ABLE Association of Biotechnology Led Enterprises

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PRICEWATERHOUSECOOPERS

# Leadership in Affordable Therapeutic Products

## A BIO PHARMA STRATEGY FOR INDIA


An **ABLE** - **PwC** Report for

सत्यमेव जयते

Department of Pharmaceuticals
Ministry of Chemicals & Fertilizers
Government of India

Evolution of new drugs continues to be an increasingly daunting task. The en-block patents expiry of older small molecule drugs with little to add by way of discovery of new ones is at once a challenge and an opportunity.

This challenge is on one hand leading to hunt of new molecules from the depths of the ocean to prospecting new chemical complexes through nanotechnologies while opening up larger market opportunities in the generics space. However the generics market will see a lot of consolidation due to entry of large global players whose energies would be diverted from the hitherto patents of small molecules, to now, in the changed context, generics, which offers the traditional low hanging fruit to profit from.

It is in this context that the development of biopharma drugs becomes very important especially in the context of India. With the advent of the product patent regime, there is an air of expectancy to develop new ideas. There can be no better area to do this than Biopharma. Biopharma as we know encompasses the range from recombinant technology based biosimilars to development of large antibodies structures – the mABs. While in the year 2009 the global biopharma market was said to be about $ 137 billion strong, India has but a miniscule share of 1.4% in it. However Indian biopharma is growing at a scorching pace and registered a 17% growth over the last year, which is really the bright silver lining.

The Department of Pharmaceuticals in the Government of India has taken up the task of addressing this opportunity. In partnership with the premier biotechnology industry body ABLE and pre-eminent consultant leader in the life sciences sector – PwC, the Department of Pharmaceuticals has sought to prepare a detailed document – The Vision 2020 BioPharma Strategy. This would for the first time bring out the multifaceted challenge and the break-through possibilities in the biopharma sector for the Indian industry.

I am sure that the industry would benefit from it and so would the government for finding new ways to address the growth and development of the biopharma industry in India for making it the future leading global hub. Thank you.

**Ashok Kumar**
Secretary, Department of Pharmaceuticals
Ministry of Chemicals & Fertilizers
Government of India
New Delhi
12th July 2010

The Vision 2020 BioPharma Strategy: This would for the first time bring out the multifaceted challenge and the break-through possibilities in the biopharma sector for the Indian industry.

**The Biopharma Challenge**

The biopharma drugs sector is the next big block-buster awaiting right techno-scientific entrepreneurship. India cannot afford to miss this opportunity. The present growth rates of over 30% but scratch the surface.

The challenge is how to do it given the promises on one hand and constraints of world class human resources, infrastructure, discovery funding and the appropriate policy mix on the other. The Vision 2020 BioPharma Strategy document would be path-breaking in pointing out direction to accomplish this difficult task. ABLE and PwC have come together through painstaking research and wide experience including first hand interviews to prepare this document.

I hope the industry, the academia and all the stake-holders find it useful. We encourage them to contribute to it and join us in the task of building India as the next big destination for global biopharma.
Thank you.

**Devendra Chaudhry**
Joint Secretary
Department of Pharmaceuticals
Ministry of Chemicals & Fertilisers
Government of India
12th July 2010

The Vision 2020 BioPharma Strategy document would be path-breaking in pointing out direction...

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The Indian Pharmaceutical Industry has been a global leader in the cause of providing high quality affordable medicines to the world. With a gradual shift from small molecules to biologics, the vision, the mission and the tactical planning for the Indian Biopharmaceutical Industry has yet to be evinced. This was the task given to us by the Department of Pharmaceuticals and this report is the result. At the outset we would like to thank the Department for reposing faith in ABLE & PwC to deliver on this important task.

This report analyses the global environment with reference to markets, regulations, government initiatives and identifies key areas for the Government to play a major role in building the required capacities and capabilities. An enabling ecosystem - infrastructure, regulatory framework and a skilled workforce are some of the factors that will ensure that India becomes a leading producer of affordable biopharmaceutical drugs in the next decade.

Recognising that the strategic way forward is through Innovation and the ability of Indian companies to create Intellectual Property, the report identifies long term initiatives that the Government can implement to foster innovation.

We hope this report presents an understanding of the opportunity for Indian Biopharma and a direction for all stakeholders to realize this opportunity.

**Vijay Chandru**
President - ABLE

**Sujay Shetty**
Leader – Pharma Life Sciences
PricewaterhouseCoopers

Recognising that the strategic way forward is through Innovation and the ability of Indian companies to create Intellectual Property...

