Deloitte.

Winning with biosimilars
Opportunities in global markets

While most players will want a presence in developed markets, a considerable opportunity exists in emerging markets for biosimilars. To win in these markets, biosimilars players will need to adopt a long-term strategy to provide affordable products and improved access to the large pockets of non-consumption. This will entail growing sales – though at a smaller margin than in developed markets – among an increasingly affluent and health-conscious population. It will also require selecting therapeutic areas (TAs) that have the largest potential impact for the local population. Participating companies will need to provide access, partner for local capabilities, and understand the importance of branding and building customer engagement in meaningful ways. Although selling lower-cost biosimilars in emerging markets may appear to be a less attractive strategy than selling in established, developed markets, particularly for high-margin branded players, winning in these markets can help position biosimilars companies for long-term success.

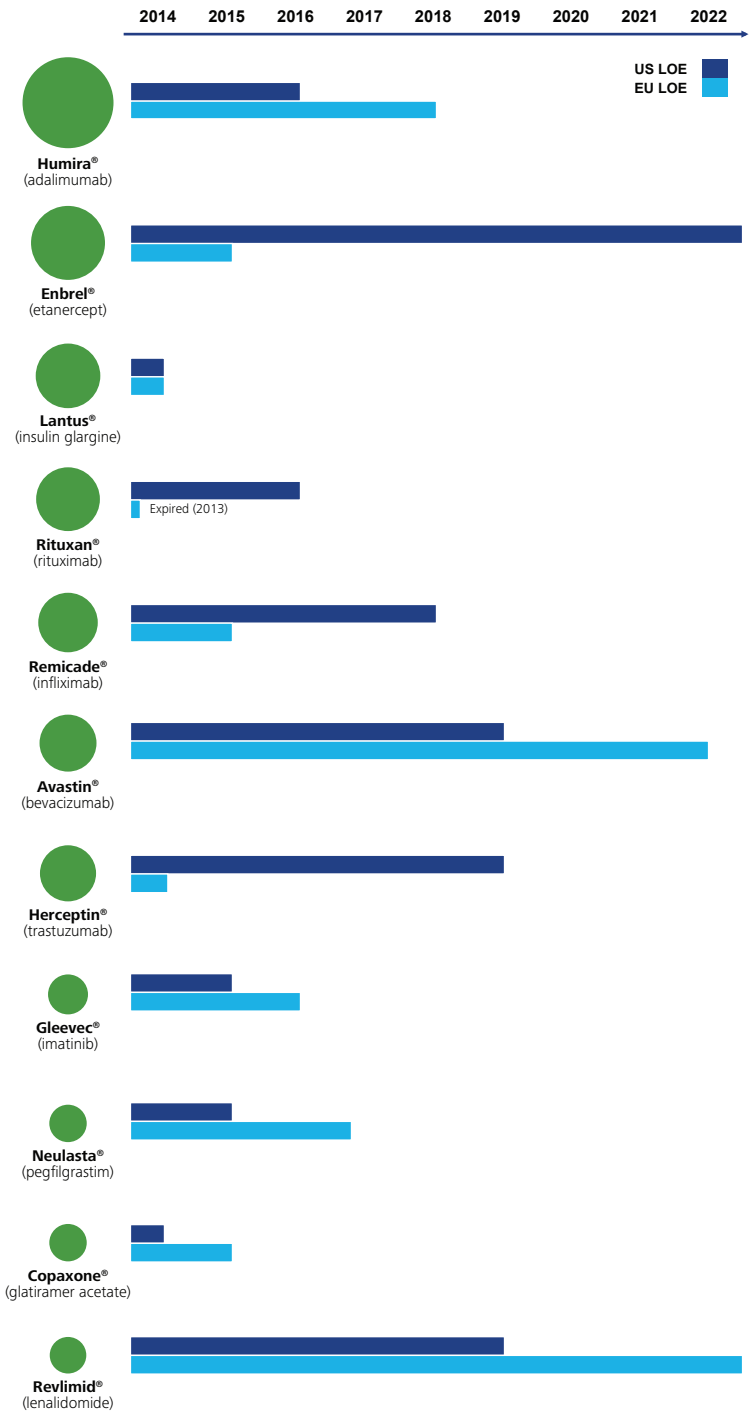
Introduction

Over the past several years, biologics have gained significant traction in the pharmaceutical industry, representing more than $150 billion in global sales in 2013. By 2020 they are predicted to generate $290 billion in revenue and comprise 27 percent of the pharmaceutical market.[i] Forty-eight percent of sales come from 11 biologics that face loss of exclusivity over the next seven years (Figure 1).[ii] This, along with the increasing worldwide focus on improving health care access and the cost of care, presents an attractive opportunity for biosimilars manufacturers.

Analysts expect the worldwide biosimilars market to reach $25-$35 billion by 2020.[iii] Since the first biosimilar approval in the European Union (EU) in 2006, there are now more than 700 biosimilars approved (~450) or in the pipeline (~250) globally.[iv] In major markets like the EU, regulators and payers have recognized the potential financial benefit of biosimilars and are driving their uptake. For example, France has initiated automatic substitution of select biosimilars over the reference products.

In the United States alone, the cost savings from switching to biosimilars are projected to be between $40[v] and $250 billion over the next 10 years, with the first biosimilar to hit the US market expected to contribute about $5-7 billion in savings.[vi]

Figure 1: Patent expirations of major biologics



Note: The size of the circle represents the drug's global sales in 2013
Sources: Company websites and SEC filings, USPTO, EvaluatePharma

What are biosimilars?

Biosimilars are biologic products that are similar but not identical to reference/originator biologic products. Although described differently by various global health agencies (Figure 2), biosimilars generally are large-molecular-weight, complex molecules that are produced in living cells through genetic engineering. The recent recommendation by the United States Food and Drug Administration (FDA) to approve an oncology supportive care drug developed by Sandoz represents a landmark for the United States launch and commercialization of biosimilars.

Early biologics, such as insulin, erythropoietin (EPO), and growth hormones, have been invaluable in the treatment of serious illnesses such as diabetes, anemia, and renal diseases. More complex biologics, such as monoclonal antibodies (mAbs), cytokines, and therapeutic vaccines, are helping to revolutionize treatment of cancer, autoimmune disorders, and other difficult-to-treat diseases. For such higher-cost disease areas, biosimilars should be instrumental in expanding access to populations who need these therapies but are unable to access them today.

