Healthcare Industry
Biosimilars

Biosimilars: A marathon, not a sprint

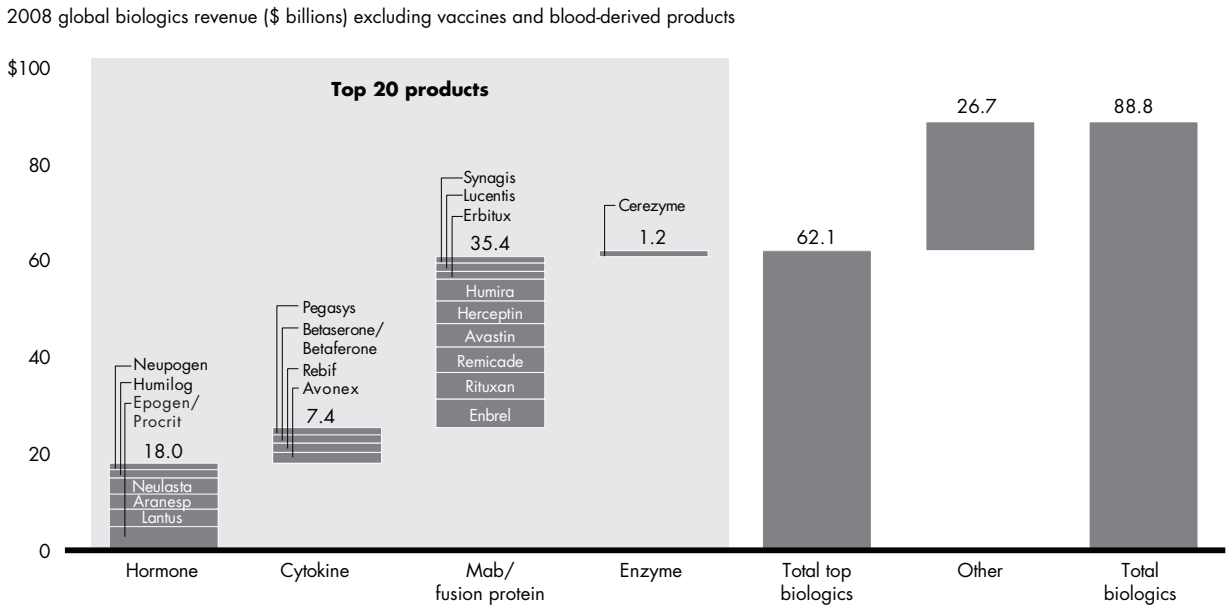
Biologics represent breakthrough drug therapies that are changing the pharmaceuticals industry. Accounting for nearly 20 percent of global drug sales, they are a critical area of investment for the industry. The growth rate for biologics is projected to increase at double-digit levels, in sharp contrast to the declining rates for chemically derived, small molecular weight ("small molecule") drugs, which comprise the historic franchise of large pharma companies. In addition, a relatively small number of currently licensed biologics comprise the vast majority of the market. (See Figure 1.)

While biologics are addressing significant unmet medical need, they are expensive. Some of these therapies cost upwards of $100,000 per treatment course on an annualized basis and are increasingly attracting the attention of public and private payers in their efforts to control medical expenditures. Currently, payers find it difficult to manage the burgeoning cost of biologics through mechanisms that try to control the utilization of these therapies. In oncology, for example, where monoclonal antibodies (MAbs) and other proteins are widely used, payers hesitate to restrict access to these life-saving treatments.

Given these challenges, biosimilars are viewed as a central tenet for future cost containment. Europe has already established the legislative framework and regulatory guidelines for at least some biosimilars. In the US, the model will be dictated by pending congressional legislation.

While the details are not final, biopharma companies can expect certain legislative and regulatory principles to be enacted in the US—such as the granting of exclusivity for innovator products (likely span: 10–14 years), a

Figure 1: Biologics revenue: Concentrated in a small number of products



Source: EvaluatePharma, Bain analysis

"505(b)2-like" approval pathway and requirements for some degree of clinical development. FDA guidelines for biosimilars' clinical protocols are likely to vary by biologic class, and will be guided by factors such as molecular weight and complexity, the existence of reliable biomarkers, the safety experience of innovator products and the nature of the indication and patient populations.

