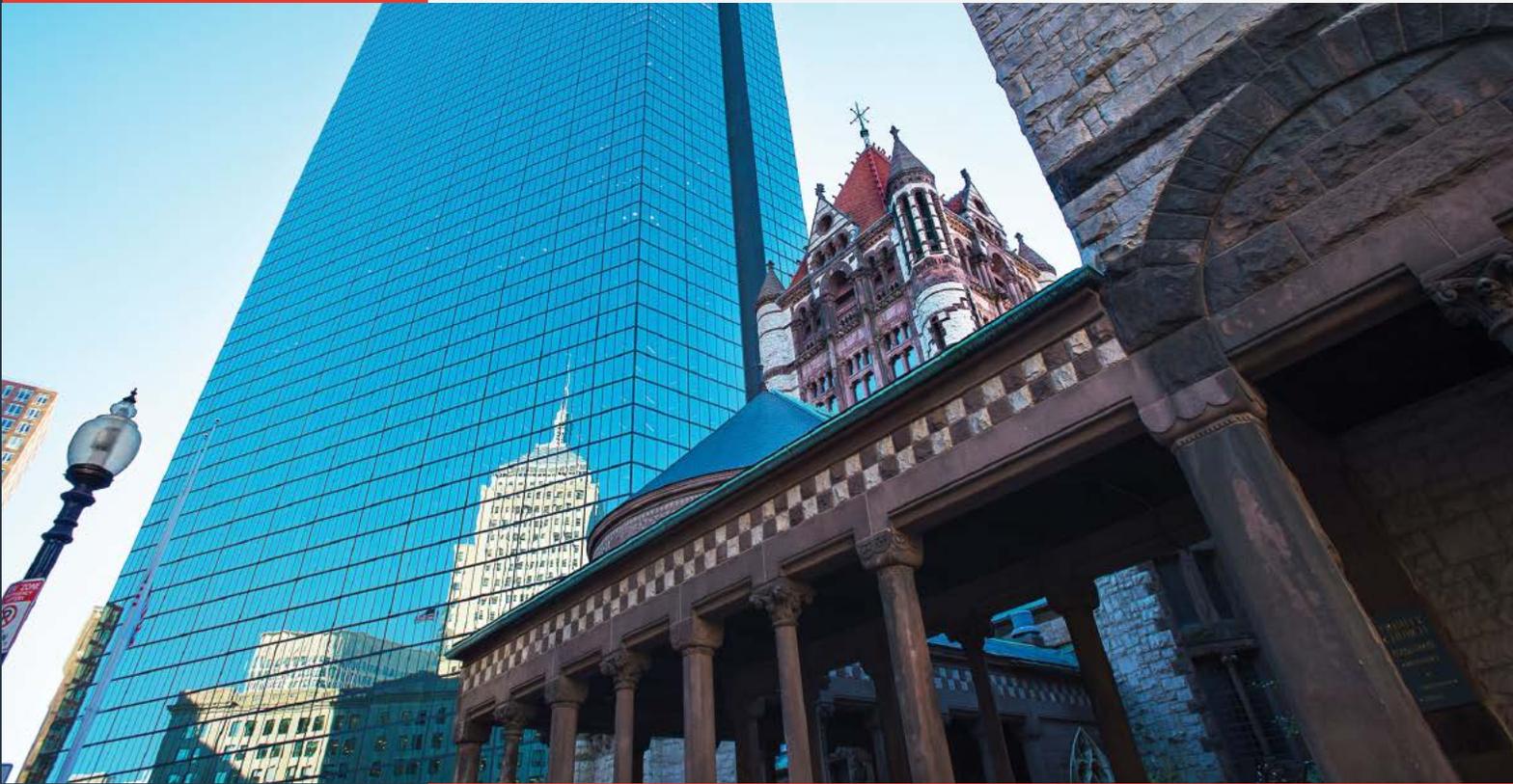


BACK BAY WHITEPAPER

# US Biosimilars 2018: Opportunities and Challenges

January 2018



# US Biosimilars: The Hope and the Hype

---

By Michelle Hoffmann, PhD, and Jonathan Barry, MD

For nearly a decade, biosimilars have loomed large over every facet of the US healthcare debate. Depending on where you sit, biosimilars represent either a dreaded threat to innovation or a hoped-for answer to sky-high drug prices. However, neither scenario has fully come to pass, and although we still expect biosimilars to effect change in the biologics market, when it will happen and to what degree are still unknown. In this white paper we outline trends and potential scenarios for US biosimilars based on current European and US market dynamics. We examine the biosimilar landscape and conclude with thoughts on how developers of biologics can best adapt to an evolving market.