Figure 2: "Biosimilar" definitions by global health agencies

FDA

A biological product that is highly similar to a United States licensed reference biological product not with standing minor differences in clinically inactive components, and for which there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity and potency of the product.[1]

WHO

A biotherapeutic product which is similar in terms of quality, safety and efficacy to an already licensed reference biotherapeutic product.[2]

EMA

A biosimilar is a biological medicinal product that contains a version of the active substance of an already authorized original biological medicinal product (reference medicinal product). A biosimilar demonstrates similarity to the reference product in terms of quality characteristics, biological activity, safety and efficacy based on a comprehensive comparability exercise.[3]

Source:

1 United States Food and Drug Administration. Guidance for Industry: Quality considerations in demonstration biosimilarity to a reference protein product. Washington DC: United States Food and Drug Administration, 2012.

2 World Health Organization. Expert Committee on Biological Standardization. Guidelines on Evaluation of Similar Biotherapeutic Products (SBPs). World Health Organization. October 23, 2009.

3 European Medicines Agency. Questions and Answers on biosimilar medicines (similar medicinal products). European Medicines Agency. September 27, 2012.

Challenges facing biosimilars

Despite their promise, biosimilars face competition from non-original biologics and bio-betters:

Non-original biologics: Non-original biologics are copies of innovator drugs, frequently found in markets with less stringent intellectual property (IP) protection, and/or markets that do not have a dedicated regulatory pathway for approval.

Bio-betters: While biosimilars are approved via a dedicated regulatory pathway, bio-betters follow the same regulatory pathway as the innovator drug and are step-wise improvements on innovator molecules. For example, Gazyva® is a bio-better of Rituxan®, both from Roche. Manufacturers of originator biologics often use bio-better strategies to strengthen market positioning with an improved product, while continuing to command premium prices. Depending on the therapeutic area, a clinically differentiated bio-better with the market access proficiency of an established biologics player may be more successful than biosimilars in capturing market share.

Although it is generally expected that biosimilars will emerge as a rapidly growing segment of the biopharmaceutical industry, their uptake faces several challenges (Figure 3 illustrates the key differences between biosimilars and generic medications).

Regulatory uncertainty

The regulatory policies governing biosimilars are still in flux, with major markets like China lacking consistent and clear pathways. The United States issued draft biosimilars guidance in 2013, and although the FDA recently approved the filgrastim biosimilar, the agency has yet to finalize a formal approval pathway.

Production complexity

Unlike generics, the cost, time, and risk of biologics production are higher, and these are typically passed on to the consumer in terms of higher prices. While generics cost between $1 million and $5 million to develop, biosimilars cost between $100 million and $200 million.[vii] Biosimilars are more complex to develop and manufacture due to the inherent variability between one living cell and another, and the inability to exactly replicate the manufacturing or structure of the originator biologic.

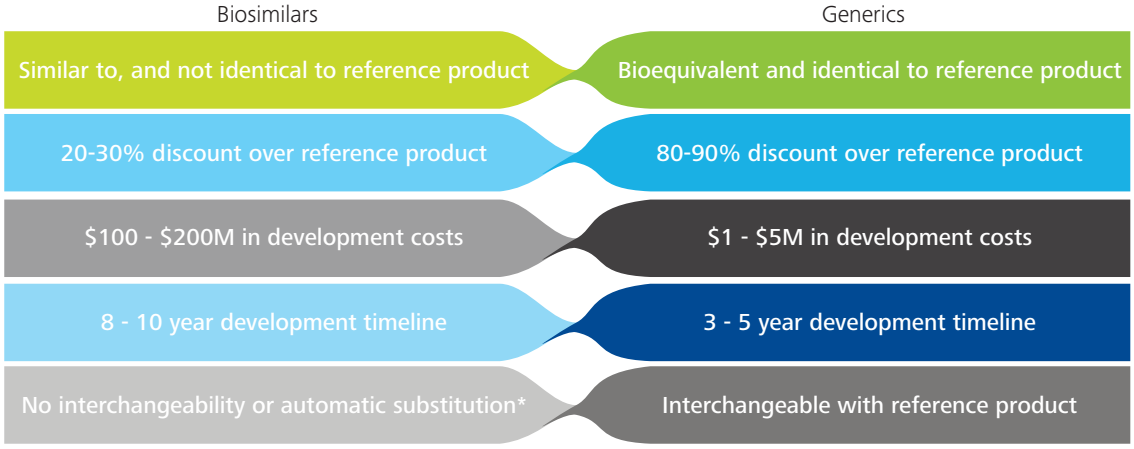
Interchangeability

The lack of clear guidelines on substitutability and interchangeability with reference biologics will likely cause physicians to exercise more caution in prescribing biosimilars until they gain comfort with the quality and efficacy of biosimilars. When the FDA reviewed Sandoz's filgrastim, there was much speculation on whether interchangeability would be recommended. However, the FDA only focused on biosimilarity. This means that Sandoz may need to show comparative data and engage in market education to drive prescriptions and increase market share.

Competition

Biosimilars face competition from at least two sources: bio-betters from branded companies and brand consciousness from consumers. Biosimilars are anticipated to engage primarily in "brand-on-brand" competition with their reference therapies, unlike Hatch-Waxman generics. Also unlike generics, which are heavily discounted, biosimilar discounts can be offset by rebates and service agreements for branded biologics, thereby making biosimilars less attractive. With more sophisticated and long-term biologic treatments (e.g., monoclonal antibodies and growth hormones) and the associated treatment chronicity, it could take longer to demonstrate and convince stakeholders of the benefits of switching.