In 2010, the Department of Pharmaceuticals (DoP) of the Government of India (GOI) set the nation's biopharmaceutical industry (BioPharma) a lofty goal: to become a leading global producer of affordable "biopharmaceutical" products by 2020. The market is currently worth about US $137 billion, but it is growing very rapidly. Indeed, industry experts estimate that it could be worth US $319 billion by 2020. Moreover, at least 48 products with combined sales of nearly US $73 billion in 2009 are due to come off patent over the next decade. So the potential is huge.

However, biopharmaceutical products are very much more difficult to develop and manufacture than traditional pharmaceuticals. The competition – both from manufacturers of branded products and from other emerging countries keen to make their mark in the biopharmaceutical space – is also likely to be intense.

If India is to achieve its aim, it will therefore have to act fast – and the GOI will have to play a major supporting role by creating a suitable physical, financial, legislative and regulatory infrastructure. The private sector will invest in building the necessary manufacturing capacity, if that enabling infrastructure is in place. But it cannot provide the roads and ports, fiscal incentives, laws, regulations and other such features that will also be needed to put India at the forefront of biopharmaceutical production.

This report focuses on the changes that will be required to provide such an infrastructure. It explores the key differences between biopharmaceutical therapies and conventional therapies, together with the implications for development and manufacturing; analyses the competitive landscape; and identifies the measures the GOI will need to implement within the next five and 10 years, respectively. It does not attempt to quantify the precise amount of manufacturing capacity that will be required; it focuses, rather, on the big picture.

We believe that India should aim to capture 10% of the global market for biosimilars – i.e., follow-on versions of original biopharmaceutical products – by 2020, and become one of the top five producers in the world. We estimate that the GOI will need to invest at least US$1 billion over the next five years to implement the measures we have identified. Doing so could yield rich returns; if India's Biopharma industry succeeds in realising this aspiration, it will bring in additional revenues of US $4.3 billion a year.

**The GOI will have to play a major supporting role by creating a suitable physical, financial, legislative and regulatory infrastructure.**

# The Vision for 2020

## Chapter 1

**India should aim to become one of the world's five leading producers of affordable biopharmaceutical drugs by 2020. Biopharmaceutical products include: vaccines, blood and blood components, somatic cells, gene therapies and recombinant therapeutic proteins.**

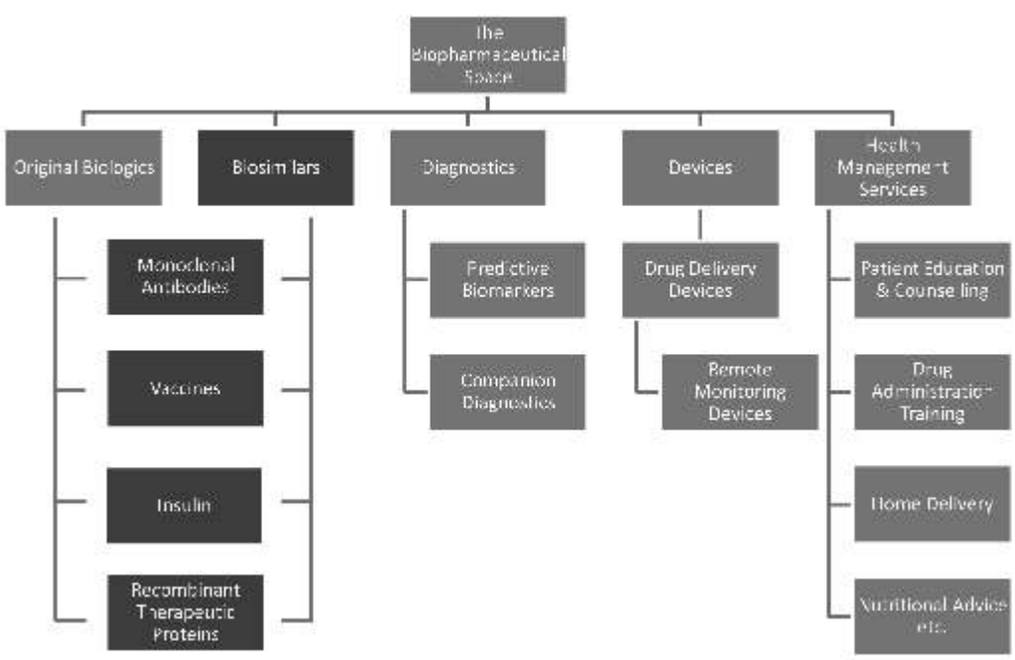
### 1.1 WHAT ARE BIOPHARMACEUTICAL PRODUCTS?

