Global & USA Biosimilar Market Analysis to 2021

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CUTTING-EDGE MARKET INTELLIGENCE

Global & USA BioSimilar Market Analysis to 2021; BioBetters, Erythropoietin (EPO), Human Growth Hormone (HGH), Granulocyte Colony-Stimulating Factor (G-CSF), Anti-Tumor Necrosis Factor (Anti-TNF), Monoclonal Antibodies (MAbs), Insulins, Interferons, Product Pipelines, Trends, Key Players, Regulations and Strategic Outlook.

TABLE OF CONTENTS

INDEX OF FIGURES

INDEX OF TABLES

1.0 Introduction

Biosimilars are highly-similar versions of biological drugs that are indicated for cancer, kidney disorders and a wide range of autoimmune diseases. Originator biologics are the most expensive drugs in the pharmaceutical industry and many of them cost nearly $100,000 per patient per year. These expensive biologics impose a heavy financial burden on patients and healthcare systems, limiting easy access and optimal care. Patent protection for some of the biologics has already expired and many more are to lose patent rights between now and 2020. This has given an opportunity to biotechnology companies to develop and market biosimilars with a cost benefit of about 20% to 30%.

In order to gain a slice of the $190 billion worth of biologic's market, many biotechnology companies have ventured into the biosimilar sector bringing out less-expensive copies of reference biologics. Biosimilars have been in the E.U. market since 2006 and less-regulated markets such as China, India, and South Korea have a number of biosimilars in their domestic markets. After a long delay, finally, the FDA took a historic decision to approve the first biosimilar Zarxio from Sandoz on March 6, 2015. The coming years will witness the flooding of large number of biosimilars into the U.S., which happens to be the largest market for biopharmaceuticals.

1.1 Executive Summary

The last ten years have witnessed an impressive growth rate for biologic medicines. Nearly 75% of the biopharmaceutical industry research and development (R&D) pipeline includes only biologics. Currently, about 10 of the global top 20 bestselling medicines are biologics and revenues from biological medicines represent 49% of the world's top one hundred drugs in terms of value by 2018. Biologic drugs are quite expensive and the cost per month of treating rheumatoid arthritis with Humira (Adalimumab) can be as high as $1,800 per month. This cost is over 30 times the cost of the small molecule drug Rheumatrex (Methotrexate).

By espousing competition, biosimilars are expected to bring the advantages of biological drugs to more patients at affordable costs. Nearly, $600 million per year is spent globally on genuine biosimilars, with the major part of the investment going to manufacturing facilities and trials. As of now, 44 biosimilars have hit the market in different parts of the world and eventually, all biologics will become candidates for biosimilars. Some biopharmaceutical firms are also developing biobetters (biosuperiors). These have the potential to improve on existing medicines and further develop the market, benefiting pharmaceutical companies and patients alike.

For the first time, in 2005, the European Medicines Agency (EMA) created biosimilar guidelines to enable faster approvals than for biologics. As of now, 19 biosimilars have been authorized in Europe for Erythropoietins (EPO), granulocyte-colony stimulating factors (G-CSF); human growth hormone (HGH); follicle inducing hormone; and anti-tumor necrosis factor (anti-TNF) monoclonal antibodies. More biosimilars are anticipated to be launched in the next few years as most of Europe's market leading biologics having an estimated $81 billion in global annual sales are facing patent expiration.

Herceptin lost its patent protection in 2014, Enbrel will lose its patent in 2015, Lucentis is to lose patent in 2016, Humira's patent will last to 2018 and Avastin will lose its patent in 2019. A competitor drug in development is Amgen's ABP 215, and it is a biosimilar of Roche's monoclonal antibody Avastin (Bevacizumab). Clinical outcome from a comparative evaluation, submitted at the European Society for Medical Oncology congress in September 2014, revealed that ABP 215 which is now in phase III trials is very similar to Avastin in multiple sensitive preclinical pharmacologic evaluations.

Even if biosimilars are cheaper and less risky to develop than reference biologics, the cost involved in developing a biosimilar is about $100 to $200 million and takes about eight to ten years. Consequently, biosimilar companies offer products with a small discount of 10% to 35% on the cost of the reference biologic. However, biosimilars are prompting competition and reducing healthcare

costs in Europe. For example, the adoption of biosimilar EPO in Germany between 2007 and 2012 resulted in more than $550 million in savings.

Sales revenue for biosimilars in the U.S. alone is expected to be $1.9 billion in 2015 and increase to $11 billion by 2020. The U.S., Europe and Japan are spending the most on biologics and therefore will become the largest markets for biosimilars. But, the U.S. is yet to have a definitive biosimilar approval pathway. To date, biosimilars represent only 0.5% of the revenues for biologics and they claim 10% of global biologic sales only if there is a strong biosimilar market in the U.S. In August 2014, the FDA accepted the filing of two biosimilars. One is from Sandoz for Neupogen and another from Celltrion for Remicade. It is expected that about five to ten biosimilars will be approved in the U.S. by 2020.