# The Hope

Biologics are therapeutic agents extracted from, or partially synthesized from, biological sources. Unlike manufactured drugs, which are generally pure compounds, biologics can be more complex mixtures of cellular products, including sugars, proteins, and nucleic acids. Biologics are currently available in many drug categories, including anti-inflammatory therapies (anti-TNF therapies, interferons), Erythrocyte Stimulating Agents (epoietin), and oncology therapeutics (VEGF inhibitors, monoclonal antibodies). A bloom of biologics in the early 2000s is now bringing the market to a new level of maturity: As these biologics have begun to come off patent, there has been increased interest in developing and marketing “generic” versions, or “biosimilars,” that have similar therapeutic properties, and which could potentially compete with, and ultimately replace, currently approved and widely used biologics.

When the concept was first introduced, biosimilars were seen as a potential replacement for many biologics, offering comparable benefits at reduced cost. But despite the passage of the Biologics Price Competition and Innovation Act (BPCIA) of 2009 — intended to encourage the development of low-cost biosimilars — the potential impact of these treatments on the US market remains largely undetermined. With only eight biosimilar products having received US approval since 2015, the domestic market lags behind Europe’s, where 37 biosimilars have already been approved<sup>5</sup> and where more than 60 drugs are in development, including many in Phase III clinical trials. Despite a relatively slow start, however, the US market will change, and the manufacturers of both biologics (“innovators”) and biosimilars need to be ready for it.

2010

*“The Congressional Budget Office estimates that over the next decade, the (BPCIA) legislation will reduce direct spending on biologics by \$10 billion in Medicare Part B alone.”<sup>1</sup>*

2012

*“The pharma industry has begun a new chapter of the biosimilars story. We now have much-anticipated guidance from the FDA on what the approval pathway will look like.”<sup>2</sup>*

2015

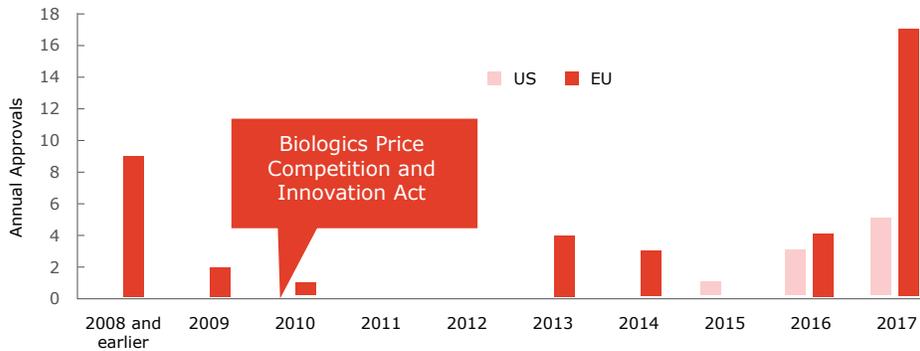
*“The [2009] BPCIA represents one of the more significant overhauls to the pharmaceutical industry in recent decades.”<sup>3</sup>*

2017

*“After years of speculation, consternation and excitement about the arrival of biosimilars in the United States, the competition is at last playing out.”<sup>4</sup>*

- 1 Buzzard J, Dalgaard K, Evers M, Kanda V, Moller M, Srinivasan R. US Healthcare Reform: A Legislative Pathway for Biosimilars Will Spur Growth—and Present New Challenges. New York: McKinsey and Company; 2010. Available at: <https://tinyurl.com/y8knj7ce>. Accessed Dec 21, 2017.
- 2 Howell P. How Much Cheaper Will Biosimilars Be? FiercePharma (website). March 2, 2017. Available at: <https://tinyurl.com/y8kvwrc5>. Accessed Dec 21, 2017.
- 3 Timmis R. The Biologics Price Competition and Innovation Act: potential problems in the biologic-drug regulatory scheme. Northwest J Tech Intellect Prop. 2015;13(2). Available at: <https://tinyurl.com/ybravbev>. Accessed Dec 21, 2017.
- 4 Mullard A. Bracing for the biosimilar wave. Nat Rev Drug Discov. 2017;16:152-154. doi:10.1038/nrd.2017.36.
- 5 European Public Assessment Reports (EPAR) for Human Medicines. European Medicines Agency (website). Available at: <https://tinyurl.com/8542jvp>. Accessed December 12, 2017.  
Purple Book: Lists of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations. Food and Drug Administration (website). Available at: <https://tinyurl.com/ybpcet5v>. Accessed December 12, 2017.

