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The Biologics Inflection Point: Managing The Risk From Biosimilar Competition

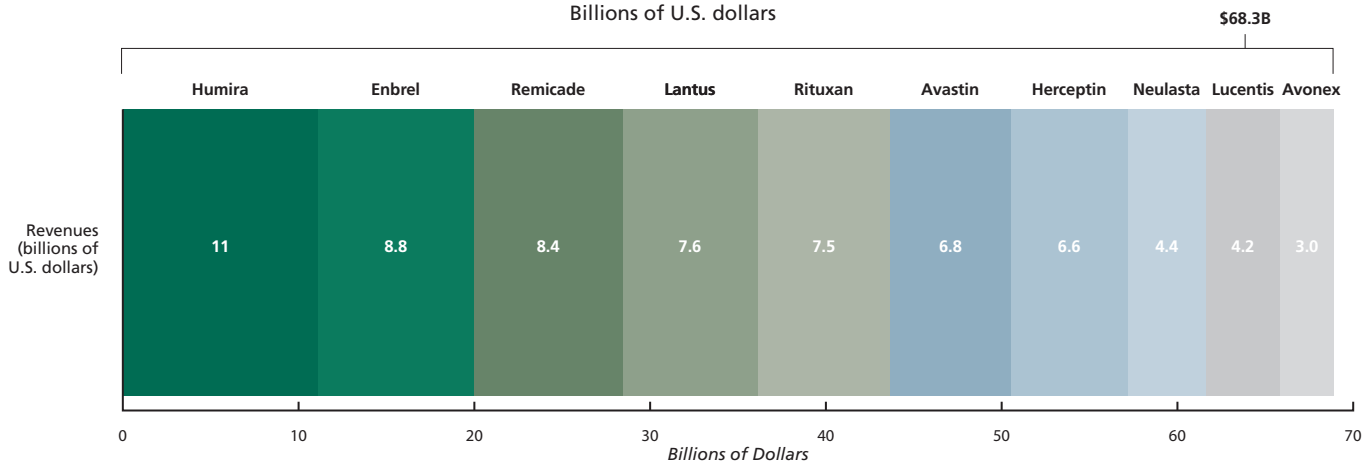
In September 2013, the European Medicines Agency announced its approval of Remsima and Inflectra, biosimilar versions of the blockbuster drug Remicade for a range of indications that Remicade already treats, including rheumatoid arthritis and Crohn's disease. With an estimated $8.4 billion in global sales for Remicade in 2013, the arrival of these biosimilar copies marked a turning point in a once secure market, and sent shockwaves through branded biologic drug manufacturers – who generated more than $100 billion in aggregate sales from biologic products in 2013. Remisima and Inflectra demonstrated unequivocally that the future profitability of branded biologic drug manufacturers will be determined by how they can compete in the face of an evolving biosimilar threat.

The stakes of this new contest for many biopharma companies are high, as many top 10 best-selling biologic drugs are expected to roll off patent in the next several years — including Lantus, Rituxan, Humira, and Avastin. And while the regulatory landscape that will govern biosimilar approval and use is far from defined across many key markets, the innovators of these pioneering products must continue to adapt in order to shore up market and patient share and protect themselves from the approaching biosimilar tidal wave.

Figure 1

Top 10 biologics by 2013 worldwide sales

Billions of U.S. dollars



Notes: *Rituxan's patent in the EU has already expired; **Enbrel's EU patent expires in 2015
Source: Evaluate Pharma, Nature Biotechnology, Pipeline

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In our view, the success of today's branded biologics and the next generation of biologic blockbusters hinges on the response of the three key stakeholder groups that will likely play a central role in determining the trajectory of biosimilar adoption – prescribers, patients and payers. Pharmaceutical players must bolster efforts to proactively engage these stakeholders in expanded or new ways in order to protect and strengthen their market position and brands. This *Executive Insights* examines these key stakeholders in detail and explores a subset of strategies for engagement that will underpin an enhanced ability to compete and win in this new market landscape.

