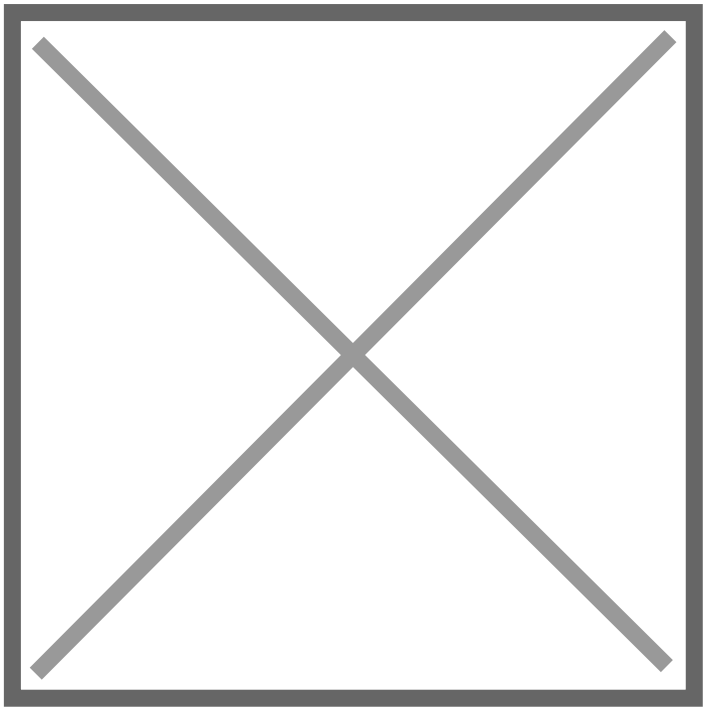
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Bionomics of Biosimilars

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biosimilars

Biosimilars are said to be the next big cash cow for India. However, players have many knots to untangle before they can have a firm grip over the economics of
the market.

Biopharmaceuticals continue to outperform the pharmaceutical market with the US alone predicted to touch a figure of about Rs 2.79 lakh crore ($60 billion) by 2010. The latest agenda for many companies now is to utilize the opportunities in biosimilar market. An increasing use of biologics in disease areas such as cancer, auto-immune and orphan diseases, in addition to healthcare cost containment, has driven the growth of biosimilars.

In a short term, biosimilar market growth will be driven by drug classes including erythropoietin, filgrastim, human growth hormone (HGH) and insulin. Gradual expiry of patents will create significant market opportunities for developers through to 2016. Between 2012-19, the market will see a patent expiry of a whopping Rs 2.79 lakh crore ($60 billion) of biotech drugs with Amgen being the most hard out of all the companies. Its blockbuster drug for anemia, Epogen which had a sale of about Rs 11,600 crore ($2.5 billion) in 2008 will lose its patent in 2013. Other blockbuster drugs, Neupogen will lose its patent in 2013 while arthritis drug, Enbreal, will lose its patent in 2012. Epogen, Neupogen
and Enbrel together accounts for half of Amgen's total revenue. Companies like Merck, Novartis and Pfizer are already on the run to make biosimilar versions of Epogen while Pfizer is also looking at coming up with a biosimilar version of Sanofi Aventis' Lovenox.

Indian scenario

India is not far behind as biosimilars spell big opportunities especially for companies like Dr Reddy's Labs, Ranbaxy, Biocon, Shantha Biotech and Intas Biopharmaceuticals, who are actively involved in the space. The Indian biosimilars market in 2008 was around about Rs 930 crore ($200 million), with an expectation to reach around about Rs 2,698 crore ($580 million) by 2012.

Jay Desai, founder and CEO, Universal Consulting, says, "In India, the interest in biosimilars is additionally spurred on by multiple factors. Firstly, under the Trade Related Intellectual Property Rights (TRIPS) agreement, pre-1995 product patents

were exempted thus granting some biologicals, the rights to continue manufacturing. Secondly, biotechnology drugs (besides insulin) are free from the government's price control act, allowing independence in price setting. There seem to be signs of acceptance of locally manufactured biosimi lars among healthcare professionals within the country."

The upcoming oncology market is one of the prime targeted areas for many companies. The current size of the Indian oncology market is about Rs 86.50 crore($18.60 million), which is expected to be over about Rs 232 crore ($50 million) by the end of 2010. Tapan Ray, director general, Organization of Pharmaceutical Producers of India (OPPI), says, "Oncology being one of the fastest growing therapy segments, sharp focus on this area is indeed a step in the right direction."

There are around 25 Indian players in the space with around 40-50 products already being sold in the Indian market and some being sold in the unregulated markets too. "Around 15 brands of EPO, eight-nine GCSF and three-four insulin products are being sold in the Indian market," informs Dr Dhananjay Patankar, COO, Intas Biopharmaceuticals. According to estimates, in India, EPO has clocked a sales of $22 million (about Rs 102 crore), c-GSF has sales of about Rs 51 crore ($11 million), interferon has a sales of $22 million, (about Rs 102 crore) streptokinase has sales of about Rs 74.40 crore ($16 million), and insulin has a sales of about Rs 255 crore ($55 million).

Dr Reddy's Labs created a niche in the oncology with the launch of its affordable biosimilar product, Reditux, in 2003. Biocon has four products developed in India; viz EPO, insulin, GCSF and streptokinase with its human insulin product being sold in the market at a discount of almost up to 80-85 percent. Glenmark is planning to come out with its first biotech product by 2010 from its biological research establishment located in Switzerland. Similarly,Ranbaxy with its strategic collaboration with Zenotech Laboratories is planning to market G-CSF oncology products in various markets of the world like Brazil, Mexico, CIS and Russia. Reliance Life Sciences launched three biosimilars - ReliPoietin Erythropoietin (EPO), ReliGrast Granulocyte Colony Stimulating Factor (G-CSF), and ReliFeron (Interferon Alpha 2b) in the domestic market in 2008.