Figure 1: Biosimilar Approvals to Date: 37 in EU, 8 in US<sup>5,6</sup>



Biosimilars and their relationship to generic medications have been extensively described by both [commercial](#) and government sources ([US](#) and [European](#)), so this report will not aim to cover that ground again. Although biosimilars and generics share many features as alternatives to established therapeutics, their differences will shape the market. Notably, biosimilars differ in three ways:

1. While biosimilars are essentially copies of innovator treatments, they are similar, but not chemically identical, to an existing biologic/reference product.
2. Because biosimilars are not identical to their reference product, they are not considered “interchangeable” (automatically substitutable for an innovator’s product), and so must undergo independent approval through clinical trials.
3. Because biosimilars mimic approved biologics, their clinical trials are less risky and complex than those performed for the innovator drug. Such trials are generally thought to incur lower costs and overhead.

Biologics account for almost 40% of US prescription drug spending and 70% of drug spending growth from 2010 to 2015.<sup>7</sup> Insurers, the government, and other purchasers of healthcare have hoped that biosimilars would offer comparable clinical utility at a lower cost. Independent analysts agree: A recent RAND analysis projects the impact of biosimilars on the US market to be high, with an estimated reduction in direct spending on biologic drugs of \$54B between 2017 and 2026, (~3% of the total estimated amount of biologic spending).<sup>8</sup>

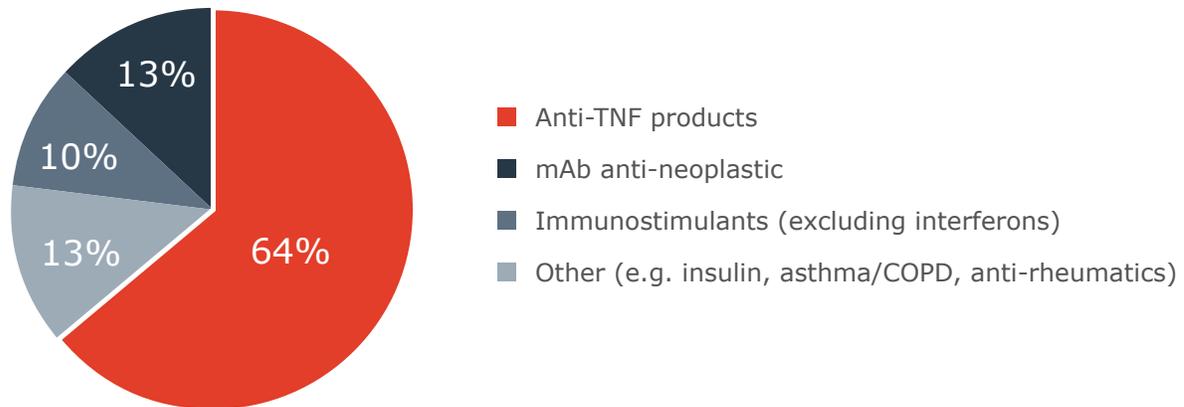
As of this writing, biosimilars have been approved for three of the top ten biologics sold in the United States: Humira (Amgen’s Amjevita, with an expected 2023 US launch and 2018 EU launch, due to a patent agreement with AbbVie); Remicade (Pfizer’s Inflectra; Merck’s Renflexis); and Enbrel (Sandoz’s Erelzi). Of those, two are already on the market: Inflectra and Renflexis. Zarxio (for Neupogen) is also available. The 60+ biosimilars in the development pipeline include medications in therapeutic areas such as oncology, immunology, and diabetes, with biosimilar producers showing particular interest in leading biologics with recent or pending patent expiry, including Avastin, Humira, and Levemir. The potential reach of such biosimilars is fueling enthusiasm in the United States, especially given the success of these drugs in Europe and the ever-present national interest in driving down healthcare costs.

6 Reinke T. Biosimilars ready, at last, to make their entrance: stars are born or do they fizzle? *Manag Care*. 2017;26(3):20-23.

7 Mulcahy AW, Hlavka JP, Case SR. Biosimilar Cost Savings in the United States: Initial Experience and Future Potential. Santa Monica, CA: RAND Corporation; 2017. Available at: <https://tinyurl.com/y7re6ecn>. Accessed Dec 20, 2017.

8 Ibid.

Figure 2: Projected US Savings by Biosimilar Molecule Class, 2017–26<sup>9</sup>



## The Hype

Despite predictions that biosimilars would become as disruptive a force in the market as generics, this has not yet occurred. While biosimilars have been approved and are entering the US market, the rate at which they are coming to market and the pace of their subsequent growth in market share have been [slower](#) than [anticipated](#). This slow rate of adoption could be due to several factors, including, in some cases a lack of interchangeability, the drug's breadth of label and targeted indications, and the need for increased physician awareness. The most important factor, however, could be that biosimilar drugs are simply not yet cheap enough.