Figure 3: Key differences between biosimilars and generics

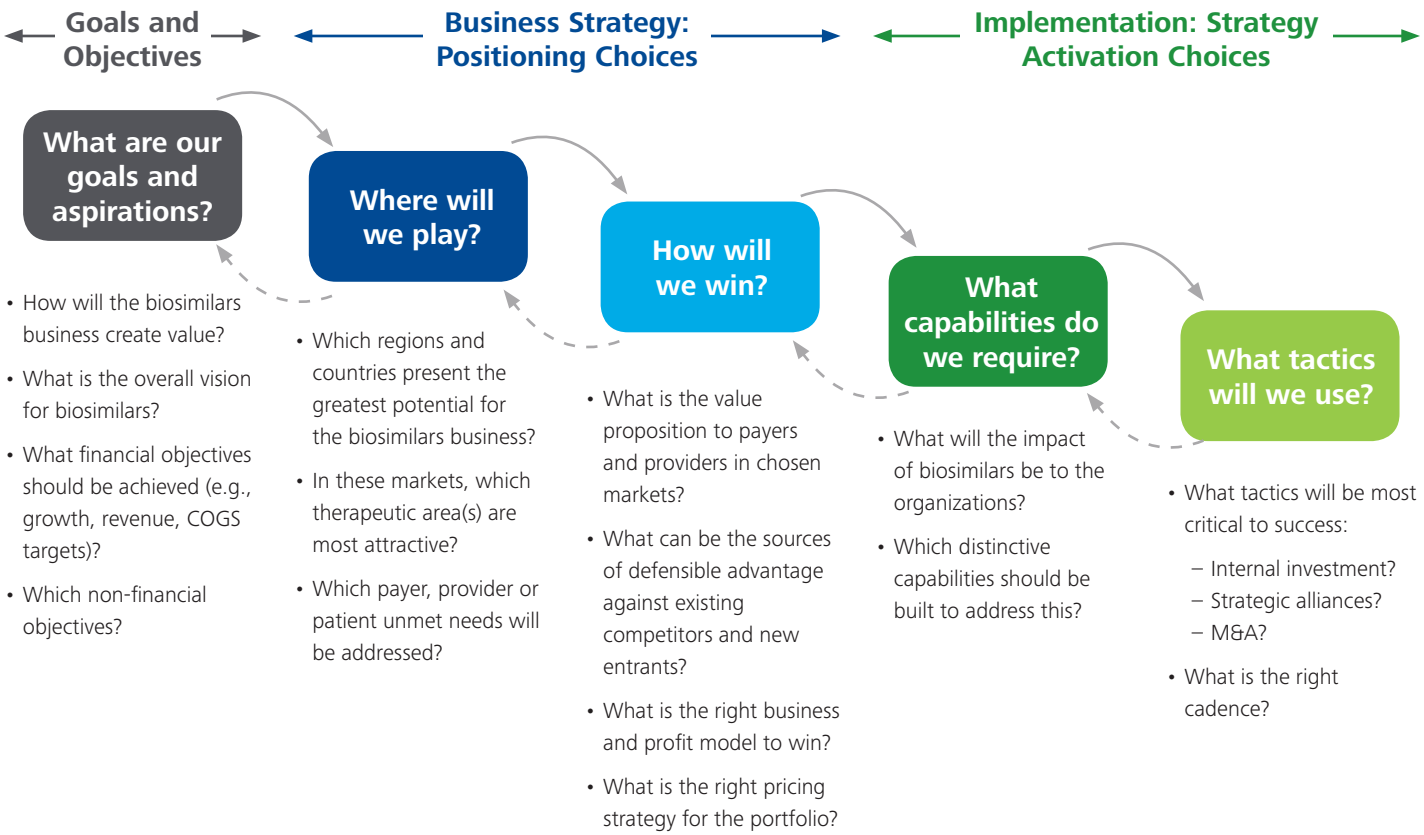


*France allows automatic substitution for biosimilars under certain conditions

Developing a global biosimilars strategy

To develop a global biosimilars strategy, manufacturers will need to address a set of strategic choices – including "where to play" and "how to win." These choices are part of the Strategic Choice Cascade (Figure 4), a framework developed by Deloitte to help companies address strategy through a set of five integrated questions. Once a manufacturer answers the first question about organizational goals and aspirations, the next two choices on the Cascade will guide how to fulfill these goals and aspirations. The choices of "where to play" and "how to win" are the focus of this paper.

Figure 4: Strategic Choice Cascade



Where to play

To help biosimilars manufacturers understand which regions present the greatest potential for growth in the near and longer term, Deloitte evaluated the developed markets of the United States, EU5 and Japan, and emerging markets including the BRICS (Brazil, Russia, India, China and South Africa) and MIST (Mexico, Indonesia, South Korea and Turkey) countries. The analysis focused on six dimensions: access to affordable biologics, regulatory environment, payer assessment and access, prescriber acceptance, patient acceptance, and biosimilars presence. A summary of findings for each market is presented in Figure 5, and more complete information on select countries is found on Page 6.

Figure 5: Summary of cross-country analysis

Variables (Ranked by importance)		Access to affordable biologics Physical and financial ability to receive biologics	Regulatory environment Presence of an abbreviated or dedicated pathway	Payer assessment and access Engagement and advocacy from payer in favor of biosimilars	Prescriber acceptance Willingness to prescribe biosimilar vs. reference molecule	Patient acceptance Patient attitude towards biosimilars	Biosimilars presence Number of approved biosimilars in the market
Developed	US	Large access	In development	Low	Low	Low	0–5
	EU5	Large access	Established	High	Medium	Medium	>10
	Japan	Large access	Established	Medium	Low	Low	>10
BRICS	Brazil	Poor access	Established	High	Medium	Medium	0–5
	Russia	Fragmented	In development	Low	Low	Medium	0–5
	India	Poor access	Established	Low	Medium	Medium	>10
	China	Poor access	In development	Medium	Medium	Low	0–5
	South Africa	Poor access	Established	High	High	Medium	0–5
MIST	Mexico	Fragmented	Established	High	Low	Medium	0–5
	Indonesia	Poor access	No	Medium	Medium	Low	0–5
	South Korea	Fragmented	Established	High	Medium	Medium	>10
	Turkey	Fragmented	Established	Low	Medium	Medium	6–10

Favorable for biosimilars Moderate/neutral for biosimilars Unfavorable for biosimilars

Sources: Secondary research, Deloitte Subject Matter Advisors, and Deloitte analysis

