-world evidence and cash flow.
- Partner selection must reflect regional strengths in access and tendering; local or regional players can often outperform global firms in complex, procurement-driven markets.
- Revenue-sharing and royalty terms need to be flexible enough to accommodate rapid price erosion, evolving competition, and indication expansions over the product's life cycle.
- Label carve-outs and staged indication launches may enable earlier entry where full-label approval is blocked by residual use patents, but they require careful medical and market-access planning to avoid confusion or limited uptake.

Together, these alliance, licensing, and carve-out structures have enabled biosimilars to expand rapidly into global markets, while balancing legal risk, capital intensity, and the need for specialized local market expertise.

Biosimilar companies are expanding globally mainly through targeted partnerships, focused US/EU pushes, and aggressive moves from Asia into the rest of the world. Overall, 2025 global expansion in biosimilars is driven less by singlecountry plays and more by integrated portfolios, crossborder licensing networks, and coordinated launches that treat US/EU leadership, AsiaPacific manufacturing strength, and emergingmarket tenders as parts of one connected strategy.

# India Pharmaceutical Outlook (2026–2030)

## From Volume to Value: Redefining Global Biopharma Leadership

India has established itself as a global hub for biosimilar production, the growth fueled by a strategic pivot toward becoming a primary exporter to regulated markets and a massive domestic disease burden (Diabetes, Oncology). Building on the recent regulatory shifts, the year 2025 has seen a surge in "first-in-world" launches and strategic global alliances. Indian players are no longer just followers; they are increasingly challenging innovators in courtrooms and international markets.

## I. The "Big 5" Powerhouses: Establishing Global Dominance

### A. Biocon Biologics: Integrated Global leader

Transitioned into a wholly owned subsidiary of Biocon Ltd (completion set for March 2026) to unify its "lab-to-market" capabilities. It is the only global player offering a full spectrum of diabetes care (Insulins + GLP-1 peptides). Announced a massive 17-asset oncology pipeline, including biosimilars for *Keytruda and Opdivo. Similarly*, reached a global settlement with Regeneron in late 2025, clearing a path for its (Aflibercept) *Eylea biosimilar* launch. **Biocon and Civica (US)**, partnership is set to bypass US PBM "rebate walls," selling directly to hospital systems.

### B. Zydus Lifesciences: The "First Mover" Disruptor

Specializes in "world-first" launches to capture the first-to-market advantage and redefine pricing benchmarks. Launched **Tishtha™** (biosimilar Opdivo) in January 2026 the world's first Nivolumab biosimilar, following a landmark Delhi High Court victory against BMS. Signed an exclusive deal with **Formycon** (Dec 2025) to commercialize a Keytruda biosimilar in the US/Canada, marking its major North American entry.

### C. Dr. Reddy's Laboratories: The "Patent Cliff" Strategist

Focuses on high-value immunology and obesity molecules with a long-term eye on the multi-billion dollar expirations in 2028. Plans to launch generic **Semaglutide** (Wegovy/Ozempic) in 87 countries starting in 2026. Announced US/EU filing for biosimilar *Orencia*, with US approval expected by late 2026. Strategic alliance with **Coya Therapeutics** for a novel subcutaneous combination biologic. Alvotech has a strategic partnership to co-develop, manufacture, and commercialize high-value biosimilars, notably a biosimilar for Keytruda (pembrolizumab) and AVT03 (denosumab). **Helinus partnership**

### D. Intas Pharmaceuticals (Accord Healthcare): The European Leader

India's primary representative in Europe, holding a ~15% market share for Filgrastim and leading in oncology launches. First Indian company to receive a positive CHMP opinion for **Pelgraz®** (Pegfilgrastim) in the EU, leveraging its EU-GMP certified domestic facility. With deep collaborative ties with European regional payers, it stays the "preferred supplier" in tender-based markets.

### E. Lupin Limited: The New US Contender

Successfully pivoted from oral generics to complex injectables and biologics. Received US FDA approval for ARMLUPEG™ (biosimilar Neulasta) in December 2025. Exclusive licensing deal with Valorum Biologics for US commercialization, allowing Lupin to focus on its Pune-based high-scale manufacturing.

## II. High-Growth "New Entrants"

These companies are disrupting the "Big 5" through technical niches like continuous manufacturing or specific therapeutic depth.

| Company | Parent | Strategic Contribution | Key 2025-26 Event |
|---|---|---|---|
| **Enzene Biosciences** | Alkem Labs | **Continuous Manufacturing**: Disrupting cost structures with its EnzeneX™ platform. | Launched Discovery Services division; partnered for US Lucentis supply. |
| **CuraTeQ Biologics** | Aurobindo Pharma | **Regulated Market Specialist**: Built specifically for US/EU compliance from day one. | Received Notice of Compliance (NOC) from Canada for Dyrupeg™ (Jan 2026). |
| **Shilpa Biologicals** | Shilpa Medicare | **Complex Modalities**: Moving beyond simple biosimilars into ADCs (Antibody-Drug Conjugates). | Received US FDA Orphan Drug Status (Jan 2026) for a novel oncology MAb. |
| **Eris Lifesciences** | NA | **Domestic Commercial Aggregator**: Acquired Biocon's India business to dominate local distribution. | Rapidly scaling Insulin Aspart across the Indian private market. |

## III. Other Player

a. **Specialized Biologics & Vaccine Giants:** Companies like the Serum Institute of India (SII), Bharat Biotech and Reliance lifesciences focus on large-molecule manufacturing, often dominating the global vaccine and recombinant protein markets.

b. **Niche Players:** Firms like concord biotech (immunosuppressants like Tacrolimus, Sirolimus) used in organ transplants, Gennova Biopharmaceuticals (mRNA technology) and Hetero Biopharma often focus on specific therapeutic areas or high complexity "niche" molecules.

c. **CDMOs & Research Services:** They for the backbone, that do not always sell under their own brand but provide the R&D and manufacturing muscle for global pharma. Companies like Syngene International, Anthem Bioscience, Sai Lifesciences and Aragen Life Sciences contribute as Contract Research Organization or CDMO (Contract Development and Manufacturing Organization).

# IV. Market Limiters & Drivers

### A. Legal Risks: "The Patent Thicket" & At-Risk Launches

Originator companies have shifted from defending single molecules to building "Patent Thickets". As seen with Zydus's 2026 launch of Nivolumab, Indian firms are increasingly launching "at risk" (before all secondary patent litigation is settled). A lost court battle could lead to massive triple-damage penalties.

### B. Regulatory Risks: The Compliance "Bifurcation"

The USFDA has entered a "post-pandemic hyper-scrutiny" phase. Unlike simple pills, biologics are "living" drugs. Recent 2025 inspections have flagged "stagnant liquids" and "data integrity" in older Indian facilities. One major Warning Letter can delay a biosimilar launch by 2–3 years, causing a company to miss the "first-to-file" window. Further, While India's CDSCO 2025 Guidelines allow for Phase III trial waivers, the USFDA still frequently demands them if there is any "residual uncertainty" in analytical data. Indian firms (like CuraTeQ or Lupin) face the risk of spending $100M+ on trials that regulators might later deem insufficient.

### C. Commercial & Policy Risks

Starting in 2026, the US government can negotiate prices for the top-selling biologics. If the government forces a 60-80% price cut on a brand-name drug (like Stelara), the "price floor" for an Indian biosimilar can drop. Within India, the "Ayushman Bharat" tenders are driving prices down so low (60-90% discounts) that some manufacturers are finding it difficult to maintain the high-quality standards required for export-grade biologics while remaining profitable.