When Back Bay Life Science Advisors recently analyzed this sector, we spoke with US payers representing large, national health plans. All indicated that biosimilar manufacturers had not offered them an anticipated 30% to 40% reduction relative to the net price (i.e., wholesale price less rebates) of corresponding biologics. Without significant price reductions, US payers are reluctant to switch from the innovator therapy, which can offer more substantial cost savings to the payer than the biosimilar therapy, as well as a demonstrably reliable drug supply.

It is important to note that thus far physicians are not clamoring for biosimilars. The physicians we interviewed understand that biosimilars can be as effective as reference products. But they also expressed a wariness regarding using a biosimilar to treat a therapeutic indication for which the consequences of failure would be disastrous. They want to see more rigorous data before switching among drugs with curative potential.

*"Without 'shock and awe' pricing, we won't endorse biosimilars as a country and as a payer community. And then biosimilars will fail and we'll never get 'Phase II' of biosimilars [in oncology and MS]."*

—US payer

*"Biosimilars have already taken costs out of the system, but it hasn't been enough yet...."*

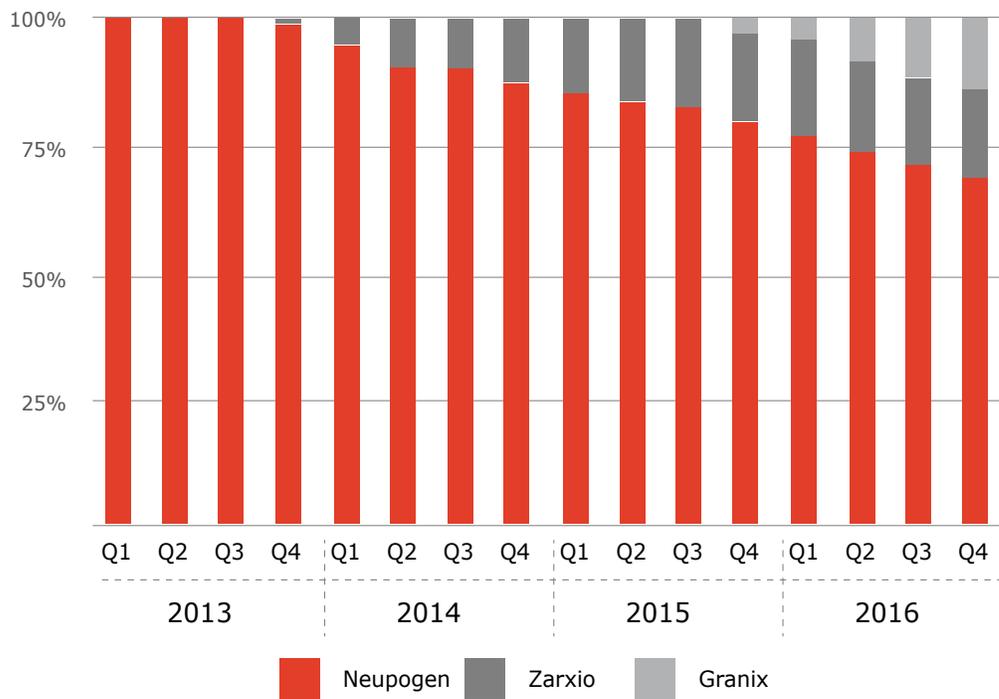
—US payer

<sup>9</sup> Ibid.

Nevertheless, when biosimilarity can be demonstrated, a lower price appears to be a motivating factor. For example, oncologists point to cost savings as a factor for adopting the biosimilar Zarxio for Neupogen (filgrastim). Another factor in Zarxio’s favor is its use in treating a chemotherapy side effect, neutropenia, rather than the primary cancer.

Patients may slow uptake as well. An additional barrier to the adoption of biosimilars may be consequential clinical differences between biosimilars and their reference biologics. A recently published trial showed that nearly 25% of patients with autoimmune diseases (rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis) discontinued biosimilar treatment when converted from the originator, having reported worsened subjective symptoms.<sup>10</sup> In fact, the potential for patient pushback against biosimilars may lead physicians to choose the established innovator biologic.

Figure 3: Zarxio Sales As a Percentage of Filgrastim Sales, 2015–17<sup>11</sup>



Uncertainty as to which indications are appropriate for biosimilar use poses still another challenge. For example, many biologics are well established for use in treating multiple indications. Approval for one indication can be followed by documented effectiveness in treating other indications. A biosimilar, however, lacks the same clinical history as a biologic, and so it is often unclear whether the similarity of a biosimilar would translate to the same

*"[Zarxio] has long periods of data published on its single indication. When you are dealing with a biologic that has six to ten indications, you need more data for longer periods to be certain."*  
 —US payer

<sup>10</sup> Tweehuysen L, et al. Subjective complaints as the main reason for biosimilar discontinuation after open-label transition from reference infliximab to biosimilar infliximab. *Arthritis Rheumatol.* 2018 Jan;70(1):60-68. doi:10.1002/art.40324. Epub 2017 Dec 7.