The word "biopharmaceutical" is a composite of the words "biotechnology" and "pharmaceuticals", and reflects the convergence of what were once two distinct industries. So it is probably helpful to begin by discussing precisely what biopharmaceutical products comprise. They are medicines typically derived from living systems and produced using biotechnology – e.g., vaccines, blood and blood components, somatic cells, gene therapies and recombinant therapeutic proteins.

Over the past decade, the BioPharma industry has developed many such "biologics", as they are also called. And follow-on versions of some of the earliest biologics made via recombinant DNA technology, including biosynthetic "human" insulin and human growth hormone, are now available. These are known as "biosimilars".

However, the biopharmaceuticals market extends well beyond medicines. It also includes diagnostics, sophisticated drug delivery and remote monitoring devices, and health management services. Only a few biopharmaceutical companies – e.g., Fresenius and Baxter Healthcare – currently offer such services, but other companies are likely to follow suit as the spotlight switches to the secondary-care sector (see Figure 1). Diagnostics, devices and health management services are major subjects in their own right. This report therefore focuses on the burgeoning market for biosimilars – and, more specifically, on how India can best prepare to capture a share of that business.

**Figure 1: The Biopharmaceutical Space**



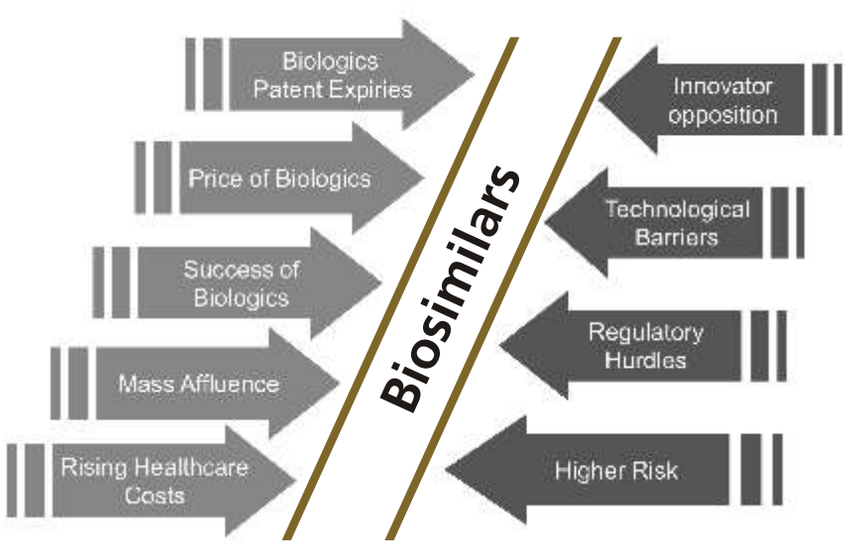

Source: PricewaterhouseCoopers

### 1.2 THE SIZE OF THE PRIZE

The biosimilars market is still in its infancy, and is largely concentrated in less heavily regulated regions such as Latin America and Asia at present. But industry analysts estimate that it could be worth more than US $43 billion by 2020. (All subsequent references are to US dollars, and all figures have been converted into dollars for ease of comparison, using the exchange rates detailed in Appendix 1.)

Aging populations and higher expectations are boosting demand for good medicines, and biologics now have a very successful track record. However, many biologics cost thousands – or even hundreds of thousands – of dollars. Biosimilars, by contrast, typically sell for between about 15% and 75% of the price of the original versions. So they are more affordable – in both mature economies with increasingly cash-strapped healthcare systems and emerging economies with increasingly affluent inhabitants (see Figure 2).

**Figure 2: The Forces Shaping the Biosimilars Market**




Source: PricewaterhouseCoopers

Biosimilars have considerable commercial potential, but exploiting that potential will not be easy. For one thing, biosimilars are much more difficult to develop and manufacture than traditional generics. The regulatory pathways for getting them approved are also less well established, and the competition – both from innovator companies and from rival biosimilars producers – is likely to be intense. We shall discuss these challenges, and how India should respond to them in more detail in the following pages.