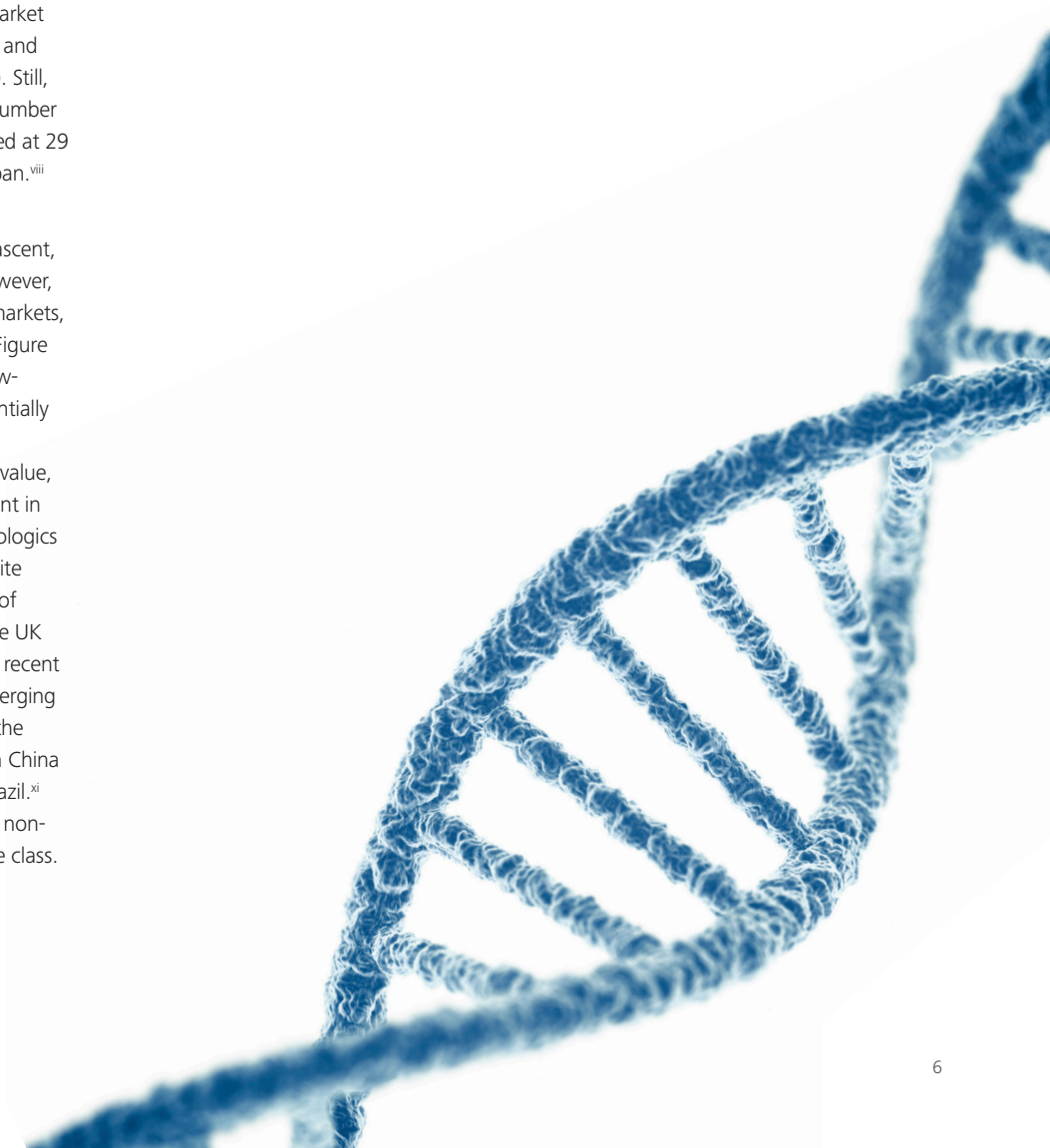
Although each country's environment is unique, there are similarities in trends across developed and emerging markets.

Developed markets

- Developed markets, with the exception of the United States, represent the greatest biosimilars presence today (Figure 5, column 6). Most biosimilars manufacturers have been and remain focused on the developed markets – whether it is for their historic and current opportunities (EU) or for their future market potential (United States, Japan). Dedicated regulatory pathways (Figure 5, column 2) set the foundation for stringent, abbreviated approval processes which, in turn, have fed investor enthusiasm. However, thus far, commercial returns on the significant investments made by manufacturers have been a source of disappointment, which emphasizes the importance of building the right conditions for success.
- Biosimilars adoption in developed markets has been primarily payer-driven (Figure 5, column 3), especially in European markets, given payers' urgent, unmet need to contain public health care expenditures. Further market uptake has been slowed by prescribers' skepticism and low patient awareness (Figure 5, columns 4 and 5). Still, developed markets continue to have the highest number of biosimilars molecules in development – estimated at 29 in Europe, 19 in the United States and seven in Japan.[viii]

Emerging markets

- In today's emerging markets, biosimilars are still nascent, with little to no presence (Figure 5, column 6). However, in contrasting emerging markets with developed markets, the limited patient access to affordable biologics (Figure 5, column 1) and the openness of physicians to low-cost therapies (Figure 5, column 4) may offer potentially significant opportunities. Today, emerging markets represent a snippet of total world biologic sales in value, less than seven to eight percent (versus 48.6 percent in the United States).[ix] Treatment rates for flagship biologics are still low compared to developed markets, despite existing demand. For example, the treatment rate of MabThera® in Brazil is three times lower than in the UK and six times lower than in the US.[x] Additionally, a recent Kantor Health Survey found that 20 percent of emerging market autoimmune patients use a biologic, with the distribution of biologics varying from 29 percent in China to 12 percent in Russia and a mere 6 percent in Brazil.[xi] This may indicate the presence of large pockets of non-consumption, especially within the growing middle class.
- Sales of biologics could be significant, but are frequently blocked by high out-of-pocket costs and consumers' low ability to pay. Therefore, sales growth often ends up being a pricing game: originators move into a biosimilars play by heavily discounting their branded product(s), and competitors move into exclusivity deals with customers. In India, a Deloitte survey found that physicians were willing to prescribe a first-line critical therapy if it was offered at a 60 to 70 percent discount. In China, getting on the essential drugs list means mandatory usage by many hospitals; however, it also comes with price cuts of 25-50 percent.[xii]
- From a regulatory standpoint (Figure 5, column 2), biosimilars pathways have been defined for most emerging markets, although they are still in flux in China and Russia. Where present, approval processes have appeared speedier than in developed markets, with less stringent comparability criteria.