<sup>11</sup> Mulcahy AW, et al.

additional indications being treated by the innovator's product. In short, considering the current lack of "interchangeability," biosimilar access will likely be limited until meaningful cost savings occur for US payers.

And although most physicians can infer how to use a biosimilar in secondary indications, reimbursement guidelines might restrict its use for only the indication for which the biosimilar was tested. Payers and clinicians are largely waiting for the FDA to weigh in on whether biosimilar studies in one indication will yield sufficient data to make the biosimilar applicable to all the indications for which an innovator has proven efficacy. So despite the pressure to reduce healthcare costs while delivering high-quality patient care, the reality is that barriers to biosimilar adoption remain significant in the United States.

*"In the end it will largely depend on the FDA approval and guidelines to make sure there are no reimbursement issues. Without these, we won't be extrapolating to patients where the FDA approval hasn't been given."*

*—US oncologist*

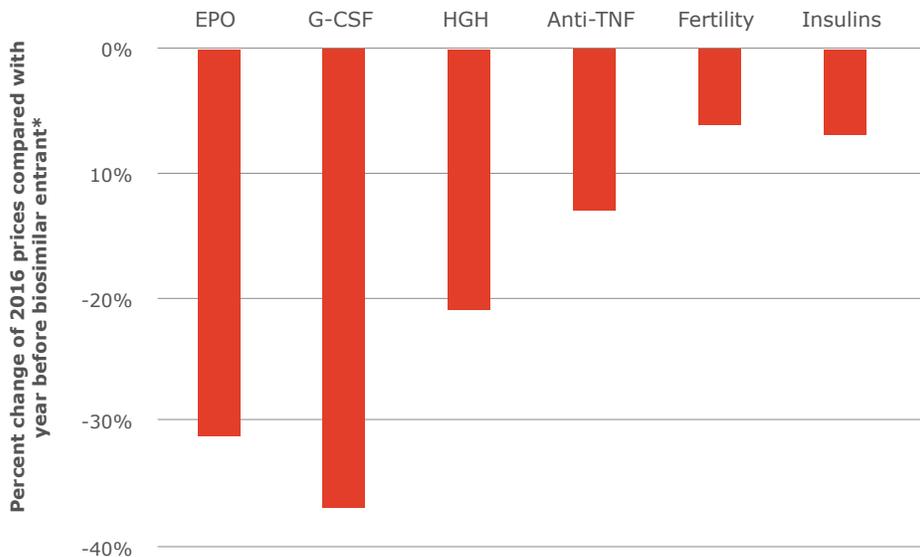
## Strategic Advice for Innovator Companies

Although many questions remain unanswered about biosimilars and the barriers to their adoption, all signs point to a changing market. Biosimilars might not have immediately taken off as expected, but innovator companies should heed the lessons learned from both US and European experiences. After carefully analyzing the history of biosimilars, we have identified several actions that innovators can take to buffer themselves against a potential market-share threat. First, innovators should be prepared to compete on net price, leveraging their manufacturing capabilities and market position to remain competitive. Second, innovators should develop approaches to securing market access and maintaining strategic market share, building on the demonstrated efficacy of their products and their established history within the market. And, third, innovators should bolster their reputation within the market to foster and preserve physician and patient trust.

Moreover, since price appears to be a major driver behind the adoption of biosimilars and their ability to capture market share, one of the most significant actions that an innovator can take is to prepare for the price decreases that will accompany the introduction of biosimilars. Although multiple aspects of the US market might slow price erosion, the European experience has nevertheless demonstrated that biosimilar entrance ultimately affects innovator prices, as well as prices for follow-on biologics.<sup>12</sup>

<sup>12</sup> The Impact of Biosimilar Competition in Europe. London: QuintilesIMS; May 2017. Available at: <https://tinyurl.com/y7zvy5cl>. Accessed December 18, 2017.

Figure 4: Total Daily Dose Price Changes After Biosimilar Entry<sup>13</sup>



\* Change is between prices for the class in the year before biosimilar entrance and 2016 in the European Economic Area (EEA).

Innovators should take solace in the fact that data from the United States and Europe demonstrate a demonstrably weak correlation between price drops and biosimilar market share.<sup>14</sup> Part of what is protecting innovators is their established position in the market. Unless the biosimilar manufacturer can access market share quickly, innovators are likely to retain their advantage. Nevertheless, innovators must remain aware of the risk that biosimilars could in some instances rapidly gain market share and hence carefully consider their reaction to any gradual reduction that could ensue in their own market share.