The evolving competitive landscape for biosimilars

To date, traditional small-molecule generics companies have been the most aggressive players in pursuing biosimilars. Generics manufacturers such as Teva Pharmaceuticals Industries, Mylan, Sandoz and Hospira already have licensed oncology adjuvant therapies such as epoetin-alfa (EPO) and granulocyte-colony-stimulating factors (G-CSF), which are being marketed in Europe. So far, the results have been mixed. The highest penetration of these products has been in Germany, due to the greater ability of the payers there to influence how drugs are prescribed. In other European countries the demand for these therapies has been quite low for several reasons: The overall penetration of generics is lower; legislation in some countries has been passed that prohibits automatic substitution of biosimilars for innovator products; and payers and providers are sometimes hesitant to promote the use of biosimilars until more robust safety data is accumulated.

In addition, emerging market manufacturers, particularly Indian biopharmaceutical companies, are developing biosimilars for local markets. Since its launch in 2007, Reditux, Dr. Reddy's biosimilar for Roche's Rituxan product, has captured nearly a third of the Indian market for Rituxan. Such programs are currently not designed to meet Western regulatory guidelines (which, in the case of biosimilars, don't exist yet for the most part) and thus are unlikely to be eligible for distribution in markets such as the US, Europe and Japan for some time. However, in the interim, the development, manufacturing and commercial expertise acquired by emerging market-based biopharma companies may prove valuable to potential Western biopharma partners, as they pursue biosimilars globally.

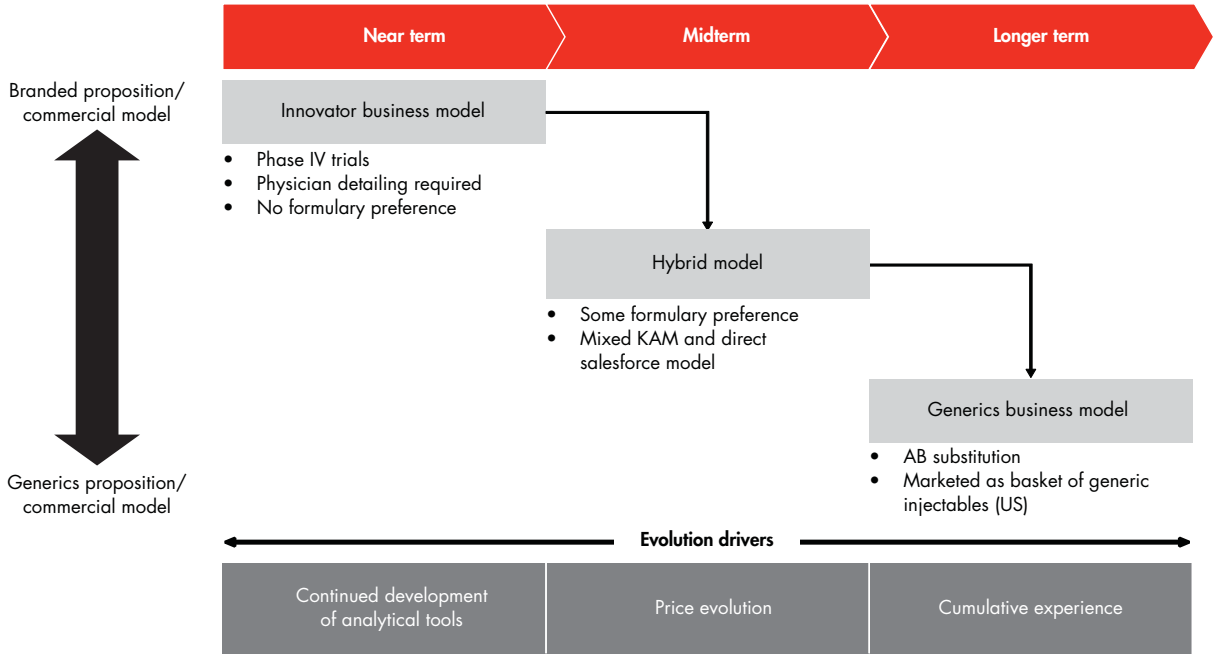
Finally, a number of large global pharmaceutical and biotech players are considering the development of "biobetters"—drugs that are similar to innovator biologics but are characterized by some change in the structure of the protein or the process by which they are made, with the goal of improved efficacy, safety or immunogenicity. While this strategy may be compelling for certain players, we believe that the clinical development requirements will not greatly differ from those of the referenced innovator product, and the commercial strategies for these products will be akin to traditional branded pharma approaches.