### D. The "Biopharma SHAKTI" Infrastructure

The ₹10,000 crore ($1.2B) government infusion (Budget 2026) is solving the industry's biggest bottleneck: Clinical Infrastructure. By expanding the national clinical trial network, India is slashing the time-to-market for complex biosimilars by 30%, allowing domestic players to compete for the "First-to-File" slot globally.

### E. Technical Disruption

Companies like Enzene Biosciences and Shilpa Biologicals are moving away from traditional batch manufacturing. By adopting Continuous Bioprocessing and AI-driven Digital Twins, they are reducing the physical footprint of plants while ensuring 100% batch consistency—effectively neutralizing the manufacturing advantages of high-cost Western facilities.

### F. The "Obesity & Diabetes" Global Reset.

With the launch of Liraglutide (Biocon) and upcoming Semaglutide (Zydus/DRL) biosimilars in 2026, Indian firms are set to democratize the "GLP-1" market. In the next decade, India will become the primary supplier of affordable weight-loss and diabetes biologics to the US and EU, potentially reducing global healthcare costs in this segment by 40–60%.

### G. ADC and mRNA Frontier

The next decade belongs to Antibody-Drug Conjugates (ADCs) and mRNA. Indian players are no longer just "copying" old drugs; they are partnering on novel delivery mechanisms. Shilpa's move into Orphan Drugs and Gennova's mRNA platform are early signals that India will lead in "Next-Gen" biologics, not just "Similar" ones.

## V. The Contribution to the Next Decade

The collective activity of these players is shifting the biosimilar traction in India through three pillars of price democratization, manufacturing sovereignty and building global trust. "India is no longer just following the patent cliff; it is building the bridge that allows billions of patients to cross it safely and affordably."

## Expert Perspectives and Industry Insights

### Industry Leaders

**Severin Schwan, CEO, Roche (2024)**

*"We recognize that biosimilars play a critical role in expanding access to biologic medicines. Our responsibility is to ensure innovation and accessibility go hand in hand."*[1]

**Dr. Sarah Johnson, Biopharmaceutical Manufacturing Expert**

*"When you're producing a biosimilar, you're essentially trying to reverse-engineer a complex biological product without access to the innovator's proprietary manufacturing process. It's like trying to recreate a gourmet dish without knowing the exact recipe or cooking techniques used*[2] *."*

### Biosimilar Council Insights

**Giuseppe Randazzo, Interim Executive Director, Biosimilars Council (2025)**

*"In the past year, the biosimilars industry celebrated a decade of pathbreaking progress, including new therapy areas, $56.2 billion in savings for patients and the healthcare system, and 3.3 billion days of patient therapy. However, over the next decade, 118 biologics are expected to lose patent exclusivity, presenting a $234 billion opportunity for biosimilars. But of these 118 biologics, right now only 12 molecules have biosimilars in development. This 'biosimilar void' means the sustainability of our industry is not guaranteed."*[3]

Thes statement reflects evolving industry consensus that originator biologics and biosimilar manufacturers share complementary roles in global healthcare. It emphasizes urgent need for increased biosimilar development investment to capture the patent cliff opportunity. The trajectory is clear: originator biologics will continue driving therapeutic breakthroughs while biosimilars democratize access, together reshaping the future of medicine over the coming decade.

1 Future Market Insights, Biosimilars and Follow-On Biologics Market (n.d.),.

2 Drug Patent Watch, Navigating the Complex Landscape: Key Challenges in Biosimilar Development, Drug Patent Watch Blog (Mar. 28, 2024).

3 Ass'n for Accessible Meds., Biosimilars Council, 2025 Generic & Biosimilar Medicines Savings Report (2024).

# Conclusion: The Inflection Point – Toward a Bifurcated Biologics Future

The past 15 years of biologics regulation, IP strategy, and BPCIA litigation have crystallized a paradox: while biosimilars have delivered measurable value, €50 billion in cumulative EU savings, 5.8 billion patient treatment days, and a growing market at ~$87 billion (2024), the looming "biosimilar void" threatens the sustainability of this achievement. As 118 originator biologics face patent expiration through 2035, representing a $234 billion market opportunity, fewer than 12 molecules currently have biosimilars in active development. This 10% penetration rate signals a systemic imbalance.

## Three Emerging Forces are Reshaping The Landscape

### I. Regulatory Acceleration vs. Industry Hesitation

The FDA's October 2025 guidance waiving clinical efficacy studies for monoclonal antibody biosimilars represents a watershed regulatory moment, theoretically reducing development timelines and costs by 2–3 years. Paradoxically, manufacturers have not yet responded with accelerated pipelines, suggesting that regulatory de-risking alone does not overcome the commercial uncertainty posed by the Inflation Reduction Act's Medicare price negotiation framework. The "Special Rule" allowing a two-year negotiation deferral if a biosimilar is likely to enter creates a perverse incentive: developers face potential profit-margin compression due to negotiated reference product pricing set years after development decisions are made. This regulatory-commercial mismatch is expected to delay biosimilar investment for products without a clear 5-7 year patent cliff.

### II. Litigation Consolidation as Industry Standard

BPCIA litigation has matured from binary (innovator wins vs. biosimilar wins) to a settlement-negotiated market entry model. Of the ~70 FDA-approved biosimilars, settlement appears in ~85% of completed litigation, with the confidential launch date, not FDA approval, driving actual market entry. Recent data show innovators are asserting an average of 24 patents per litigation (2020–2024), up 85% from 2014–2019. This escalation reflects a deliberate strategy to create settlement leverage rather than achieve patent validity. The emerging risk: regulators may eventually challenge this pattern as an abuse of the BPCIA's negotiation framework, particularly if settlements delay market entry beyond 12–18 months post-approval in cases where patent merit is weak.

## III. Geographic Divergence: A Permanent Carve-Out World

The biosimilar market will not harmonize globally; instead, it will calcify into three distinct tiers:

- Tier 1 (EU, Australia, Canada): High biosimilar penetration (35–50% for off-patent products by 2030), aggressive tendering, and rapid adoption driving prices down 25–40%.
- Tier 2 (US): Moderate penetration (15–25% by 2030) due to rebate complexity and interchangeability barriers, with settlement-driven launch delays preserving innovator leverage.
- Tier 3 (Asia-Pacific, emerging markets): High volume but low price, fragmented by local regulatory standards and compounded pharmaceutical production, limiting innovation incentives.

For biosimilar sponsors, this geographic stratification means that global development programs optimized for single-pathway approval are economically inefficient. Strategic manufacturers will adopt tiered development and label carve-outs, obtaining first approval and launch in Tier 1 markets (6–9 months) to establish real-world evidence and cash flow, before navigating the complex US settlement landscape (9–18 months) and staging Asian regulatory submissions based on post-launch data.

# Looking Forward

The decade 2025–2035 will determine whether biosimilars become a systemic competitor to biologics or a niche segment dependent on select high-value molecules. The critical inflection points are: (1) FDA enforcement of timely market entry post-BPCIA settlement, (2) IRA price negotiation outcomes for the first "Subject to Negotiation" biologics (2027–2029), and (3) investment in manufacturing capacity and CDMOs. Without intervention, the 118-molecule opportunity may yield only 20–30 new biosimilars, leaving a $180+ billion savings gap unrealized for global healthcare systems and patient access initiatives stalled.