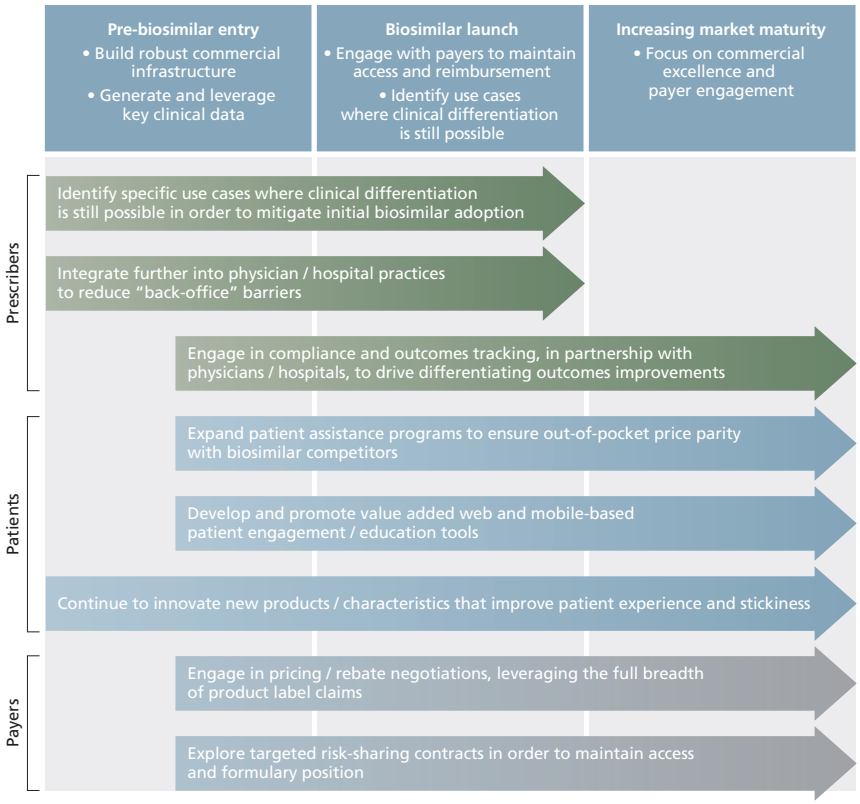
Prescribers: Enabling Improved Care Delivery

Historically, biologic drug manufacturers have leveraged their considerable commercial infrastructure to employ a high-touch physician communication strategy aimed at establishing a value proposition that emphasizes clinical efficacy and safety as key competitive differentiators. This strategy has largely relied on the basic tenants of physician education and brand strategy in order to build up a well-articulated use case for products across prescriber segments. Placebo-controlled efficacy and safety data have been the historic backbone of these efforts, with relatively limited data vs. active comparators.

Going forward, however, a branded biologics commercial case that relies solely on differentiation through traditional evidence will likely face diminishing returns as physicians overcome initial hesitance around biosimilar prescribing and gain comfort with biosimilar's core clinical performance. Given this, branded biologic manufacturers should take two steps: first, leverage rich, long-term efficacy and safety data (often spanning more than 10 years) to build a defensive bulwark of preferential use cases for key patient segments and label indications of opportunity; and second, evolve their relationship with prescribers into one that emphasizes improved drug access and value-added services that boost patient compliance and improve outcomes. While to some extent the manufacturers of anti-TNFs have undertaken these steps in an effort to differentiate themselves from competing brands, achieving true differentiation relative to what are likely to be less expensive biosimilar alternatives will take greater focus and dedication.

Efforts should target specific areas of opportunity where biosimilar competitors lack comprehensive clinical data, including key patient segments and/or indications that were not well-studied in the biosimilar product's clinical development

Figure 2
Key engagement strategies and timing by stakeholder group



program and long-term safety profile. For example, the core of Remsima and Inflectra's clinical data resulted from a pharmacokinetic study in ankylosing spondylitis patients and a pivotal efficacy and safety study in rheumatoid arthritis patients, leaving open a significant opportunity to establish clinical differentiation for a branded product across additional indications and/or patient sub-segments (for example, Crohn's disease patients). These efforts may act to blunt early share erosion across the aggregate patient base, and encourage prescribers to stage-gate biosimilar adoption (at least initially) to smaller patient segments.

Biologics manufacturers should develop a relationship with prescribers that more closely resembles a care partnership, and that makes outcomes the focus.

Many manufacturers have expanded their commercial infrastructure to move beyond traditional "front-office" engagement and deeper into "back-office" support (for example, navigating prior authorizations) with a focus on ensuring seamless access to branded products. Nonetheless, there remain additional opportunities to expand the prescriber relationship, including, for example, assisting physicians in maximizing patient outcomes through drug compliance tracking and support systems. Promoting patient compliance to a prescribed drug regimen has traditionally fallen outside of a manufacturer's purview; however, as outcomes-based, integrated healthcare systems become increasingly the norm (more than 400 ACOs were created in the past two years alone), drug manufacturers should evolve their capabilities to track and promote patient compliance beyond that which is conducted by prescribers. Systems to track daily patient compliance and the timely filling of prescriptions, along with reminders sent to physicians and patients to encourage prescription refills or alert prescribers when prescriptions go unfilled, can underpin increasingly valuable clinical and economic outcomes. A number of emerging players are developing web and cloud-enabled systems that link patients, prescribers, and manufacturers to track and promote sustained patient compliance and drive outcomes improvements (for example, MediSafe Project and HealthPrize Technologies).