# Overview of the Global Biologics Sector

Chapter 2

**With global sales of biologics reaching nearly $137 billion in 2009 and the patents on at least 48 biologics due to expire over the next decade, industry experts predict that the global biosimilars market could be worth more than $43 billion by 2020. But biologics differ from conventional pharmaceuticals in some fundamental ways.**

## 2.1 THE SIZE AND COMPOSITION OF THE GLOBAL BIOLOGICS MARKET

In 2009, global sales of biologics totalled $136.6 billion (see Table 1). Avastin (bevacizumab) headed the list of best sellers, with sales of $5.74 billion, while Rituxan (rituzimab) and Humira (adalimumab) came second and third, respectively (see Table 2).

**Table 1: The Global Market for Biologics in 2009**

| Country | 2009 Sales ($ bn) |
|---|---|
| US | 69.02 |
| Europe | 41.68 |
| Japan | 10.29 |
| Asia/Africa/Australasia | 14.40 |
| Latin America | 1.20 |
| **Total Biologic Drugs Market** | **136.59** |

Source: visiongain & PricewaterhouseCoopers analysis

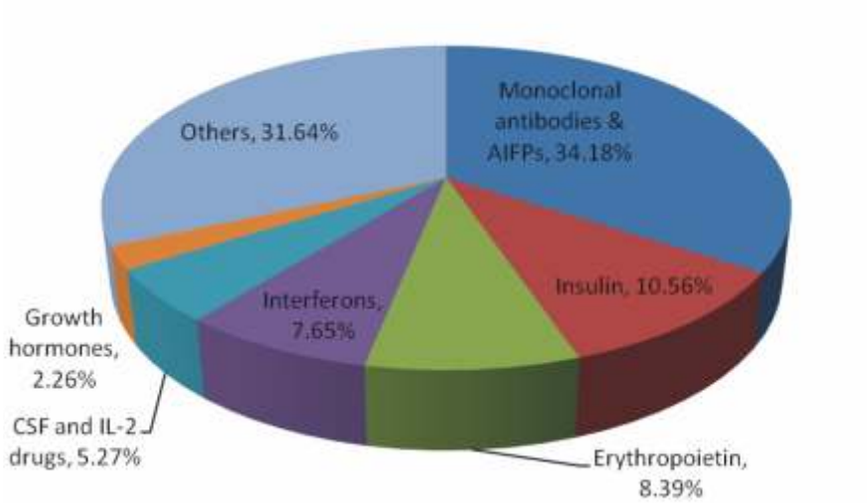
**Table 2: The 10 Top Selling Biologics in 2009**

| Brand | Drug Name | 2009 Sales ($bn) |
|---|---|---|
| Avastin | bevacizumab | 5.74 |
| Rituxan | rituximab | 5.62 |
| Humira | adalimumab | 5.48 |
| Herceptin | trastuzumab | 4.86 |
| Lantus | insulin glargine | 4.29 |
| Enbrele | tanercept | 3.87 |
| Remicade | infliximab | 3.51 |
| Neulasta | pegfilgrastim | 3.35 |
| Epogen | epoetin alfa | 2.56 |
| Avonex | interferon beta-1a | 2.32 |

Source: EvaluatePharma

Measured by drug type, monoclonal antibodies (MAbs) led the market. They accounted for more than one-third of all sales of biologics in 2009, followed by insulin and erythropoietin (see Figure 3).

**Figure 3: Share of the Total Biologics Market by Drug Type in 2009 (%)**




Source: visiongain

## 2.2 THE SIZE AND COMPOSITION OF THE GLOBAL BIOSIMILARS MARKET

Biosimilars accounted for sales of just $1.23 billion – less than 1% of the total biologics market – in 2009 (see Table 3). However, there is considerable potential for growth.

**Table 3: The Global Market for Biosimilars in 2009**

| Country | 2009 Sales ($ bn) | Market Share of Biosimilars (%) |
|---|---|---|
| US | 0.06 | 4.9 |
| Europe | 0.14 | 11.4 |
| Other Countries (incl. China and India) | 1.03 | 83.7 |
| **Total Biosimilars Market** | **1.23** | **100.0** |

Sources: IMS Health & visiongain

Some 30-odd biosimilars are currently in development or close to securing regulatory approval. The patents on at least 48 biologics with combined sales of nearly $73 billion in 2009 are also due to expire within the next 10 years, paving the way for the development of additional follow-on products. (Please see Appendices 2 and 3 for further information on the biosimilars pipeline and biologics with patents expiring between 2010 and 2020.) Furthermore, healthcare payers around the world are becoming increasingly interested in biosimilars, as they struggle to contain healthcare bills that are soaring as a result of aging populations – and, given that treating a single patient with a MAb can cost as much as $100,000 a year, it is easy to see why more economic alternatives might appeal. Lastly, the US, which is the world's largest biopharmaceuticals market, has just created a new regulatory pathway for approving complex biosimilars. For all these reasons, industry experts predict that the global biosimilars market could be worth more than $43 billion by 2020.