The path forward requires coordinated action: simplified regulatory harmonization for the 80%+ of biosimilars addressing identical reference products across jurisdictions; transparent settlement timelines to prevent BPCIA abuse; and clearer investment signals from policymakers regarding IRA price negotiation schedules. The biologics revolution is incomplete without ensuring the biosimilar half of the promise, democratized access, keeps pace with the innovator half.

# Appendix: Biologics Patent Litigation Landscape

## Adalimumab: Litigation Landscape & Approval to Launch Timeline

| Case Name & Docket No. | Accused Biosimilar (INN) | FDA Approval Date | US Launch Date | Complaint Filed | Litigation Outcome | Settlement Date (Dismissal Order) |
|---|---|---|---|---|---|---|
| **AbbVie v. Amgen (16-666, D. Del.)** | AMJEVITA (adalimumab-atto) | Sep. 23, 2016 | Jan. 31, 2023 | Aug. 4, 2016 | Settlement (Stipulation & Order of Dismissal) | Sep. 28, 2017 |
| **AbbVie v. Boehringer Ingelheim (17-1065, D. Del.)** | CYLTEZO (adalimumab-adbm) | Aug. 25, 2017 | Jul. 1, 2023 | Aug. 2, 2017 | Settlement (Stipulation & Order of Dismissal) | May 15, 2019 |
| **AbbVie v. Sandoz (18-12668, D.N.J.)** | HYRIMOZ (adalimumab-adaz) | Oct. 30, 2018 | Jul. 1, 2023 | Aug. 10, 2018 | Settlement (Stipulation & Order of Dismissal) | Oct. 16, 2018 |
| **AbbVie v. Alvotech (21-2258/2899, N.D. Ill.)** | AVT02 (adalimumab) | Feb. 23, 2024 | May 20, 2024 | Apr. 27 & May 28, 2021 | Settlement (Stipulation & Order of Dismissal) | Mar. 9, 2022 |
| **Alvotech v. Abbvie (2-21-00265, E.D. Va.)** | AVT02 (adalimumab) | Feb. 23, 2024 | May 20, 2024 | May 11, 2021 (Declaratory Judgment) | Voluntarily Dismissed (after transfer) | Oct. 22, 2021 (Transfer Order) |

| Biosimilar | FDA Approval | Settlement/Dismissal | US Launch | Lag (Approval to Launch) |
|---|---|---|---|---|
| **AMJEVITA** | Sep. 2016 | Sep. 2017 | Jan. 2023 | 6 years, 4 months |
| CYLTEZO | Aug. 2017 | May 2019 | Jul. 2023 | 5 years, 11 months |
| HYRIMOZ | Oct. 2018 | Oct. 2018 | Jul. 2023 | 4 years, 8 months |
| AVT02 | Feb. 2024 | Mar. 2022 | May 2024 | 3 months (Note: Settlement pre-dates approval) |

## Key Observations (Analysis)

- **Consistent Outcome:** All primary AbbVie infringement suits resulted in a settlement and a stipulated dismissal, indicating a clear pattern of negotiated market entry for the biosimilars rather than a full trial.
- **Reference Product:** HUMIRA is the sole reference product involved in all five actions, highlighting its dominant market position and the focus of biosimilar competition.
- **Launch Delays:** The initial three biosimilars (Amjevita, Cyltezo, Hyrimoz) faced a significant delay of over four years between FDA approval and their US market launch (with a cluster launch in early/mid-2023), likely due to the terms of the confidential settlements.

- **Newer Launch Pattern:** The launch of AVT02 (May 2024) is much closer to its recent FDA approval (Feb. 2024), suggesting a different, potentially more immediate market entry condition for this later-approved biosimilar.

## Aflibercept: Litigation Landscape

Aflibercept (EYLEA) litigation landscape, covers two distinct phases: completed cases (Mylan and Sandoz) and ongoing cases (Celltrion, Samsung Bioepis, Formycon, and Amgen).

### i. Completed Litigation Landscape (Mylan & Sandoz)

| Feature | Regeneron v. Mylan (1:22-CV-00061) | Regeneron v. Sandoz (1:24-cv-00085) |
|---|---|---|
| **Accused Biosimilar** | **YESAFILI (aflibercept-jbvf)** | ENVEEZU (aflibercept-abzv) |
| **Reference Product** | **EYLEA** | EYLEA |
| **District Court** | **N.D. West Virginia (N.D. W. Va.)** | N.D. West Virginia (N.D. W. Va.) |
| **Complaint Filed** | **Aug. 2, 2022** | Aug. 26, 2024 |
| **FDA Approval Date** | **May 20, 2024** | Aug. 9, 2024 |
| **Final Outcome** | **Settlement/Dismissal (Stipulated Order entered Apr. 22, 2025)** | Settlement/Dismissal (Stipulation and Order entered Sept. 9, 2025) |
| **Notable Event** | **Complex trial and appeal process; Permanent Injunction issued then vacated; MDL-Centralized.** | Consolidated into MDL shortly after filing. |

## Key Observations

- The Mylan case is notable for the procedural history, including a full trial and a permanent injunction, which was ultimately vacated as part of the settlement. This suggests that settlement terms, not the court's prior order, govern the biosimilar launch timeline.

### ii. Ongoing Litigation Landscape & Multi District Litigation

| Accused Biosimilar (Brand) | Competitor | FDA Approval Date | Complaint Filed | Key Patent Asserted | Preliminary Injunction Outcome | Federal Circuit Appeal |
|---|---|---|---|---|---|---|
| **CT-P42 (aflibercept)** | Celltrion | Not Approved | Nov. 2023 | U.S. 11,084,865 ('865) | Granted (June 28, 2024) | Affirmed (Mar. 5, 2025) |
| **OPUVIZ (aflibercept-yszy)** | Samsung Bioepis | May 20, 2024 | Nov./Dec. 2023 | U.S. 11,084,865 ('865) | Granted (June 14, 2024) | Affirmed (Jan. 29, 2025) |
| **AHZANTIVE (aflibercept-mrbb)** | Formycon | July 1, 2024 | Nov. 2023 | U.S. 11,084,865 ('865) | Granted (June 21, 2024) | Affirmed (Jan. 29, 2025) |
| **PAVBLU (aflibercept-ayyh)** | Amgen | Aug. 23, 2024 | Jan. 2024 | U.S. 11,084,865 ('865) | Denied (Sept. 23, 2024) | Affirmed (Mar. 14, 2025); Launch occurred |

Timeline and Analysis of the EYLEA MDL: The litigation against the proposed biosimilars for EYLEA (Aflibercept) is a classic example of an innovator using all BPCIA tools to enforce patents and control market entry, but with a highly fractured result.

### A. Centralized, Focused Litigation (Nov. 2023 – Apr. 2024)

1. **Complaint Filing:** Regeneron filed complaints against four key competitors (Celltrion, Samsung, Formycon, Amgen) between November 2023 and January 2024.
2. **MDL Consolidation:** In April 2024, the cases were consolidated into a Multidistrict Litigation (MDL) in the Northern District of West Virginia. The MDL focused on a "common set of thirteen U.S. patents," streamlining the defense efforts.
3. **The Injunction Race:** Anticipating the May 18, 2024, expiration of EYLEA's regulatory exclusivity (and potential FDA approvals), Regeneron aggressively pursued Preliminary Injunctions (PI) and even Temporary Restraining Orders (TRO) to block launches.