Analysis of selected countries

United States

- FDA approval of the first biosimilar in March 2015 with Sandoz's Zarxio (filgrastim)
- About 19 pipeline biosimilar molecules in development[viii]
- Represents about 50% of the global biologics market value and generates about 50% of the sales value growth[i]
- Pending legislative decisions on data exclusivity period, naming conventions and interchangeability likely to have important implications

EU5

- Most mature biosimilar market representing 80% of global biosimilar spending
- Performance to date viewed as "disappointing" by select manufacturers
- Nineteen biosimilar products authorized in four molecule classes: human growth hormone, erythropoietin, G-CSF and tumour necrosis factor (TNF)-inhibitor[xiii]
- About 29 pipeline biosimilars molecules in development[viii]
- World-class dedicated pathway leaving questions of substitutability at the pharmacy level to member states
- Payer-driven uptake
- Challenged by continued pressure from strict regulatory decisions, lingering fear from prescribers around biosimilars' "similarity", safety and efficacy, debates on automatic substitution and INN prescription

Japan

- Limited maturity of the biosimilar market
- Dedicated regulatory pathway
- About seven pipeline biosimilar molecules in development[viii]
- Growth potential considered limited today based on the reluctance from both prescribers and patients as well as the general mistrust toward "generic makers"
- A push from payers, which has yet to be seen, may help open up the market

Brazil

- Led the way with the development of biosimilars regulations in Latin America and released biosimilars guidance in 2010
- Reducing the reliance on imported (and high-cost) medicines through policies that favor the expansion of the domestic pharmaceutical industry and public-private partnerships to expand access to drugs[xii]
- International companies have entered the market through partnerships and acquisitions (e.g., Pfizer's 40% stake in Teuto, Sanofi's acquisition of Medley and Merck's joint venture with Supera, co-owned by Cristalia and Eurofarma)
- The regulatory environment and interest of domestic and international manufacturers are major drivers in expanding the biosimilars market
- Approximately five biosimilar molecules in the development pipeline[viii]
- Seventy-five percent of physicians surveyed in Brazil considered rituximab difficult to access due to high costs and 77% said they would increase prescription of rituximab if a cheaper alternative were available[xiv]

Analysis of selected countries

Russia

- Aims to boost its domestic pharmaceutical market and increase the market share of domestic players from 20% in 2012 to 50% by 2020
- The strong preference for local manufacturers will require international companies to engage in cooperative partnerships with Russian companies
- Indicative of the burgeoning domestic industry, a rituximab biosimilar, developed by Russian company Biocad, was the first mAb biosimilar approved in Russia in April 2014
- About eight biosimilar molecules in the development pipeline[viii]

India

- Biosimilar guidelines established in 2012
- 80% of pharmaceutical spend is out of pocket
- Indian companies have extensive experience with generics and have made in-roads in other countries as well through exports
- Indian companies grapple with the image of manufacturing as unsafe with poor quality drugs
- Partnerships between global pharmaceutical companies and domestic companies are helping to improve the quality of biosimilars marketed in India
- Approximately 19 biosimilars in the development pipeline[viii]; large proliferation of non-original biologics
- Large middle class with growing disposable income who prefer brand name products, so there is a good opportunity for branded biosimilars
- Approximately 70% of the country's population is considered rural and will focus on the cost of therapy – a 20-30% discount on originator biologics may not be sufficient

China

- Issued draft biosimilars guidelines in 2014; once a clear regulatory pathway for biosimilar approval is established, the market will be very attractive – not only due to the volume potential but also the growing ability to pay
- Similar to the tight controls requiring international companies to create partnerships or use domestic pharmaceutical distributors, the successful manufacturing and marketing of biosimilars will also require partnerships with domestic companies
- Lack of physician trust and enthusiasm for non-branded drugs exacerbated by unsafe and counterfeit drugs

South Africa

- Sophisticated market; generics make up more than 50% of the market
- Biosimilars guidelines were established in 2010
- There is a financial pressure on the system overall, and great pressure to utilize generics including biosimilars
- Several Indian companies have entered the South African market and are key to keeping drug costs low
- There is a cost containment focus from the government and payer side and a quality focus from the physician and patient side
- Companies will have to bring in a cost structure that is lower than what currently exists along with the highest quality and safety profiles of their biosimilars

Mexico

- Established, government-incentivized market for biosimilars
- Demand spurred by high out-of-pocket health care spending (estimated at +90%)[xv]
- Significant presence of non-original biologicals known as "biolimbos" who have not undergone marketing authorization review consistent with globally accepted standards
- Biosimilars development led locally by Probiomed which won six biosimilars approvals, including a version of Rituxan®

South Korea

- Most mature biosimilar "development" market
- Enabled by unprecedented support from the South Korean government: 35% of the national medical R&D budget was invested into biosimilars development in 2012[xvi]
- Government-set goal for domestic biopharmaceutical companies to win 22% of the global biosimilars market by 2020
- Twelve biosimilars have been approved and another 36 biosimilars are in the pipeline[xvii]
- Leading the race in the high-risk and complex development of monoclonal antibody (mAb) biosimilars with 17 mAbs in the pipeline

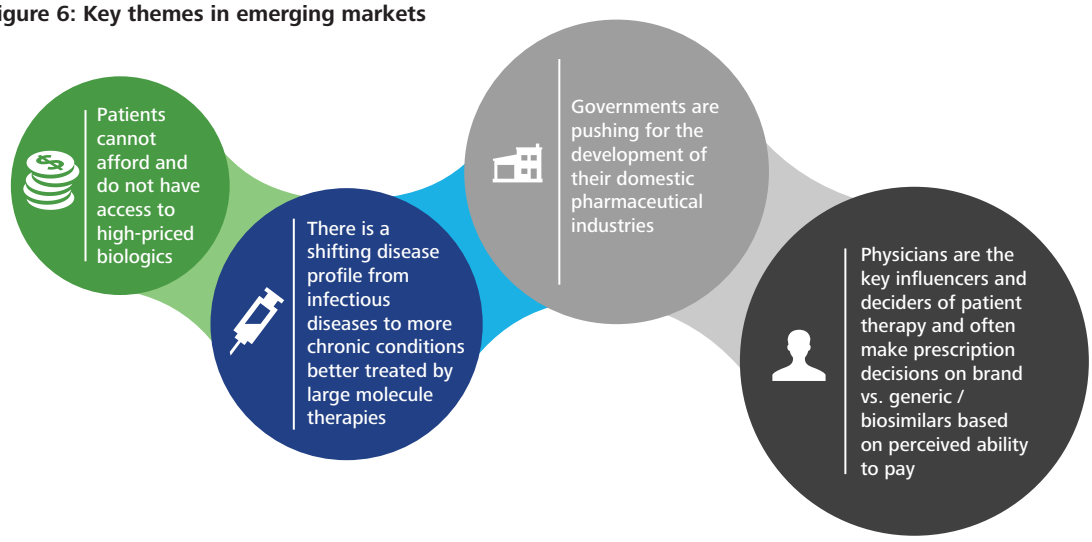
Different markets, different opportunities