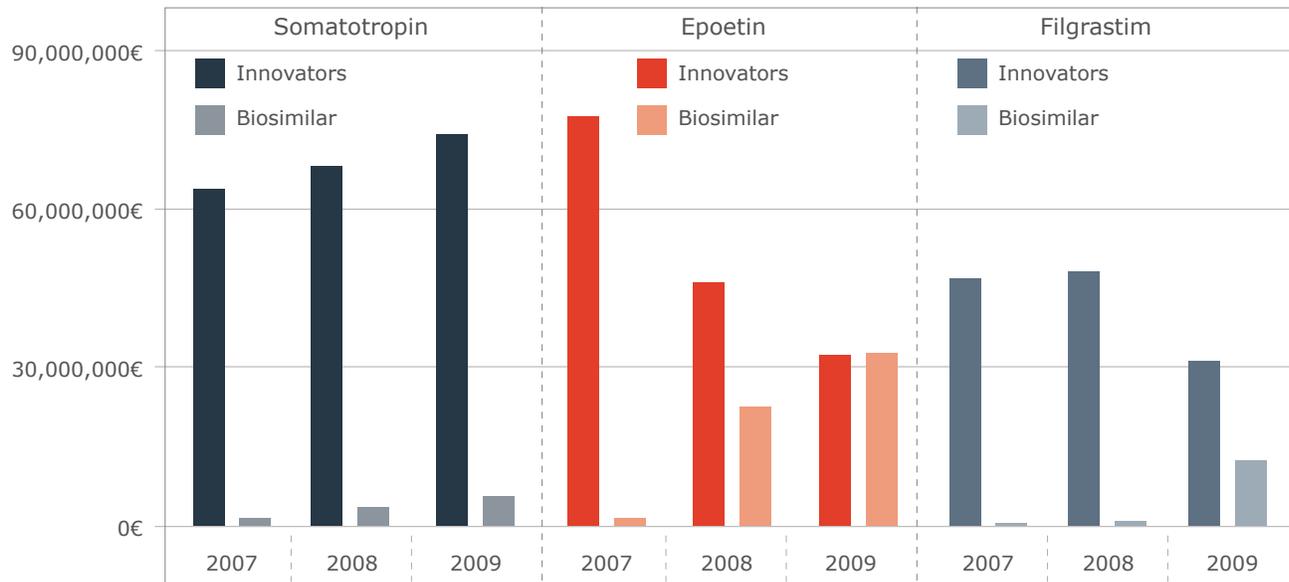
Consider the case of Germany, where insurers incentivize hospitals and clinics to use cheaper alternatives when possible. In the German system, a reference pricing system is in place for specific groups of biosimilars, and there are regional biosimilar quotas.<sup>15</sup> As Figure 5 shows, while these factors alone do not guarantee biosimilar uptake, the drug epoetin (biosimilar to the biologic erythropoietin) enjoyed early and rapid success, and quickly gained substantial market share while the introduction of the biosimilars somatotropin and filgrastim did not.

<sup>13</sup> Ibid.

<sup>14</sup> Ibid.

<sup>15</sup> Grabowski H, Guha R, Salgado M. Biosimilar competition: lessons from Europe. *Nat Rev Drug Discov.* 2014 Feb;13(2):99–100. doi:10.1038/nrd4210. Epub 2014 Jan 21.

Figure 5: German Uptake of Biosimilars, 2007-09<sup>16</sup>



So what made epoetin such a successful biosimilar? In this case, it was a combination of price and market acceptance. Epoetin was introduced at a discount of 20% off net price, a clear but not radical discount to the innovator product.<sup>17</sup> This discount, however, prompted early adoption by the Kuratorium für Dialyse und Nierentransplantation (Kuratorium for Dialysis and Renal Transplantation; KfH), the largest network of dialysis centers in Germany, which manages 30% of Germany’s dialysis patients.<sup>18,19</sup> The KfH uses a limited, centralized set of Group Purchasing Organizations (GPOs) to negotiate with manufacturers, and thus delivered a large set of accessible patients. Although there was no mandated substitution, uptake was spurred by peer-to-peer education among practicing nephrologists and associations regarding epoetin and its efficacy. But in the end, it was the price discount and approval by a leading national network, along with coordinated delivery via a network of providers, that allowed this biosimilar to outperform others.