### B. The Pivotal Preliminary Injunction Rulings (June – Sept. 2024)

The entire market entry hinged on the court's ruling on the PI, which Regeneron eventually narrowed to a single formulation patent (the '865 patent).

- **Innovator Victory (Blockade)**: The Court granted the PI motions against Celltrion, Samsung Bioepis, and Formycon in June 2024. These injunctions were swiftly affirmed by the Federal Circuit (Jan./Mar. 2025), legally blocking these three companies from launching their approved or pending biosimilars.
- **Innovator Defeat (Launch Achieved):** The Court denied the PI motion against Amgen in September 2024, finding non-infringement of the same '865 patent. This critical distinction allowed Amgen to launch PAVBLU in October 2024, marking the first US biosimilar launch for EYLEA.
    - Regeneron's subsequent emergency request to the Federal Circuit for an injunction pending appeal was denied (Oct. 2024), confirming Amgen's right to launch while the legal process continues.

### C. Market Impact: The Split Result

The EYLEA litigation is remarkable for its split outcome, demonstrating that patent-by-patent analysis holds significant weight, even within consolidated litigation:

- Regeneron successfully protected the market against three biosimilars by securing a preliminary injunction.
- Amgen achieved market entry by successfully defending against the same injunction motion based on non-infringement, paving the way for the first wave of EYLEA competition.

## Bevacizumab: Litigation Landscape & Approval to Launch Timeline

| Case Name & Docket No. | Accused Biosimilar (Brand) | Reference Product | FDA Approval Date | US Launch Date | Complaint Filed | Final Outcome | Settlement/ Dismissal Date |
|---|---|---|---|---|---|---|---|
| **Genentech v. Amgen (17-1407, D. Del.)** | MVASI (bevacizumab-awwb) | AVASTIN | Sep. 14, 2017 | Jul. 18, 2019 | Oct. 6, 2017 | Settlement | Jul. 7, 2020 |
| **Genentech v. Pfizer (19-638, D. Del.)** | ZIRABEV (bevacizumab-bvzr) | AVASTIN | Jun. 28, 2019 | Dec. 31, 2019 | Apr. 5, 2019 | Settlement | Sep. 20, 2019 |
| **Genentech v. Centus (20-361, E.D. Tex.)** | FKB238 (bevacizumab) | AVASTIN | Not Approved | N/A | Nov. 12, 2020 | Settlement | Jul. 2, 2021 |
| **Genentech v. Samsung Bioepis (20-859, D. Del.)** | SB8 (bevacizumab) | AVASTIN | Not Approved | N/A | Jun. 28, 2020 | Voluntary Dismissal | Sep. 7, 2022 |

| Biosimilar | FDA Approval | US Launch | Lag (Approval to Launch) |
|---|---|---|---|
| **MVASI (Amgen)** | Sep. 2017 | Jul. 2019 | ~ 1 year, 10 months |
| **ZIRABEV (Pfizer)** | Jun. 2019 | Dec. 2019 | 6 months |

## Key Observations

Pattern of Settlement (Genentech v. Pfizer & Centus)

- The cases against Pfizer (ZIRABEV) and Centus (FKB238) followed a typical pattern: a lawsuit was filed, and the case was dismissed shortly afterward based on a stipulated settlement. The ZIRABEV settlement was entered three months after its FDA approval and three months before its US launch, indicating the settlement likely dictated the launch date. The Centus case was settled even though the biosimilar was not yet approved, suggesting a "design around" or early, conditional market entry agreement was reached.

Contested Litigation and Appeal (Genentech v. Amgen): The MVASI case against Amgen stands out as the most litigated:

- Key Court Action: Genentech actively sought to stop the launch by filing motions for a Preliminary Injunction (PI) and Temporary Restraining Order (TRO). The District Court denied Genentech's motions.
- Appeal: Genentech appealed the denial of the PI/TRO to the Federal Circuit which affirmed the District Court's decision, allowing the biosimilar's launch to proceed without an injunction.
- Conclusion: Despite winning the motion phase and launching the product, the parties ultimately entered a stipulated settlement a year after the launch (July 2020), formally ending the litigation.

Voluntary Dismissal (Genentech v. Samsung Bioepis): The case against Samsung Bioepis for SB8 was Voluntarily Dismissed by Genentech two years after the complaint was filed. This often suggests that either a non-confidential settlement was reached, the biosimilar program was abandoned, or the claims were dropped for strategic reasons.

## Denosumab: Litigation Landscape & Approval to Launch Timeline

### i. First Wave: Settled Case

| Accused Biosimilar (Brand) | Reference Products | FDA Approval Date | US Launch Date | Complaint Filed | Litigation Outcome | Injunction/ Consent Judgment Expiry |
|---|---|---|---|---|---|---|
| **STOBOCLO/ OSENVELT (Celltrion)** | PROLIA, XGEVA | Feb. 28, 2025 | Jul. 7, 2025 | May 28, 2024 | Voluntary Dismissal (Consent Judgment) | Jun. 1, 2025 |
| **JUBBONTI/ WYOST (Sandoz)** | XGEVA, PROLIA | Mar. 5, 2024 | Jun. 2, 2025 | May 1, 2023 | Voluntary Dismissal (Stipulated Order) | Feb. 19, 2025 |
| **FKS518 (Fresenius Kabi)** | PROLIA, XGEVA | Mar. 26, 2025 | Jul. 1, 2025 | Oct. 4, 2024 | Dismissed (Settlement) | N/A |
| **Denosumab Biosimilar (Accord Biopharma)** | PROLIA, XGEVA | Not Approved | N/A | Nov. 13, 2024 | Dismissed (Consent Judgment) | Oct. 1, 2025 |
| **OSPOMYV/ XBRYK (Samsung Bioepis)** | PROLIA, XGEVA | Feb. 13, 2025 | N/A | Aug. 12, 2024 | Dismissed (Consent Judgment) | N/A |

### ii. Second Wave: Ongoing Litigation

| Feature | Amgen v. Hikma | Amgen v. Shanghai Henlius | Amgen v. Biocon Biologics |
|---|---|---|---|
| **Accused Biosimilars** | ENOBY / XTRENBO | BILPREVDA / BILDYOS | BOSAYA / AUKELSO |
| **Reference Products** | PROLIA, XGEVA | PROLIA, XGEVA | PROLIA, XGEVA |
| **FDA Approval Date** | Sept. 26, 2025 | Aug. 29, 2025 | Sept. 16, 2025 |
| **Complaint Filed** | June 25, 2025 | June 25, 2025 | June 30, 2025 |
| **Venue Status** | Pending (D.N.J.) | Pending (D.N.J.) | Pending (D.N.J. via transfer) |
| **Litigation Status** | Pending (Settlement or Trial TBD) | Pending (Settlement or Trial TBD) | Pending (Settlement or Trial TBD) |

| Biosimilar | FDA Approval | Injunction Expiry (Settlement Date) | US Launch |
|---|---|---|---|
| **JUBBONTI** | Mar. 2024 | Feb. 19, 2025 | Jun. 2, 2025 |
| **STOBOCLO** | Feb. 2025 | Jun. 1, 2025 | Jul. 7, 2025 |
| **FKS518** | Mar. 2025 | N/A | Jul. 1, 2025 |