While developed markets will remain an important focus area for biologics manufacturers, our analysis indicates that long-term growth likely will be fueled by emerging markets. These markets have not yet attracted as much attention in the biosimilars environment and are poised to drive growth but, will require specific strategies and tactics.

- **Developed markets**, such as the United States, EU5 and Japan, provide near-term growth opportunities for biosimilars, aided by governments which are issuing clear regulatory pathways and payers which are pushing uptake to contain costs. Yet, the growth potential thus far has been a mix of reality and hype, as illustrated by the perceived underperformance of biosimilars in Europe in the last seven to eight years. Continued regulatory uncertainty, lingering fears from patients and physicians about biosimilars' "similarity," safety and efficacy, and the ongoing (frequently heated) debates on automatic substitution and International Nonproprietary Naming (INN), will likely build long-term barriers for widespread uptake. In these markets, innovation (in the form of bio-betters) is likely to beat imitation (in the form of biosimilars), especially in the United States.
- **In emerging markets**, the large pockets of non-consumption and untapped demand – characterized by poor physical and financial access to currently high-priced biologics – provide favorable long-term growth opportunities (Figure 6). In addition to macroeconomic factors such as high Gross Domestic Product (GDP) growth rates, and increasing purchasing power parity and health care spending, there is a strong regulatory focus on containing costs and increasing treatment access (especially where there is a growing middle class). Although the emerging market countries each have different health care and payer systems, studies have shown that cost is a big barrier to the use of biologics in all of these markets, and physicians would increase prescription rates if less expensive biosimilar alternatives were available.[xiv, xviii] In most of these countries, patients have high out-of-pocket costs for medicines and are unable to afford branded biologics – a powerful driver of biosimilar uptake. In addition, many of these countries already have biosimilar approval pathways in place or are finalizing guidelines. Finally, emerging markets have driven the growth of the generics industry, with almost 90 percent generics penetration in some markets[xix, xx] while developed countries have served as the innovation hubs for new therapies. Similar strong growth may be attainable for biosimilars.

While developed markets will remain important to the biosimilars market, based on this assessment, answers to the "how to win" question will focus primarily on emerging markets.

Figure 6: Key themes in emerging markets



How to win

Winning in emerging markets poses considerable challenges but the opportunity to create a market in many cases, along with the growth potential, should make it worthwhile for biosimilars companies to establish and/or expand in these markets. In considering "how to win," companies should assess each market's unique characteristics and opportunities, in order to develop strategies (Figure 7) that can enable them to leverage the unique value proposition they offer stakeholders (including, physicians, patients, payers and policy makers), and gain a defensible competitive advantage.

Choose wisely

When considering which products to offer in specific markets, biosimilars companies should choose therapeutic areas wisely. In evaluating their emerging markets portfolio, companies should consider the diseases that are most prevalent and costly for payers to treat in that market, in order to strengthen the case for reimbursement and market access. As part of this process, biosimilars companies may have to adjust their R&D and commercial focus, as some emerging markets are eradicating infectious diseases and shifting health care treatment and spending to lifestyle diseases and other complex conditions that require large-molecule therapies.

To help drive physician and patient uptake, manufacturers should also examine patient unmet needs or the diseases that provide the most burden to the community. These may be very different from those that burden payers as they could include diseases that limit patients' abilities to work, care for families, etc., and diseases that impact patients' sense of wellbeing. Doing so may enable biosimilars companies to use grassroots marketing campaigns to promote adoption.

To minimize risks, companies may want to enter new markets by focusing on TAs in which they have established expertise and strength, and use that to expand into areas that address broader local needs. For example, Merck established a partnership with Samsung Bioepis in 2013 and is pursuing biosimilars opportunities based on its strengths in diabetes, anti-TNF, and oncology.

Figure 7: Strategies for success in emerging markets

It is also important to consider the likely comorbidities of prioritized disease areas. If a condition has several comorbidities, treatment of just one disease might not be enough to make the case for reimbursement. Similarly, if other medications (biologic or not) are required to treat a disease, manufacturers should look to provide bundles of drugs through the same representative (either in a single formulation or separate). This will help drive uptake of the biosimilar (e.g., metformin and DPP-4 inhibitors or methotrexate and etanercept). Even if patients can access the biosimilar, if comorbidities or concurrent therapies are required, access to the biosimilar may be dampened if access to other treatments are not available or affordable. Partnering with local companies, particularly generics manufacturers, to bundle products for comorbid conditions or to gain greater efficacy at an affordable price may be a more patient-centric approach and help to drive uptake of the biosimilar. In addition to strengthening the company's experience in the TA, this approach may help create marketing and operational efficiencies and, ultimately, provide the physician and patient with a single value-oriented bundle.

Once a company selects a TA or specific treatment, it should prioritize and sequence its target markets. Each market will require a tailored approach due to regional, country and local complexities.

Unlock access

After TA selection, the next step for biosimilars manufacturers is to consider how to drive adoption. Growth in emerging markets may be hampered by a lack of regulatory oversight and / or compliance, nascent distribution networks, underdeveloped health care infrastructure, fragmented demand, and pressure on manufacturers' margins. In response, companies may have to adapt traditional sales, marketing, and distribution models. Two major issues to address are market access and infrastructure.