By focusing new efforts on improving outcomes through compliance and adherence tracking, manufacturers can begin to play a more central role in the delivery of care by making their products central to an outcomes-based care delivery model. These efforts will allow manufacturers to develop a relationship with prescribers that more closely resembles a care partnership, which puts patient outcomes as the primary focus.

Patients: Broadening Communities Of Support

In addition to engaging with prescribers, manufacturers should also engage more directly with patients in order to enhance product preference and loyalty. The primary focus of these efforts should be to reduce financial and access restrictions and to broaden communities of support that encourage treatment adherence and enable expanded patient communication.

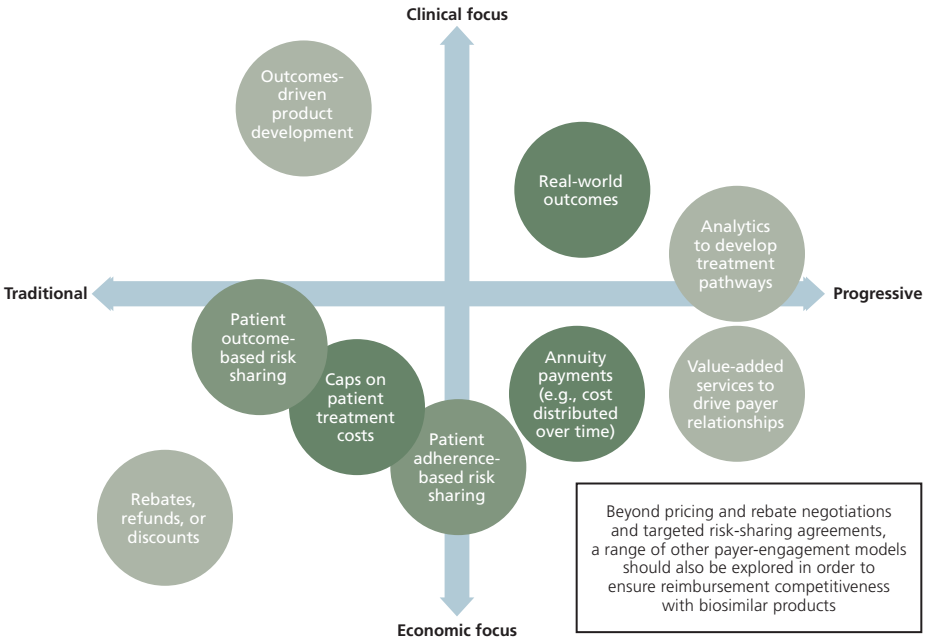
As a key step, branded biologics manufacturers should act to remove any financial barriers to their products' utilization vis-à-vis biosimilars through the expansion of patient assistance and support programs. Given that biosimilar products are expected to undercut innovator biologics on price and achieve preferred reimbursement positioning over time, it is critical that any resulting cost or insurance coverage differentials do not impact the net out-of-pocket cost borne by patients. Viewing cost parity for out-of-pocket costs to be table stakes in this evolving market, manufacturers can begin to identify and engage patient segments who are likely to see out-of-pocket discounts as key drivers for biosimilar switching, and engage with them proactively to mitigate concerns.

Beyond financial engagement, branded biologics manufacturers should also promote patient stickiness in other ways – primarily through the development or expansion of communities of

support. For many serious and often chronic conditions that are treated with biologic drugs (for example, lupus and Crohn's disease), manufacturers should begin to expand and/or support online and mobile applications that connect patients with information on their condition and treatment, as well as with other patients. These support communities and tools will not only provide patients with direct access to educational resources and engagement with a broader patient community, but will also allow manufacturers the opportunity to support patients by promoting therapeutic regimen compliance and connecting patients to their respective patient-assistance programs.

Figure 3

A range of other payer-engagement models



As an additional value driver, branded biologics manufacturers should prioritize efforts to improve the patient experience associated with the usage of their drugs. When possible, manufacturers should continue to innovate and seek to develop more convenient and easier-to-use products such as patient-friendly injectors, smaller gauge needles, longer acting formulations, and products that do not require mixing or refrigeration. By focusing on easing the patient burden and differentiating on non-efficacy dimensions, branded-drug manufacturers can further enhance patient stickiness and drive preferential usage of their products.