While many companies are involved in the development of biosimilars, some of the companies are actively involved in developing biobetter therapeutics. Biobetters are developed by modifying an existing biologic molecule and incorporating slight differences in the active ingredient. For instance, a MAb can be PEGylated or tagged with a cytotoxic drug to make it better than biosimilars and biologics. Roche's Kadcyla is a biobetter of its own Herceptin. Similarly, TrasGEX is a biobetter of Herceptin, being developed by Glycotope. Currently, there are 452 biobetters in development compared to 655 biosimilars and 1,241 biologics.

Just like biologics, biobetters also have to meet stringent regulatory requirements. Yet, the cost of development and risks are lower, as the core molecular structures are similar to the originator biologics. They also do not infringe patents and can circumvent biosimilar competition. Companies with successful biologic drugs can bring out biobetters of their own molecules and retain their hold on the market.

1.2 Objectives of This Report

This report provides a comprehensive overview of the size of biosimilars' market, the segmentation of the market, key players and the vast potential of therapies that are in clinical trials. On total, about 44 biosimilars are available in the global market and currently the E.U. is the major market with 19 approved biosimilars in use. A significant number of biosimilars are available in the markets of China, India, South Korea and Latin America. Biosimilars from these emerging countries are approved by a less-stringent approval pathway and therefore, the commercialization of their products is mostly confined to the domestic markets. The report describes how the long-awaited FDA approval of Zarxio from Sandoz (biosimilar for Amgen's Neupogen) in March 2015 is to transform the otherwise nascent market. The report includes:

- An overview of biosimilars that includes differences between biologics; biosimilars and generics, definition of biosimilars by different agencies, barriers in developing biosimilars, cost of developing biosimilars.
- A summary of regulatory pathways in various geographic regions.
- Development of biosimilars in Europe, China, India, South Korea, Latin America and the sudden spurt in the development of biosimilars in the U.S.
- A list of biosimilar developers in different geographic locations.
- An overview of biobetters that includes regulatory considerations, differences between biosimilars and biobetters, various biobetters that are in developmental stages, and the companies with the largest biobetter pipeline.
- An overview of approved biosimilars in the E.U., U.S., India, South Korea and Latin America.
- The market impact of biosimilars on their reference biologics such as Epogen, Humira, Remicade, Neupogen, Neulasta, Enbrel, Rituxan, Herceptin, Avastin and Lantus through 2021.
- The top ten biologics on the focus of biosimilar developers.

- The five major classes of biologics and their biosimilar counterparts.
- The current landscape of originators of biosimilars.
- Global market for biologics by region, through 2021.
- Global market for biologics by indication, through 2021.
- Global market for biologics by drug class, through 2021.
- Global market for biosimilars by region, through 2021.
- Global market for biosimilars by indication, through 2021.
- Global market for biosimilars by drug class, through 2021.
- Profiles of 95 biosimilar developers, their products in the market and their product pipeline.
- A newsletter in the appendix gives the latest news of biosimilar sector as of February 2015.

1.3 Key Questions Answered in This Report

- How do biologics, biosimilars and generics vary from each other?
- What are the different quality, safety and efficacy assessment tests for biosimilars?
- How much is being spent for developing a biosimilar molecule?
- How many years does a biosimilar take to reach the commercial market?
- How do regulatory pathways differ from region to region?
- What is the need for biosimilars?
- What are the different platforms for the development of biosimilars?
- What is the success rate in the development of a biosimilar when compared to a biologic and generic?
- What are the most attractive target biologics for the development of biosimilars?
- How many biosimilars are being developed for Avastin, Enbrel, Herceptin, Humira, Neulasta, and Rituxan, and what are they?
- How many biosimilar MAbs are being developed and what are they?
- How much can the U.S. save by the introduction of biosimilars, through 2024?
- Which companies are involved in developing biosimilar MAbs in South Korea?
- Who are the Indian players active in Indian biosimilar industry?
- What are the biosimilar drugs being developed by the Indian biosimilar developers?
- Name the biosimilars approved in the E.U., India, South Korea and Latin America?
- What is the current utilization rate of biosimilars in the E.U. countries?
- The biosimilars approved for use in Germany, Netherlands, U.K., South Korea, Japan, Latin America and India?
- How far the markets of Epogen, Humira, Remicade, Neupogen, Neulasta, Enbrel, Rituxan, Herceptin, Avastin and Lantus will be affected by the entry of biosimilar counterparts?
- What are the top ten biologics that have become the focus of biosimilar developers?
- What are the five major classes of biologics that have attracted the attention of biosimilar developers and what are their current market shares?
- What are the top ten biologic drugs from 2009 to 2014?
- Which biologic drugs dominated the U.S. market, between 2010 and 2014?
- How much is the Medicare Part B spending on biologics in the U.S.?
- What are the top-eight biologic drugs in the E.U. market?
- How many biologics maintain absolute dominance in the German market?
- What is the average cost of a biologic drug in the U.S.?
- How did the market for biosimilars perform between 2007 and 2014?
- How small is the market for biosimilars, when compared to that of biologics?
- What favorable signs are there in the industry to hope for an accelerated growth for biosimilars?
- What is the projected global and regional market for biosimilars from 2014 to 2021?
- What is the projected market for biosimilars by major drug classes from 2014 to 2021?
- Who are the market leaders in the biosimilar sector?