Market access

Biosimilars manufacturers will need to secure broad access to succeed in emerging markets. Manufacturers will need to work closely with policy makers and payers to implement reimbursement policies built on solid evidence. With increased purchasing power and demand for biopharmaceuticals, governments and payers in emerging markets are facing the challenge of containing health care spending. Therefore, the strategies most likely to be successful in driving access and reimbursement will be grounded in value and health economics. An important nuance is that companies need to understand what "value" means in each market. To identify the sources of value, companies will need to develop an integrated stakeholder approach that supports the dynamic policy and stakeholder landscape in emerging markets. In many markets, policy makers change with every election cycle, and many policies are implemented to manage short-term budgets constraints rather than longer-term health expenditures. This presents a challenge to manufacturers with evidence packages solely built on five plus year economic analyses. Instead, manufacturers should balance short- and long-term benefits of the product. The benefits can be modeled relative to the current standard of care, the cost in local currency, near-term safety and efficacy endpoints, and longer-term outcomes.

Emerging markets typically lack an integrated approach to care that includes services and collaboration with other health care players, such as providers and retail outlets. In addition to providing the drug, biosimilars companies can provide added services, partner with other health care players to build patient engagement and awareness (currently low in emerging markets), and gather real world evidence (currently lacking). Biosimilars companies who can bring this approach to emerging markets stand to gain significant market access advantages, including a potential seat at the policy table. Biosimilars companies also can enhance market access by providing supporting services and technologies such as smart-phone apps, support groups, and educational forums that are targeted to the unique challenges and circumstances of patients in emerging markets. For example, Genentech recently created an app to educate breast cancer patients on the disease and treatment options. In addition to providing a support system for patients, such services can foster patient engagement while providing companies with valuable data, including the much-needed real-world evidence for therapies.

Similarly, the pricing strategy for biosimilars in emerging markets should keep patient out-of-pocket costs low. In markets where patients subsist on $4-6 USD[xxi] per day, paying as little as $5 USD for a biologic on a daily or weekly basis – even if it saves a life – is untenable. Companies may still achieve a pricing advantage by lowering costs (cost of goods sold, selling and administrative costs) and shifting toward lower cost manufacturing techniques. Partnering with low-cost and lean manufacturers, as well as investing in research and technology for innovative low-cost manufacturing approaches, may ultimately help biosimilars companies own the low-cost position and keep patient / payer prices lower.

In addition to pricing considerations, biosimilars companies should evaluate innovative financing approaches and patient-access programs. For example, biosimilars companies could consider providing monthly installment plans for acute / non-chronic medications. These plans are proving popular with the rapidly growing middle class in emerging markets and may enable purchases that would otherwise be beyond reach. Additionally, biosimilars companies could consider cost-sharing models with governments and payers, especially for chronic medications, as a way to drive adoption and further reduce the cost for consumers.

Finally, communicating a product's value to all stakeholders is particularly important for biosimilars. Due to non-consumption and access issues, stakeholders have generally low awareness of and familiarity with the safety and efficacy of these drugs. Later sections of this paper discuss engagement and communication with two important stakeholders – physicians and patients.

Infrastructure

Biosimilars companies must address infrastructure (e.g., transportation, availability of clinicians) limitations in many emerging markets. Access can also be limited if patients do not have the flexibility to visit a physician or drive a family member because they must work to support their family. Further, in many emerging markets such as India, doctors still make house calls. In such instances, companies can engage physicians serving remote geographies to build a grassroots network of key opinion leaders (KOLs) who can help penetrate the most under-served areas.

From a manufacturer's perspective, many biologics require cold chain logistics and storage, so intermittent power and refrigeration in rural areas can present challenges. Tapping into the expertise of local manufacturers to develop formulations suited for emerging markets is already a tactic employed in the small-molecule world. While the complexity of the manufacturing process makes this more challenging for biologics, these local partnerships could have an even bigger impact, given the more prevalent issues of stability and immunogenicity with large molecules.

Partner locally

Through partnerships, local companies can help multinational biosimilars companies improve sales by providing an understanding of the local operating environment and patient needs, making stakeholder introductions, and providing some local credibility (coupled with the power of the biosimilars company's global brand). Many emerging markets are implementing local manufacturing regulations that require a product to be manufactured (at least in part) in-country. Partnering with resident players may be a cost-effective and flexible way to meet this requirement, and to help multinational companies navigate local regulations, customs and other challenges. In addition to leaning on local players' market understanding and low-cost manufacturing excellence, multinational biosimilars companies can benefit from and leverage resident players' R&D capabilities, as evidenced by several recent partnerships (e.g., Lilly's strategic alliance with Chinese drug-maker Innovent and South Korean company Hanmi Pharmaceuticals). In addition to commercial, R&D and / or manufacturing partnerships with other companies, biosimilars companies may also engage in public-private partnerships (PPP). Several countries including Brazil and China are increasingly encouraging PPPs between local and global pharmaceutical companies. Through PPPs, private companies gain low-cost financing and government benefits, while public companies improve access of biosimilars based on the country's specific public health needs.[xxii]

Business model differences

Lower margins, higher volumes

Biosimilars companies may need to adapt traditional business models in several ways when entering / expanding in emerging markets (Figure 8). First, emerging markets will not provide the margins typically earned in developed markets. Margins will be lower due to lower prices and upfront investments required to build the markets. Manufacturers will need to shift approaches to seek higher volumes at a lower margin. This represents a fundamental shift for many potential players — one that will likely require extensive change management with company shareholders, leadership and the Board of Directors. While companies playing in the generics space already may be better equipped to manage this change, even those organizations should be prepared for the upfront investment and lower margins associated with providing biosimilars in emerging markets.

Brand matters

A second fundamental shift may be required in the way biosimilars are developed and marketed in emerging markets. While biosimilars are, by definition, similar to the associated branded drug, biosimilars companies should not look to promote any differentiation (other than price). Differentiation from the branded drug could create fears in customers, especially in markets where counterfeiting can be rampant in both the life sciences industry and in consumer goods in general. A recent study revealed that a third of anti-malaria drugs sold were found to be counterfeit,[xxiii] and 100,000 deaths per year in Africa were linked to counterfeit drugs.[xxiv] Physicians and patients in emerging markets are particularly wary of non-brand name drugs. In our experience, brand matters more in emerging markets than developed markets, and there tends to be a willingness to pay for the brand (assuming there is the ability to pay). Seventy-five percent of emerging markets pharmaceutical growth is expected to come from branded generics.[xxv] According to a 2013 Roper Report, 79 percent of consumers in developing Asian markets and 61 percent of consumers in Latin American markets only buy products and services from a trusted brand.