## Key Observations

- **Settlement is the Uniform Outcome:** Consistent with industry trends, all completed cases resulted in dismissal/settlement rather than a full BPCIA trial. The settlement process effectively moves the determination of the launch date from the court to a private agreement.
- **Strategic Use of Injunctions to Control Entry:** Amgen used the threat or process of a Preliminary Injunction to secure **Consent Judgments** and **Stipulated Orders.** These legal agreements often include an injunction expiring shortly before an agreed-upon, **delayed US launch date** (e.g., Sandoz's injunction expired in February 2025, but the launch date is June 2025).
- **Centralized Multidistrict Litigation (MDL):** Amgen successfully consolidated the first wave of cases into an MDL in the District of New Jersey (D.N.J.). This centralization streamlines discovery, pretrial motions, and scheduling, allowing Amgen to coordinate its defense against multiple biosimilars simultaneously and apply consistent legal pressure.
- **Proactive Litigation:** Lawsuits for the second wave of biosimilars (Hikma, Henlius, Biocon) were filed in June 2025, before the FDA granted final approvals in August/September 2025. This is a common BPCIA tactic to initiate the patent dispute well in advance of a potential market launch.

## Eculizumab: Litigation Landscape & Approval to Launch Timeline

| Feature | Detail |
|---|---|
| **Case Name & Docket No.** | Alexion v. Samsung Bioepis, 1-24-cv-00005 (D. Del.) |
| **Accused Biosimilar (Brand/Code)** | EPYSQUALI (eculizumab-aagh) / SB12 |
| **Reference Product** | SOLIRIS (eculizumab) |
| **Complaint Filed** | January 3, 2024 |
| **FDA Approval Date** | July 19, 2024 |
| **US Launch Date** | April 7, 2025 |
| **Final Outcome** | Settlement (Stipulated Order of Dismissal) |
| **Settlement/Dismissal Date** | August 30 / September 3, 2024 |

| Date | Event/Outcome | Key Detail (Litigation Timeline) |
|---|---|---|
| **Jan. 3, 2024** | **Complaint Filed** | Initiation of the patent infringement suit. |
| **Feb. 12, 2024** | **PI Motion Filed** | Alexion files a Motion for Preliminary Injunction (PI) to stop the launch. |
| **May 6, 2024** | **PI Motion Denied** | District Court denies Alexion's PI motion. |
| **May 14, 2024** | **Appeal Filed** | Alexion appeals the PI denial to the Federal Circuit (CAFC). |
| **May 17, 2024** | **Emergency Motion Filed** | Alexion files an emergency motion for injunction pending appeal in the District Court. |
| **June 17, 2024** | **Emergency Motion Denied** | District Court denies the emergency motion, noting it was essentially a motion for reconsideration. |
| **June 21, 2024** | **CAFC Injunction Motion** | Alexion files a motion for an injunction of marketing/sales directly with the Federal Circuit. |
| **Jul. 19, 2024** | **FDA Approval** | EPYSQUALI receives FDA approval. |
| **Jul. 29, 2024** | **CAFC Injunction Denied** | Federal Circuit denies Alexion's motion for an injunction pending appeal. |
| **Aug. 30, 2024** | **Stipulated Dismissal** | Parties file a Stipulated Order of Dismissal (Settlement). |
| **Sep. 4, 2024** | **Appeal Dismissed** | Federal Circuit dismisses the pending appeal following the settlement. |

## Key Observations

- **Aggressive, Multi-Forum Defense:** The litigation is characterized by Alexion's extremely aggressive defense, attempting to block the biosimilar launch via three separate motions for injunctive relief across two courts (District Court and Federal Circuit):
  - Motion for Preliminary Injunction (D. Del.)
  - Motion for Injunction Pending Appeal (D. Del.)
  - Motion for Injunction Pending Appeal (Fed. Cir.)
- **Consistent Judicial Denial:** All three attempts by Alexion to obtain an injunction were denied by the courts.
- **Settlement Despite PI Denials:** Despite being denied all injunctions, the parties still reached a settlement, leading to a stipulated dismissal. This confirms the industry trend where patent litigation rarely goes to trial, even after early skirmishes are decided against the innovator.
- **Launch Control:** The settlement agreement was reached in August/September 2024, leading to a controlled US launch date of April 7, 2025. This lag of nearly 8.5 months between settlement/dismissal and launch is likely the negotiated market entry period.

## Epoetin alfa: Litigation Landscape & Approval to Launch Timeline

| Feature | Detail |
|---|---|
| **Case Name & Docket No.** | Amgen v. Hospira, No. 15-839 (D. Del.) |
| **Accused Biosimilar** | RETACRIT (epoetin alfa-epbx) |
| **Reference Products** | EPOGEN / PROCRIT (epoetin alfa) |
| **Complaint Filed** | September 18, 2015 |
| **FDA Approval Date** | May 15, 2018 |
| **US Launch Date** | November 12, 2018 |
| **Final Outcome** | Jury Verdict for Amgen, Affirmed on Appeal |

| Date | Event/Outcome | Key Detail (Litigation Timeline) |
|---|---|---|
| **Sept. 18, 2015** | **Complaint Filed** | Initiation of the patent infringement lawsuit. |
| **Sept. 22, 2017** | **Jury Verdict (Trial)** | The jury found Hospira infringed the ' 298 patent and awarded Amgen $70 Million in damages. |
| **May 15, 2018** | **Biosimilar Approval** | RETACRIT receives FDA approval. |
| Aug. 27, 2018 | **Post-Trial Motions Denied** | District Court denies Hospira's post-trial motions (for judgment as a matter of law, new trial, or damages recalculation). |
| Nov. 12, 2018 | **US Launch** | RETACRIT launches in the US market. (Launch occurred after the trial judgment but before the appeal decision). |
| Dec. 17, 2019 | **Federal Circuit Decision** | The Federal Circuit affirms the District Court's judgment of infringement and the jury's verdict. |
| Mar. 16, 2020 | **Rehearing Denied** | Federal Circuit denies Hospira's petition for rehearing. |

## Key Observations

- Rare Full Trial: This case is highly significant because it represents a rare example of BPCIA litigation proceeding to a full jury trial and verdict (unlike the majority of cases that end in settlement).
- Innovator Victory: Amgen (the innovator) secured a clear victory at trial, with a jury finding of infringement and an $70 Million damages award.
- Launch Despite Judgment: Notably, the biosimilar RETACRIT launched in November 2018, after the initial jury verdict and denial of post-trial motions, but before the Federal Circuit appeal was decided. This indicates the injunction issue or a stay on enforcement was either not sought or structured to allow the launch.
- Appellate Affirmation: The Federal Circuit's affirmation solidified Amgen's victory, confirming the validity of the patent and the finding of infringement.