Payers: Maintaining Competitive Access And Pricing

The last, and perhaps the most critical, stakeholder group to proactively engage with in new ways is payers. As healthcare costs have continued to rise, the balance of power has increasingly shifted toward payers, often making them a key arbiter of drug utilization. Not surprisingly, with biosimilars expected to be priced at a discount to branded drugs, many payers view their arrival as a key route to near-term cost savings and longer-term budget management. Still, manufacturers of biologics can counter this trend by enhancing their relationships with payers in order to protect and maintain current access and pricing levels.

Despite Remsima and Inflectra's broad label recommendations by the EMA, which permits their use across all of Remicade's label indications, it is not yet clear whether the U.S. Food and Drug Administration will allow for broad label claims or restrict biosimilar approval to the key indication(s) studied during the drug's clinical development. Under a scenario in which biosimilars receive approval for a subset of potential label indications, branded drug manufacturers will have a key lever in their negotiations with payers, allowing them to negotiate aggregate pricing and rebate levels across the range of labeled indications. In this way, branded biologics manufacturers can extend attractive product economics to payers across a broad patient population, while preserving patient access to the trusted, innovator product. It also mitigates the risk of having

to compete strictly on price within any one indication – a scenario that we believe could lead to an inevitable downward pricing spiral across indications over the mid-to-long term, as additional entrants materialize and market efficiency increases.

Further, branded-drug manufacturers should pursue additional, and targeted, payer-engagement strategies along economic and clinical dimensions that better align cost and risk for key drug / indication combinations (for example, Rituxan when used to treat leukemia or lymphoma). While these strategies would be driven by each branded biologic's unique circumstances, reducing payer cost exposure will become increasingly critical as market competitiveness ratchets up; for example, per patient price ceilings in exchange for reduced pricing concessions and/or for a continuation of preferred formulary access, or the establishment of risk-sharing deals that tie reimbursement to clinical impact/outcomes, will be increasingly important under certain competitive conditions. These new relationship structures can enable pricing and access upside for branded biologics manufacturers, more predictable and manageable budget impact for payers, and importantly, unfettered access to trusted brands for patient populations.

For today's players, a comprehensive evaluation of payer strategies should be pursued on a case-by-case basis going forward, with the overarching goal being the preservation of access and reimbursement in the face of biosimilar competition, and a shift in competitive focus to commercial execution – a move that greatly favors the branded incumbents.

No Time To Lose

It is clear to all market participants that branded drug manufacturers will face a formidable new threat in the form of biosimilar products as the intense pressure grows to drive down healthcare costs in the U.S. and abroad. However, unlike in traditional generic markets, branded biologic drug manufacturers may still be able to limit the pace and depth of erosion, if they act now to raise the bar for generic entrants. In order to do so, we recommend the following:

1. **Raise the bar on commercial excellence:** Further evolve the relationship with prescribers and patients to create a more fully integrated commercial model that positions branded biologics manufacturers as true partners in healthcare delivery and positive outcomes, and leverages their extensive commercial infrastructure and experience to raise the competitive bar for new biosimilar entrants.

2. **Shift the focus to execution:** Pursue strategies that engage payers in a way that aligns incentives, blunts economic arguments for biosimilar adoption, and allows for the continuation of access to trusted, innovator products. By maintaining access in these ways, the competitive focus will shift to commercial execution – where branded drug manufacturers have a considerable and deep-rooted advantage.

Figure 4

Key strategies to manage the risk from biosimilar competition and win in the biologics market of tomorrow

Prescribers	Become a partner in care delivery and outcomes improvement through the identification of use cases where the branded product maintains differentiated outcomes data, and through deeper integration into physician / hospital offices
Patients	Further connect patients to communities of support that can drive outcomes improvements and promote greater brand stickiness
Payers	Drive access and reimbursement vis-à-vis biosimilars through a comprehensive set of payer-engagement models in order to shift the competitive playing field towards commercial excellence

With the launch of biosimilar Remicade it is clear that the market for biologic drugs is at a key inflection point; however, we believe that branded biologic manufacturers can evolve and adapt in order to maintain and strengthen their market positions despite coming competition. Players who are facing impending biosimilar competition, as well as those with emerging biologic blockbusters, should accelerate efforts to bring unique value to key stakeholders and shift the balance to commercial execution in order to maximize the sustainability of their position in the rapidly shifting biologics marketplace.

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