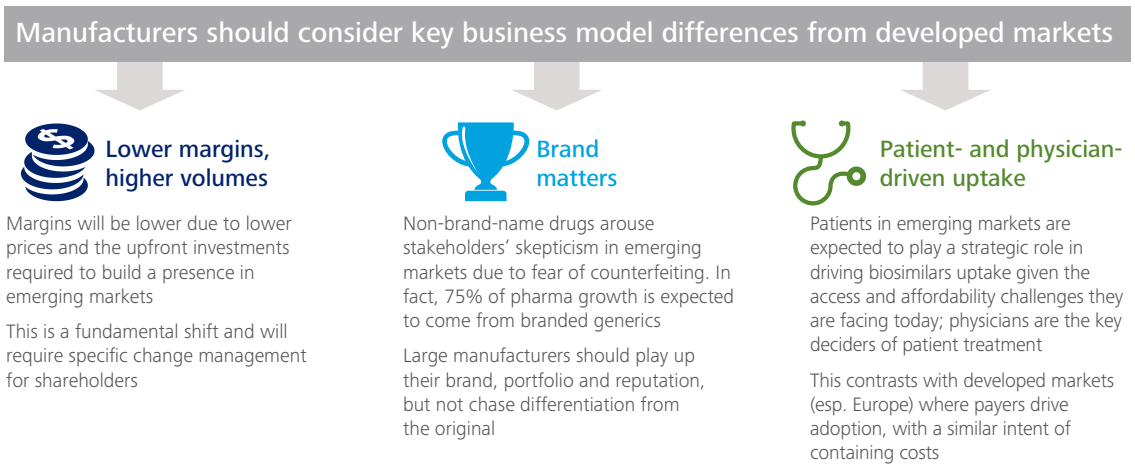
Patient- and physician-driven uptake

While regulatory agencies and payers in the EU have largely driven the uptake of biosimilars in those markets, in emerging markets, physicians and patients are expected to play a bigger role in biosimilars uptake. In many emerging markets, physicians are the sole decision makers of patient therapy based on their perception of a patient's ability to pay for high-priced therapies.

Physician awareness

One challenge facing biosimilars in emerging markets is low physician awareness of biosimilars exacerbated by low prescription rates for and familiarity with existing biologic therapies (branded or non-branded). In response, biosimilars manufacturers should develop education programs to educate physicians (and nurses) on the need to treat patients, how to administer the product, and the side-effects and benefits. While these trainings may require an upfront investment, they will likely be crucial to driving adoption. Companies should likely start these efforts with local KOLs and large medical centers but quickly look for opportunities to expand into smaller practices (depending on the market) while leveraging other educational and training materials through web portals, smartphones, sponsored mobile clinics and health camps. Additionally, even if there are no stringent regulatory approval requirements for clinical research in the local population, companies should be strategic about their clinical development plans to potentially include patients from emerging markets in clinical studies. This could help to drive initial adoption and physician awareness, and convince physicians of the safety and efficacy of the medication within the local populations.

Figure 8: Key business model differences



Patient awareness

Patient awareness may be another way to drive biosimilars adoption. Patients in emerging markets are typically deferential to their physicians and rarely question physician decisions. While direct-to-patient marketing is not permitted in most markets, many emerging markets have growing patient advocacy groups that can drive market access, and physician and patient awareness. This presents an opportunity for biosimilars companies to work with these groups to educate patients on the therapy options available, including the price advantage of biosimilars and the long-term benefits of the medication (and adherence to the regimen). Biosimilars' ability to more cost-effectively deliver the same efficacy as branded products is likely to resonate with many emerging markets patients who typically pay out-of-pocket. Advocacy groups, social organizations, worker groups and physicians can also help distribute patient education material (which should be made easy to read and understandable for patients with limited education or literacy). While more "grassroots" than typical pharmaceutical / biologic marketing, this method can be especially effective if there is a higher incidence of the disease among specific cohorts. All of this must be done within the requirements of local regulations.

Conclusion

A 2013 report published by the European Commission supports the idea that biosimilars will improve access to biological medicines and new treatments from medical and scientific advancement.[xxvi] Although biosimilars growth has been slow to date, more governments and payers are recognizing the savings potential of increased biosimilars penetration. We believe that long-term growth of this burgeoning class of drugs will come from emerging markets — and will accelerate as regulatory pathways around the globe are developed. We anticipate the market can be expanded by addressing non-consumption resulting from patients in emerging markets being unable to access high-priced biologics.

Developed markets, such as the United States, EU5 and Japan, are expected to provide near-term biosimilars growth, aided by governments who are issuing clear regulatory approval guidelines and payers promoting uptake in order to contain health care costs. In these markets, bio-betters, which offer a clinical advantage over existing therapies, may grow more quickly than biosimilars. However, in emerging markets, such as the BRICS and MIST, the overall growth of these markets — coupled with a lack of physical and financial access to high-priced biologics — will likely provide the best future opportunity for manufacturers of biosimilars.

While biosimilars' growth potential appears bright, winning with biosimilars in emerging markets is not a simple undertaking. Companies seeking entry or expansion should craft a strategy to address the specific challenges in the emerging markets and incorporate the lessons learned from developed markets. A unique value proposition will likely be required to tap into the large populations in emerging markets who cannot access high-priced biologics. These companies should develop robust market-access strategies that address key "Where to play" and "How to win" choices, be prepared to make upfront investments to drive adoption, and shift business models from profit to volume. Upfront investments will likely require a strong emphasis on physician and patient education to address non-consumption, as well as supply chain investments to better enable access to the medication. Part of this education may come through the sales force, who should be fully equipped to meet the needs of the patient (including strategies and products for helping treat comorbidities and side effects). Finally, manufacturers should not overlook the opportunity to work with local players to help navigate the environment. Knowledge of local market nuances and lean, low-cost manufacturing, coupled with the strong international brand and reputation of the manufacturer, will help to propel the growth of biosimilars in emerging markets.

While biosimilars' growth potential appears bright, winning with biosimilars in emerging markets is not a simple undertaking. Companies seeking entry or expansion should craft a strategy to address the specific challenges in the emerging markets and incorporate the lessons learned from developed markets.

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