Innovator companies operating in the United States need to heed this example and consider how they can fully leverage their advantage as incumbents to retain market share as prices drop. For example, Inflectra (biosimilar infliximab), which is used to treat rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn’s disease, plaque psoriasis, and ulcerative colitis, was approved by the FDA in April 2016. It launched at minus the 15% of biologic’s wholesale acquisition cost (WAC), and even dropped to minus 35% of WAC when a second biosimilar, Renflexis, was introduced in June 2017.<sup>20</sup> The innovator company, Johnson & Johnson (J&J), which has a significant amount of market share, preserved

16 Rovira J, Espín J, García L, Olry de Labry A. The Impact of Biosimilars’ Entry in the EU Market. Andalusian School of Public Health. EMI-Net; 2011. Available at: <https://tinyurl.com/y9xug22c>. December 18, 2017.

17 Back Bay Life Science Advisors expert interviews conducted December 2017.

18 Lepage-Nefkens I, Gerkens S, Vinck I, Piérart J, Hulstaert F, Farfán-Portet M. Barriers and Opportunities for the Uptake of Biosimilar Medicines in Belgium. Brussels: Belgian Health Care Knowledge Centre (KCE); 2013, KCE Reports 199. Available at: <https://tinyurl.com/ycb5p22e>. Accessed December 18, 2017.

19 Back Bay Life Science Advisors expert interviews conducted December 2017.

20 Harris R. Small Savings for Drugs Made to Mimic Biotech Blockbusters. Shots: Health News from NPR (website). October 19, 2016. Available at: <https://tinyurl.com/yc793l2h>. Accessed December 11, 2017.

Remicade’s preferred status by introducing corresponding price reductions.<sup>21,22</sup> The combination of lower prices, physician familiarity, and confidence in J&J’s product helped the company retain a dominant share of the market.

Figure 6: Infliximab and Filgrastim Coverage Summary<sup>23</sup>

Insurer	Lives Covered	Infliximab	Filgrastim
United Healthcare		Remicade preferred	Parity among options
Anthem		Remicade preferred	Parity among options
Humana		Remicade preferred	Parity among options
Aetna		Remicade preferred Inflectra preferred as of Jan 2018	Zarxio preferred
BCBS - Illinois, Michigan		Remicade preferred	Zarxio and Granix preferred over Neupogen (non-preferred, specialty)
Cigna		Remicade preferred	Zarxio or Granix preferred over Neupogen
Centene		Inflectra preferred	Parity among options
Kaiser Permanente		Inflectra preferred	Zarxio preferred

 Represents 5M people

As the example of Remicade shows, innovators can incrementally reduce prices and maintain preferred status by leveraging their majority market share while unencumbered by the need for new sales forces and other switching costs.<sup>24</sup> The same cannot be said for a comparable price reduction for the biosimilar, and so such an adaptive pricing and marketing strategy can pay off when competing with discount biosimilars. Back Bay interviewed payers from a variety of plans who were clear that unless biosimilar manufacturers offered 40% to 60% discounts off net price, an innovator’s smaller rebates, coupled with market share, made it more economically attractive for these payers to stick with the originator’s biologic.<sup>25</sup>

*“If we don’t get the ‘shock and awe’ pricing from a biosimilar manufacturer, and we can get 2 to 5 points from an innovator, we get savings from doing no work... If they compete [on price], they keep biosimilars at bay.”*