## Etanercept: Litigation Landscape & Approval to Launch Timeline

| Feature | Immunex v. Sandoz (ERELZI) | Immunex v. Samsung Bioepis (ETICOVO) |
|---|---|---|
| **Accused Biosimilar** | **ERELZI (etanercept-szzs)** | ETICOVO (etanercept-ykro) |
| **Reference Product** | **ENBREL (etanercept)** | ENBREL (etanercept) |
| **FDA Approval Date** | **Aug. 30, 2016** | Apr. 25, 2019 |
| **US Launch Status** | **Not yet launched** | Not yet launched |
| **Complaint Filed** | **Feb. 26, 2016** | Apr. 29, 2019 |
| **Patents at Issue** | **182 and 522 patents** | 182 and 522 patents |
| **Litigation Outcome** | **Immunex Victory on Validity (Affirmed on Appeal)** | Immunex Victory (Permanent Injunction) |

## Key Observations

- **Total Blockade:** Unlike many BPCIA cases that result in a settlement allowing a controlled launch, the ENBREL litigation resulted in **total judicial victories for the innovator (Immunex/Amgen),** effectively establishing a complete blockade of the US market for the first two approved biosimilars.
- **Impact of Patents:** The '182 and '522 patents proved to be **extremely robust**, successfully withstanding challenges from two different competitors at both trial and appellate levels, preventing the US launch of approved products years after their FDA clearance.
- **Long-Term Exclusivity:** As a result of the litigation, ENBREL maintains monopoly status in the US, despite both ERELZI and ETICOVO being approved years ago.

## Filgrastim: Litigation Landscape & Approval to Launch Timeline

| Accused Biosimilar (Brand) | FDA Approval Date | US Launch Date | Complaint Filed | Final Litigation Outcome | Key Result/Significance |
|---|---|---|---|---|---|
| **ZARXIO (Sandoz)** | Mar. 6, 2015 | Sep. 3, 2015 | Oct. 24, 2014 | Supreme Court/ CAFC Decisions | Defined mandatory nature of "patent dance" and timing of Notice of Commercial Marketing (NCM). |
| **GRASTOFIL (Apotex)** | Not Approved | N/A | Oct. 2, 2015 | Non-Infringement Judgment (Affirmed on Appeal) | Early innovator loss on patent merits. |
| **NIVESTYM (Hospira)** | Jul. 20, 2018 | Oct. 1, 2018 | Jul. 18, 2018 | Settlement (Stipulation & Order of Dismissal) | Typical settlement outcome for launch. |
| **Filgrastim (Kashiv/Adello)** | Not Approved | N/A | Mar. 8, 2018 | Settlement (Stipulation & Order of Dismissal) | Settled before approval. |
| **NYPOZI (TX-01) (Tanvex)** | Jun. 28, 2024 | N/A | Jul. 23, 2019 | Settlement (Stipulation & Order of Dismissal) | Settled early in the process. |

| Biosimilar (Company) | FDA Approval | US Launch | Lag (Approval to Launch) |
|---|---|---|---|
| **ZARXIO (Sandoz)** | Mar. 2015 | Sep. 2015 | 6 months |
| **NIVESTYM (Hospira)** | Jul. 2018 | Oct. 2018 | 3 months |

## Key Observations

- The lawsuit concerning ZARXIO is the most important case in the BPCIA data set, as it resulted in rulings from the U.S. Supreme Court (SCOTUS) that defined the statute's procedures.
  - Mandatory Patent Dance: Is the biosimilar applicant required to participate in the BPCIA's patent exchange process? Final Ruling (SCOTUS): No, the biosimilar applicant cannot be compelled to participate in the patent dance.
  - Timing of Notice of Commercial Marketing (NCM): When must the applicant provide the 180-day notice that it intends to launch its product? Final Ruling (SCOTUS): The NCM can be provided prior to FDA approval.
- Patent Merit Outcome: Following the Supreme Court rulings that paved the way for the biosimilar's launch, the patent infringement claims themselves were resolved in favor of Sandoz: The District Court granted summary judgment of non-infringement on the key '878 patent, which was affirmed by the Federal Circuit in 2019. The parties also stipulated non-infringement of the '427 patent.
- The ZARXIO case led to the first-ever BPCIA biosimilar launch in the US, occurring just six months after FDA approval, despite the active litigation.

## Infliximab: Litigation Landscape & Approval to Launch Timeline

| Feature | Janssen v. Celltrion (INFLECTRA) | Janssen v. Samsung Bioepis (RENFLEXIS) |
|---|---|---|
| **Accused Biosimilar** | **INFLECTRA (infliximab-dyyb)** | RENFLEXIS (infliximab-abda) |
| **Reference Product** | **REMICADE (infliximab)** | REMICADE (infliximab) |
| **FDA Approval Date** | **April 5, 2016** | April 21, 2017 |
| **US Launch Date** | **November 28, 2016** | July 24, 2017 |
| **Complaint Filed** | **March 6, 2015 (Refiled May 31, 2017)** | May 17, 2017 |
| **Litigation Outcome** | **Biosimilar Victory (Summary Judgment)** | Voluntary Dismissal (Janssen's proposal) |
| **Patent Outcome** | **Patents 471 (Invalid) & 083 (Non-Infringement/ Invalid)** | All counts dismissed |

| Biosimilar | FDA Approval | US Launch | Lag (Approval to Launch) |
|---|---|---|---|
| **INFLECTRA** | Apr. 2016 | Nov. 2016 | 7.5 months |
| **RENFLEXIS** | Apr. 2017 | Jul. 2017 | 3 months |

## Key Observations

- **The Celltrion Litigation Victory for Biosimilar (INFLECTRA):** This case is notable because the biosimilar maker achieved market entry by defeating the innovator's patents in court, rather than through a confidential settlement. The District Court granted Summary Judgment in favor of Celltrion (July 2018), effectively ending the case in the biosimilar maker's favor. The Federal Circuit affirmed the judgments (The appeal regarding the '471 patent was dismissed as moot because the PTAB had already invalidated it during ex parte reexamination).
- **The Samsung Bioepis Case Voluntary Dismissal (RENFLEXIS):** This case ended quickly, suggesting a strategic move by the innovator once the biosimilar had already launched. The case was terminated quickly in November 2017 when the District Court entered a stipulation of voluntary dismissal based on Janssen's proposal. Given the highly similar product (RENFLEXIS) launched quickly after the complex litigation loss against Celltrion (INFLECTRA), Janssen likely recognized the weakened position of its patents and chose to dismiss the remaining claims rather than pursue a second, costly, and likely losing case on the same patents.
- **Rapid Market Entry:** The REMICADE litigation highlights a major innovator failure in patent enforcement. Unlike the ENBREL or HUMIRA cases, the patents did not significantly delay the launch of the first biosimilar (INFLECTRA) and completely failed to stop the second (RENFLEXIS), allowing for a rapid, competitive market entry.

## Natalizumab: Ongoing Litigation Landscape

| Feature | Detail |
|---|---|
| Case Name & Docket No. | Biogen v. Sandoz, 1:22-CV-1190 (D. Del.) |
| Accused Biosimilar | PB006 (natalizumab) |
| Reference Product | TYSABRI (natalizumab) |
| FDA Approval Date | August 24, 2023 |
| Complaint Filed | September 9, 2022 |
| Litigation Status | Pending (Trial postponed) |

## Key Considerations

This case is a prime example of a protracted BPCIA battle focused on blocking market entry and managing complex method patents.

### A. Critical Preliminary Injunction Denial (PI)

The most significant development was the denial of Biogen's Motion for Preliminary Injunction, which is crucial for preventing "at-risk" launch:

- **PI Denied:** June 20, 2023, months before the biosimilar's approval.
- **Court's Rationale:** Biogen failed to demonstrate irreparable harm and a likelihood of success on the merits.
- **Market Impact:** The denial of the PI meant that Sandoz was legally free to launch its approved biosimilar (Tyruko is the brand name, approved August 24, 2023) at any time, as there was no court order blocking commercialization. This places the pressure on the innovator (Biogen) to secure a final judgment quickly.