"We are concurrently conducting clinical trials for two biosimilars — Erythropoietin and GCSF — in Europe," says KV Subramaniam, president and CEO, Reliance Life Sciences. Intas Biopharmaceuticals has launched four biosimilar products - G-CSF, EPO, Interferon Alpha Beta (IFN-) and Peg-GCSF in international as well as domestic markets. "Our strategy for regulated markets would be a step wise approach from API to biosimilars to contract research to collaborative research and biobetters to novel biologics. The company is aiming to replicate its biosimilar success of India and semi-regulated markets success in Europe and North America."

Wockhardt has biosimilar products at various stages of development and is targeting the US and EU markets. Cipla has entered into an 50:50 joint venture (JV) with a Chinese company for biosimilars. The JV called BioMab, expects the first product to be out by 2010.

However, it will not be a smooth road for these players. "There are five bridges that an Indian biopharma company must traverse, all of them are equally important to success. These bridges are those of affordability, assets, approvability, acceptability and availability. The ability to safely cross over these spans, will determine the level of success we are likely to see in the Indian biosimilars industry," adds Desai. Above all, industry experts fear that the market will see the mushrooming of a number of other players who are on the run to make quick money but will come out with products without any quality.

EU, US markets: Not a cakewalk

Attaining a firm grip in the EU and the US markets will not be a cakewalk for India. With EU already out with a pathway in 2006 and the US FDA scheduled to come out with one in another five years, Indian players are investing heavily keeping these two markets in mind. However, industry experts claim that it will be a different ball game altogether. Says Desai, "The current theory-in-use is that India will at some point in the not-too-distant future, replicate the relative success of its pharma generics industry in the biosimilars market worldwide. The theory-in-practice may well turn out to be quite different."

"The estimated cost to develop a biosimilar is in the range of $10-40 million, largely because of the need for extensive safety and efficacy testing when compared with $1-2 million for a traditional generic," claims Subramaniam. Post the approval of its first biosimilar product, Omnitrope, Sandoz's penetration levels in the European market is still very low. According to Peter Wittner, senior consultant, Interpharm Consultancy, "It will be a bumpy road for India. Registering a biosimilar product in the EU (EMEA) will be easier since the guidelines have already been laid out, yet the cost of compliance is extremely high. Moreover, in regions like the EU, the entry cost is high leading to low competition and fewer players."

Need for an independent regulatory body

The call of the hour is to set up an independent regulatory pathway in India for the approval of biosimilar products. At present, the Drug Controller General of India (DCGI) gives the go ahead for market approval both for generic as well as biotech drugs.

Without a regulatory body, there might be chances of low-quality products being sold, which in turn can ruin the reputation of the Indian industry.

In 2004, there was a call by a section of the industry for an independent body for approval of biologics. Nothing concrete has come up since then. Dr Patankar, who then represented the Confederation of Indian Industry (CII), recalls “The need to streamline and draft guidelines for biosimilar drugs first came about in 2004 with the setting up of the Mashelkar Task Force which had representatives both from associations and the industry.” Only a few recommendations from the task force are being implemented today.

All eyes are now on the WHO guidelines for biosimilars which can bring about some stability. “The Indian government is looking into the issue and it has been sharing details to the industry and also taking in their suggestions,” adds Dr Patankar.

Alternate options for investors

There has not been much activity from private equity and venture capitalists too. In terms of private investment, Intas Biopharma and Bharat Biotech are the two big names known where PE funding of both companies put together come up to about Rs 139.60 crore (almost $30 million). “There are not many deals happening in the PE and VC space. This is because of the huge risk involved in biosimilars. A huge chunk of investment today comes from promoters. However, I gradually see an interest picking up for this space,” mentions a well-known private equity investor who is keeping a close tab in this space.

Investors believe that a good alternative would be for Indian companies to enter into licensing agreements and alliances for biosimilars especially when it comes to the regulated markets. This, they believe, can attract some PE/VC investment. After EPO, insulin, GCSF and interferons, investors are now bullish about the Mabs space. With the patent expiry of products like Herceptin, Humira and Rituxan, Mabs are in the pipeline for many Indian players. Currently, Mabs generate global revenues of around about Rs 93,000 crore ($20 billion) and represent the fastest-growing segment within the pharmaceutical industry.

Competition from China

There are apprehensions of India facing tough competition from China. Experts are divided in their opinion as to which country has the upper hand. China at present has a number of small players operating in the space. Dragon Pharma alone has 20 GCSF products in the pipeline. “China has the edge over us in terms of manufacturing and expertise and hence they might eat up a major share of the global biosimilar market,” says Dr Arumugam Muruganandam,senior scientific manager, R&D, Biocon. However, experts also believe that India has the edge over China because of a large number of ‘big players’ in India participating in the space which is not yet to be seen in China.

Biobetters: The future

The new turf for biotechs, both innovator and biosimilar companies alike are ‘biobetters’, which are second generation biopharmaceuticals showing improved performance and efficacy over the innovator product by a slight modification of the molecule. There can be two possibilities. The first being a biosimilar company which has a drug target in mind, has the proven clinical results but then induces a slight clinical change in the molecule design which then brings out a product which is better than the innovator product. The second situation is when an existing molecule of an innovator product is modified to bring out a drug which does not exist in the market at all. Industry experts however opine that Indian players should take one step at a time and have to shift their focus on biosimilars.

Nayantara Som in Mumbai