Key issues ahead for biosimilars

Based on extensive work on this topic and research with key constituents, Bain believes there are several key issues that new entrants and marketers of currently licensed innovator biologics will need to be aware of as they formulate their strategic approach to biosimilars:

- **The model will transition over time:** Bain & Company believes a plausible scenario is a multiphased evolution, where biosimilars gradually move from a branded proposition and commercial approach to a traditional generics model. (See Figure 2.) This may not be true for all products—for example, biobetters by definition are not likely to achieve automatic substitution, the migration timeline could vary significantly by product and the number of products eligible for a generics-like model will be smaller—but public and private payers will have a strong motivation to facilitate this transition. Such an evolution has significant implications for biosimilars entrants, as many of the traditional generics players lack commercial capabilities such as strategic marketing expertise in targeted therapeutic areas, a trained field force and managed markets experience—all of which will be required to market biosimilars initially. To date, generics

Figure 2: The biosimilars business model is likely to evolve in stages



manufacturers entering the biosimilars space have created partnerships that focus on accessing biologics manufacturing and cell-line development capabilities. We expect future alliances to address gaps in commercial capabilities and will be driven by the desire to create synergies in key therapeutic areas.

- **Commercial realities are a key success factor:** While legislative and regulatory concerns have dominated the discussion so far, the future success of biosimilars will depend on commercial realities: the ability to drive acceptance and market share. The tepid demand in the US for Sandoz's Omnitrope—a human growth factor licensed through a 505(b)2 application in 2006—is a good example of that challenge. Biosimilars players will need to design clinical development programs (pre-licensure and post-marketing) and pharma-covigilance approaches that address the strategic needs of payers, key opinion leaders and physicians—and satisfy regulatory requirements.

- **Innovators will fight hard to defend their relative market share:** Leading biotech companies have too much at stake to walk away from branded franchises in which they have heavily invested, and in contrast with small-molecule drugs, the early-stage commercial characteristics (such as the need for physician detailing) for biosimilars will play to the advantage of innovators. The multiround pricing actions among biosimilars entrants and biologics innovators in Germany already indicate that both entrants and incumbents will need to carefully map out competitive strategies (including game-theory-based pricing approaches) in upcoming battleground markets—both in terms of disease areas and key geographies.

- **Payers are the key:** In the case of small-molecule drugs, multiple stakeholders in the value chain—pharmacy benefit managers, distributors, pharmacists—have both the incentive *and* the ability to drive the market share of a generic drug. However, the lack of AB substitution in many markets, at

least for an extended period of time, means that the systems will not be geared to drive biosimilars penetration. Once they are comfortable with the safety and efficacy of these products, payers will need to drive usage to realize savings; thus, informing payer perspectives and behaviors will be a key focus for entrants and innovator incumbents alike.

- **Market acceptance will vary by product:** A variety of factors—sometimes conflicting—will determine which biosimilars come to market and are in demand. The example of oncology monoclonal antibodies (MAbs) shows how these conflicting factors work. On the one hand, the market appetite for oncology MAbs biosimilars is high given the price of innovator biologics; and the likelihood of the entire class of drug being cannibalized by enhanced innovator versions is lower. On the other hand, the hurdle to prove comparability will be higher given the complexity of these biologics.

  Furthermore, the ability of a biosimilars manufacturer to increase market share through low pricing will be dictated not only by varying up-front development requirements, but also by its relative manufacturing costs, which are more significant for biologics compared with small-molecule drugs. The ability of a biosimilars manufacturer to achieve a favorable cost position will be dictated by factors such as scale, location of capacity and efficiency (i.e., yields) in protein expression and purification.

While it is hard to predict exactly how—or when—the market for biosimilars will evolve, their potential impact on the global pharmaceuticals industry cannot be ignored. Just as generics emerged as a powerful force in the last two decades, for many in the pharma industry, biosimilars will be a strong agent for change in the future—either through disruption or innovation.

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