### B. Strategic Patent Claim Narrowing

Following the denial of the PI, the parties began to streamline the case by dismissing certain patent claims, focusing the litigation:

- **'015 Patent:** Dismissed by stipulation on May 3, 2024. & '879 Patent: Dismissed by stipulation on October 31, 2024.
- **Focus Shift:** The remaining dispute likely centers on complex patents related to manufacturing, formulations, or the JCV assay (a test for a viral infection risk associated with natalizumab treatment, which is mentioned as a key area for discovery).

### C. Trial Delays and Procedural Disputes

The litigation has been characterized by repeated scheduling delays, often instigated by the innovator, Biogen:

- **Initial Trial Date:** May 5, 2025.

- **Reschedule 1:** Vacated and reset for June 9, 2025. & Reschedule 2: Vacated again (May 28, 2025) at Biogen's request for additional discovery on the defendant's JCV assays and marketing plans.
- **Pending Trial:** The trial date is currently pending reevaluation following an October 2025 status conference.

The TYSABRI litigation has successfully navigated the regulatory hurdle with FDA approval (August 2023). However, the failure of the innovator to secure a Preliminary Injunction combined with subsequent trial delays creates a situation where the biosimilar has the ability to launch at any time, subject to its own commercial strategy, while the core patent validity issues remain unresolved.

## Pegfilgrastim: Litigation Landscape & Approval to Launch Timeline

| Accused Biosimilar (Brand) | FDA Approval Date | US Launch Date | Complaint Filed | Litigation Outcome (Final) | Key Legal Action/ Significance |
|---|---|---|---|---|---|
| **LAPELGA (Apotex)** | Not Approved | N/A | Aug. 6, 2015 | Biosimilar Victory on Patent Merits (Affirmed on Appeal) | Landmark ruling on NCM/Injunction; Non-infringement ruling. |
| **ZIEXTENZO (Sandoz)** | Nov. 4, 2019 | Nov. 15, 2019 | Mar. 4, 2016 | Biosimilar Victory on Patent Merits (Affirmed on Appeal) | Summary Judgment of non-infringement. |
| **UDENYCA (Coherus)** | Nov. 2, 2018 | Jan. 3, 2019 | May 10, 2017 | Biosimilar Victory on Procedure (Affirmed on Appeal) | Dismissal for failure to state a claim. |
| **FULPHILA (Mylan)** | Jun. 4, 2018 | Jul. 26, 2018 | Sept. 22, 2017 | Stipulation of Non-Infringement | Achieved launch and stipulated to non-infringement. |
| **LAPELGA/GRASTOFIL (Accord/Apotex)** | N/A | N/A | Aug. 7, 2018 | Settlement (Stipulation & Order of Dismissal) | Typical settlement outcome for pre-approval case. |
| **NYVEPRIA (Hospira)** | Jun. 10, 2020 | Unclear | Feb. 11, 2020 | Settlement (Stipulation & Order of Dismissal) | Typical settlement outcome post-approval. |

| Biosimilar | FDA Approval | US Launch | Lag (Approval to Launch) |
|---|---|---|---|
| **FULPHILA (Mylan)** | Jun. 2018 | Jul. 2018 | 1.5 months |
| **UDENYCA (Coherus)** | Nov. 2018 | Jan. 2019 | 2 months |
| **ZIEXTENZO (Sandoz)** | Nov. 2019 | Nov. 2019 | 11 days |

## Key Observations

- Landmark Procedural Ruling (Amgen v. Apotex - LAPELGA): The District Court initially granted Amgen's PI, preventing the launch until 180 days after FDA approval and notice of commercial marketing (NCM). CAFC Affirmation: The Federal Circuit affirmed this injunction (2016), solidifying the requirement that the 180-day NCM period must begin after the FDA has approved the biosimilar application. This decision was crucial in defining a procedural lock-out for early biosimilar launches.

- Consistent Biosimilar Victories on Patent Merits:
  - Apotex (LAPELGA): The District Court granted judgment of non-infringement on the key '138 patent (Sept. 2016), which was affirmed by the Federal Circuit (2017).
  - Sandoz (ZIEXTENZO): The District Court granted summary judgment of non-infringement on the '878 patent (Dec. 2017), which was also affirmed by the Federal Circuit (2019).
  - Coherus (UDENYCA): The case was dismissed entirely for failure to state a claim (Mar. 2018), and this dismissal was affirmed by the Federal Circuit (2019).
- Market Entry and Outcome:
  - **Mylan (FULPHILA)**: Launched quickly in 2018, leading to a later stipulation of non-infringement in 2019.
  - **Coherus (UDENYCA)**: Launched early 2019, soon after the successful motion to dismiss.
  - **Hospira (NYVEPRIA) and Accord (LAPELGA)**: These cases ended in settlements, the industry's usual endpoint, after the patent landscape was already largely defined against Amgen by the Apotex, Sandoz, and Coherus losses.
- The NEULASTA litigation is characterized by strong procedural enforcement by Amgen (securing the 180-day NCM lock-out) but weak patent enforcement (repeated losses on the merits), leading to a rapid, competitive entry for the approved biosimilars.

## Pertuzumab: Ongoing Litigation Landscape

| Feature | Detail |
|---|---|
| **Case Name & Docket No.** | Genentech v. Shanghai Henlius, 2:25-cv-14648 (D. N.J.) |
| **Accused Biosimilar** | Pertuzumab biosimilar |
| **Reference Product** | PERJETA (Pertuzumab) |
| **Complaint Filed** | August 14, 2025 |
| **FDA Approval Status** | Not yet approved (Pending) |
| **Litigation Status** | Pending |

## Key Observations

This lawsuit marks the official beginning of BPCIA litigation for the reference product PERJETA.

- **First Pertuzumab Litigation**: This is the first publicly reported patent infringement lawsuit regarding a biosimilar to PERJETA (pertuzumab), a blockbuster oncology treatment.
- **Proactive Filing**: Genentech initiated the litigation in August 2025, well in advance of the biosimilar receiving FDA approval. This is the standard BPCIA strategy to trigger the statutory patent dispute process and establish venue.
- **Focus on Market Control**: Since the biosimilar is not yet approved, the lawsuit is designed to eventually lead to a confidential settlement agreement. This agreement will determine the exact, controlled date that the Shanghai Henlius pertuzumab biosimilar is permitted to launch in the US market. The pending status means the critical phase of preliminary injunction motions or settlement negotiations is currently underway.