- What was the market for biosimilars in the major E.U. countries between 2007 and 2013?
- How much is the competition between biologics and biosimilars in the German market between 2007 and 2020?
- What is the potential market for biosimilars in the U.S., through 2020?

Global Biosimilar Market

We have seldom seen the emergence of an entirely new pharmaceutical business segment in a short span of time, but it is happening in the drug development industry with biosimilars. Today, there are more than 245 biopharmaceutical, big pharmaceutical and generics companies focusing on developing or already marketing biosimilars.

While the U.S. has approved only one biosimilar therapeutic; Japan, Australia and Europe have approved six, eight and 19 biosimilars respectively. Already, biosimilars have an exemplary safety track record in the E.U., Japan, and Canada where biosimilars are regularly competing against biologics for nearly seven years. The E.U. was the first geographic market to develop the process of authorization of biosimilars, setting an example for many other developing markets to follow suit. As of 2015, the E.U. has approved 19 biosimilars, out of 21 submissions, mostly for three reference biologics such as Somatropin, Epoetin alfa and Filgrastim.

Biosimilars generated revenues of $1.1 million in 2007, which gradually rose to $86.9 million in 2014. During this period, the market penetration of biosimilars in Europe and emerging markets was only about 8%. By 2019, KellySciPub forecasts that 50% of the biologics market will belong to off-patent drugs, creating a high market potential for biosimilars.

The top five biologics targeted most by biosimilar developers are Avastin, Enbrel, Herceptin, Humira and Rituxan, which together generate revenues of about $50 billion annually.

Like most other markets, a competitive biologics market can offer benefits to consumers by lowering prices and enhancing quality. In addition, biosimilars have an unblemished safety track record in the E.U., where biosimilars have been competing against biologics since 2006. Biosimilars have also proved to have a notable impact on drug prices. In the E.U., where biosimilars are already competing with biologics, biosimilars are sold at a 30% discount compared to branded biologic drugs. In spite of the approval of 21 biosimilars in Europe, only 18% of the physicians are aware of these similar versions of biologics. This market analysis report gives cutting-edge information on the following:

- Biosimilar Market Performance, 2007-2014
- Loss of Patent Protection for Biologics: The Major Driver of Biosimilars' Market
- Biologics Losing Patent Protection, Through 2019
- Relatively Small Size of Biosimilars' Market Compared to Biologics'
- Biosimilars' Market Compared with Biologics', Through 2021
- Favorable Signs for Increased Uptake of Biosimilars
- Recent Events in Biosimilars' Market
- Biosimilars Market by Geography (Europe, US, Canada, Russia, Middle-East, Australia, Asia, Africa, South America, China, India), Through 2021
- Biosimilars Global Market by Drug Class (MAbs, TNF-alfa inhibitors, EPO, Insulin, G-CSF, Interferons, HGH), through 2021

- Biosimilar Market Leaders
- The Four Biosimilar Market Leaders and their Market Shares, 2008-2014
- Distribution of Biosimilar Companies by Geography (Europe, North America, Asia/Pacific, Latin America, Middle-East, Africa)
- Leading Biosimilar Markets in Europe (France, Italy, UK, Spain, Germany), through 2020
- Future of Biosimilars

US Biosimilar Market

With the approval of the first biosimilar in the U.S in early 2015 and the expected patent expiration of 12 biologics by 2020, biosimilars are expected to competitively penetrate the US biologic market. Biosimilars have thus become a threat and opportunity for biotechnology and pharmaceutical sectors. Zarxio (Filgrastim, Sandoz) will be launched into the U.S. market in September 2015 and will compete with Neupogen (Amgen) within the US G-CSF market.

Biosimilars will account for 4% to 10% of the biologics market total by 2020, depending on the number of biosimilars launched in the U.S. The U.S. is the largest market for biologics and the biosimilars can achieve 10% of the global sales in 2020, only if the volume growth for biologics is achieved in the U.S. market. According to the Federal Trade Commission, biosimilars can potentially save the U.S. healthcare system, more than $250 billion through 2022.

The main players looking to penetrate the US biosimilar market are currently Amgen, Mylan, Pfizer, Sandoz and Hospira. This report indicates the following key information on the US biosimilar market:

- The Market Potential for Biosimilars in the U.S.
- Projected U.S. Biosimilar Market, Through 2020
- Optimistic Predictions for the Growth of Biosimilars' Market in the U.S.
- Timeline for U.S. Patent Expiration of Branded Biologics
- Viability of Biosimilars in the U.S.
- Cost of Developing and Bringing a Biosimilar into the U.S. Market
- Projected Savings with Biosimilars in the U.S.
- Projected Savings with Biosimilars of 11 Specific Biologics in the U.S., 2012-2024
- Multiple Challenges for Biosimilars' Entry into the U.S. Market
- Break-Even Analysis for Biosimilars in the U.S.
- Biosimilars About to Enter the U.S. Market
- Top Five Players Focused on Developing Biosimilars for the U.S. Market

Figure S1: Biosimilar Market Performance, 2007-2014