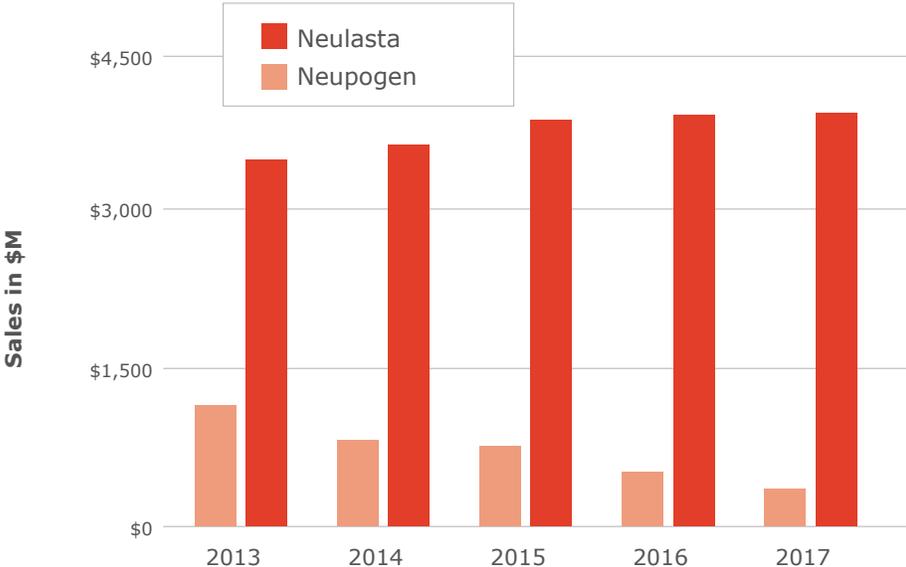
—US payer

21 Back Bay Life Science Advisors analysis: Non-exhaustive review of a sample of commercial insurance policy documents, 2017.  
 22 Back Bay Life Science Advisors expert interviews conducted in December 2017.  
 23 Back Bay Life Science Advisors analysis.  
 24 Blackstone EA, Joseph PF. The economics of biosimilars. Am Health Drug Benefits. 2013 Sep-Oct;6(8):469–478.  
 25 Stanton D. Remicade Biosimilar: J&J’s “Fear and Loathing” Subdued As Pfizer Slugs It Out. Biopharma Reporter (website). September 14, 2017. Available at: <https://tinyurl.com/yaeg3mq2>. Accessed December 11, 2017.

Finally, innovators should reinforce their brand and develop strategies to promote clinician allegiance. Currently, biosimilar filgrastim (Zarxio) occupies a preferred position on the majority of formularies of some of the US’s largest payers, ahead of the original biologic, Neupogen. When reflecting on the decision to go with Zarxio, US payers called it a “no-brainer because of the price differential.”

Nevertheless, Zarxio sales have not achieved expected levels, potentially because innovator Amgen has appealed to their physician base and encouraged them to switch to Neulasta, a longer-acting version of Neupogen. Amgen also made changes to the injector and provided ancillary patient and physician services that go “beyond the pill.” The company’s strategy of building on their clinical capital and innovator status allowed them to overcome the advantage that Zarxio’s price seemingly provided.<sup>26</sup>

Figure 7: US Neulasta/Neupogen Sales, 2013–17<sup>27</sup>



26 Johnson SR. One Year After Zarxio Approval, Future of Biosimilars Remains Unclear. Modern Healthcare (website), March 23, 2016. Available at: <https://tinyurl.com/yagx59n8>. Accessed December 11, 2017.

27 Mulcahy AW, et al.

## Conclusion

Biosimilars will likely become an increasingly important part of the pharmaceutical ecosystem. However, they continue to face barriers to adoption, including questions of interchangeability, a typical lack of approval for all the reference biologic's indications, the need for biosimilar manufacturers to negotiate with payers, the challenge of overcoming unique patent dynamics, and innovators' established positions within the physician community.

As these challenges play out in the coming years, manufacturers of biosimilars will become more adept at navigating the complex US drug market. To achieve their goals, they must demonstrate strong, evidence-based clinical value (such as switching studies) to convince payers and providers of their product's value and reliability, as well as ensure a high-quality drug and robust supply.

Given the inevitable and accelerating gains that biosimilars will make in the market, innovators should work to preserve their positions through adaptive strategies that take advantage of their market leadership. We advise the use of negotiated rebating/discounting with payers, including leveraging price and access to their portfolio of therapies, and reinforcing brand awareness and loyalty with physicians and patients. Manufacturers of biologics can also drive innovation (such as through streamlined clinical workflow, better drug delivery, or other changes) that will give them a marketplace edge.

Both innovators and biosimilar developers would benefit from adopting strategies that enable broader market access, create economic alignment with payers and providers, and, most importantly, focus on ensuring the best patient outcomes. Although it is not clear who the winners and losers will be in the biologics and biosimilars market, what is certain is that the landscape is shifting.

We hope that this white paper has provided some helpful background information and insights into why it is likely a time of risk and opportunity for both the biosimilar and the innovative biotech industries. We welcome feedback on the evidence and analysis presented here, as well as the opportunity to continue this important and timely conversation.

# About Back Bay Life Science Advisors

Back Bay Life Science Advisors is a strategic consulting and advisory firm dedicated to uncovering the deepest business insights for clients so they can thrive in a competitive, dynamic environment. We advance those recommendations into execution on the transactions that drive our industry. Back Bay combines rigorous analytics and industry expertise to arrive at solutions that are often unexpected but always realistic and actionable. Clients rely on Back Bay to create clarity for their toughest strategic decisions to drive growth and create value.

Back Bay's hands-on senior leaders are engaged with every assignment, from inception to execution. To learn more about Back Bay leadership visit [bblsa.com](http://bblsa.com).

## **Back Bay Life Science Advisors**

545 Boylston St., 12th Floor

Boston, MA 02116

Phone: 617.236.0954

Fax: 617.236.1215

[mhoffmann@bblsa.com](mailto:mhoffmann@bblsa.com)

© 2018. Back Bay Life Science Advisors.  
All Rights Reserved.