## Rituximab: Litigation Landscape & Approval to Launch Timeline

| Feature | Genentech v. Sandoz (GP2013) | Genentech v. Celltrion (TRUXIMA) | Genentech v. Dr. Reddy's/ Fresenius Kabi (DRL_RI) |
|---|---|---|---|
| **Accused Biosimilar** | GP2013 (rituximab) | TRUXIMA (rituximab-abbs) | DRL_RI (rituximab) |
| **Reference Product** | RITUXAN (rituximab) | RITUXAN (rituximab) | RITUXAN (rituximab) |
| **FDA Approval Date** | Not Approved | Nov. 28, 2018 | Not Approved |
| **US Launch Date** | N/A | Nov. 11, 2019 | N/A |
| **Complaint Filed** | Dec. 21, 2017 | Jan. 12, 2018 | Nov. 17, 2023 |
| **Final Outcome** | Settlement (Stipulated Dismissal) | Settlement (Stipulated Dismissal) | Settlement (Stipulation of Dismissal) |
| **Settlement Date** | Dec. 6, 2018 | Nov. 1, 2018 | Apr. 10, 2024 |

## Key Observations

- **Consistent Outcome of Early Settlement:** All three cases resulted in a stipulated settlement and dismissal. This demonstrates a strong and consistent pattern of negotiated market entry for rituximab biosimilars, confirming the industry trend away from full BPCIA trials. Both the Sandoz (GP2013) and Celltrion (TRUXIMA) cases were settled within a year of the complaint being filed (December 2018 and November 2018, respectively). The Dr. Reddy's case also settled quickly (April 2024) after a late 2023 filing.
- **Launch Control (TRUXIMA)**: The settlement was finalized before the biosimilar received FDA approval. The negotiated launch date was nearly a full year (11.5 months) after FDA approval, suggesting the settlement agreement included a significantly delayed market entry period for TRUXIMA in exchange for the dismissal of the patent suit.
- **Pre-Approval Settlements**: Two of the three cases (Sandoz and Dr. Reddy's) were settled before the accused biosimilar received FDA approval, demonstrating that companies often strike market-entry agreements conditional on future FDA clearance.

## Tocilizumab: Litigation Landscape & Approval to Launch Timeline

| Feature | Detail |
|---|---|
| **Case Name & Docket No.** | Genentech v. Biogen/Bio-Thera, 1:23-cv-11573 (D. Ma.) |
| **Accused Biosimilar** | BIIB800 (tocilizumab) |
| **Reference Product** | ACTEMRA (tocilizumab) |
| **Complaint Filed** | July 13, 2023 |
| **FDA Approval Date** | September 29, 2023 |
| **Final Outcome** | Settlement (Joint Stipulation of Dismissal) |
| **Settlement Date** | October 23, 2023 |

## Key Observations

- **Swift Resolution**: The primary significance of this litigation is the speed of the legal resolution relative to the regulatory process. The entire litigation spanned a very short period (Just over three months)
- **Settlement is the outcome**: Consistent with the majority of BPCIA litigation, the case ended with a joint stipulation of dismissal in view of a settlement agreement, avoiding a costly and lengthy trial.
- **Pre-Launch Agreement**: The settlement was reached just 24 days after the biosimilar (BIIB800) received FDA approval (September 29, 2023). This rapid sequence suggests the litigation was primarily a formality under the BPCIA, and the settlement terms likely governed the actual date of the biosimilar's US market launch.
- **First Tocilizumab Biosimilar**: This case resolves the litigation for what may be the first biosimilar of ACTEMRA to clear both the regulatory and legal hurdles, setting the stage for its eventual market entry according to the confidential settlement terms.
- **Trastuzumab**: Litigation Landscape & Approval to Launch Timeline

| Case Name (v. Competitor) | Accused Biosimilar (Brand) | FDA Approval Date | US Launch Date | Complaint Filed | Settlement/ Dismissal Date |
|---|---|---|---|---|---|
| **Genentech v. Pfizer** | TRAZIMERA | Mar. 11, 2019 | Feb. 15, 2020 | Nov. 17, 2017 | Dec. 4, 2018 |
| **Genentech v. Celltrion** | HERZUMA | Dec. 14, 2018 | Mar. 16, 2020 | Jan. 12, 2018 | Dec. 27, 2018 |
| **Genentech v. Amgen** | KANJINTI | June 13, 2019 | July 18, 2019 | June 21, 2018 | July 7, 2020 |
| **Genentech v. Samsung Bioepis** | ONTRUZANT | Jan. 18, 2019 | Apr. 15, 2020 | Sept. 4, 2018 | July 1, 2019 |
| **Genentech v. Tanvex** | TX05 | Not Approved | N/A | June 2, 2022 | Feb. 1, 2023 |

| Biosimilar | FDA Approval | Settlement Date | US Launch | Lag (Approval to Launch) |
|---|---|---|---|---|
| **KANJINTI (Amgen)** | Jun. 2019 | Jul. 2020 | Jul. 2019 | 1 month |
| **TRAZIMERA (Pfizer)** | Mar. 2019 | Dec. 2018 | Feb. 2020 | 11 months |
| **HERZUMA (Celltrion)** | Dec. 2018 | Dec. 2018 | Mar. 2020 | 15 months |
| **ONTRUZANT (Samsung)** | Jan. 2019 | Jul. 2019 | Apr. 2020 | 15 months |

## Key Observations

- The Pattern of Settlement: **All five lawsuits concluded via settlement and a stipulated order of dismissal**. This confirms that for HERCEPTIN biosimilars, Genentech's strategy was to negotiate controlled market entry rather than pursue a full trial. For the first four approved biosimilars, the settlements were reached well before the US launch date, indicating the confidential agreements explicitly dictated the launch timing.

- Contested Litigation and Appeal (Genentech v. Amgen): The case against Amgen (KANJINTI) stands out as the most actively contested. Genentech sought to block the launch by filing motions for a Preliminary Injunction (PI) and Temporary Restraining Order (TRO), but the District Court denied these motions (July 2019). KANJINTI launched immediately on July 18, 2019, one month after its FDA approval, and while the appeal was pending. Notably, despite the innovator's loss at the motion and appellate stage, the parties still formalized the end of the litigation with a settlement (July 2020).
- The KANJINTI case, due to the denial of the preliminary injunction, achieved a rapid market entry (~1 month post-approval). The other three approved biosimilars faced a significant, negotiated delay, launching in a cluster 11 to 15 months after their respective approvals in early 2020. This stark contrast highlights the importance of the preliminary injunction ruling in the overall market dynamic.

## Ustekinumab: Litigation Landscape & Approval to Launch Timeline

| Feature | Detail |
|---|---|
| **Case Name & Docket No.** | Janssen Biotech v. Amgen, 1:22-CV-1549 (D. Del.) |
| **Accused Biosimilar** | ABP 654 (ustekinumab) |
| **Reference Product** | STELARA (ustekinumab) |
| **Complaint Filed** | November 29, 2022 |
| **FDA Approval Date** | October 31, 2023 |
| **Final Outcome** | Settlement (Joint Stipulation of Dismissal) |
| **Settlement/Dismissal Date** | May 22/23, 2023 |

## Key Observations

- **Swift Resolution by Settlement:** The litigation was extremely brief, concluding with a joint stipulation of dismissal in view of a settlement just under six months after the complaint was filed.
- **Pre-Approval Agreement:** The settlement was finalized and the case dismissed in May 2023, a full five months before the ustekinumab biosimilar (ABP 654) received its FDA approval in October 2023.
- **Conclusion:** This pattern strongly suggests that the lawsuit was primarily a formality under the BPCIA framework, which quickly led to a confidential settlement agreement that dictated the commercial terms and the US launch date for Amgen's biosimilar, effectively avoiding a drawn-out patent battle.

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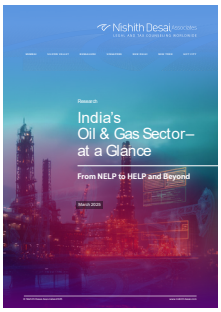


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