## 2.3 THE KEY DIFFERENCES BETWEEN BIOLOGICS AND CONVENTIONAL PHARMACEUTICALS

However, biologics differ from conventional pharmaceuticals in some fundamental ways. In the next section, we shall discuss these differences, together with their implications for the development, manufacturing and marketing of biosimilars.

### 2.3.1 Differences in Therapeutic Targets

Biologics typically address diseases conventional drugs cannot treat very effectively – such as cancer and genetic disorders. They can therefore command premium prices in most markets when they are first launched, because there are no effective therapeutic alternatives.

### 2.3.2 Differences in Product Attributes

But biologics are very complex products. Conventional drugs are derived from chemicals, consist of relatively few molecular ingredients, are quite small and can easily be characterised through their chemical structures, using established analytical techniques such as mass spectrometry. Biologics, by contrast, are derived from genetically modified microorganisms or animal cell lines. Most biologics also consist of many molecular ingredients, are much larger than conventional drugs (between 100 and 1,000 times larger) and have complex structures that cannot be completely characterised by the methods used for conventional drugs.

### 2.3.3 Differences in Manufacturing Processes and Infrastructure Required

Biologics likewise differ crucially from conventional drugs in that the methods by which they are manufactured greatly influence their therapeutic characteristics. The same starter ingredients may deliver quite different results, depending on the system that is used. Similarly, a slight variation in the starter ingredients or external manufacturing conditions may yield a different product, even if the living system from which it is derived is the same. These differences can render a biologic unsafe or ineffective. Hence the fact that the patents protecting biopharmaceuticals often include the processes used to manufacture them as well as their chemical composition.

Moreover, the process flows typically used to manufacture proteins or antibodies, and the unit operations involved in those process flows, have very little overlap with the process flows and unit operations typically involved in the production of small molecules (see Tables 4 and 5). These differences in the manufacturing processes and infrastructure required to produce small molecules and proteins or MAbs mean that the latter are more expensive to manufacture in terms of both capital costs [per square feet (sq. ft.)] and operating costs.

**Biologics likewise differ crucially from conventional drugs in that the methods by which they are manufactured greatly influence their therapeutic characteristics.**

| Table 4: Typical Process Flows | |
|---|---|
| **Small Molecules** | **Proteins/MAbs** |
| Chemical reaction | Cell banking |
| Solvent extraction | Seed fermentation (or inoculum development) |
| Crystallization | Production fermentation/cell culture |
| Vacuum or air drying | Harvesting (cell separation) |
| Milling | Concentration and purification (multiple steps depending on product and host organism) |
| Blending | Bulk formulation, bulk lyophilisation |
| | Aseptic fill-finish (vials, cartridges, syringes, etc.) |

Source: PricewaterhouseCoopers

| Table 5: Key Differences in Manufacturing of Conventional Drugs and Biologics | |
|---|---|
| **Small Molecules** | **Proteins/MAbs** |
| Chemical synthesis | Expressed in micro-organisms (bacteria,yeast, fungi, mammalian cells) |
| May involve harsh conditions like extremes of pH, temperature and pressure, flammable organic solvents | Generally aqueous processing using mild conditions |
| Bulk active pharmaceutical ingredient available as a stable solid at room temperature | Requires formulated bulk solution with cold storage |
| Formulated for oral delivery (tablets, capsules, syrup) or topical application (ointment, spray) | Formulated as a sterile vial, pre-filled syringe or cartridge for injection or infusion without terminal steam sterilization |
| Manufacturing facility is generally not designed for aseptic processes | Manufacturing facility is designed for aseptic processes |
| Supply chain may include different manufacturers for drug intermediate, bulk drug and formulated drug product | Vertically integrated up to formulated bulk; at most fill-finish can be decentralized. No concept of drug intermediate |

Source: PricewaterhouseCoopers

More specifically, whereas most of the equipment needed to manufacture small molecules can be sourced locally, most of the equipment needed to manufacture biologics must be imported, although some subsidiaries of European and US vendors have now set up shop in India (e.g., Millipore Corporation, Sartorius and Clestra). The initial capital investment is therefore much greater. The skills required to manufacture biologics – e.g., a knowledge of cell line engineering, fermentation, microbiology, protein purification (chromatography, membrane separations, lyophilisation, protein folding, etc.) and aseptic processing – are also much more demanding.

### 2.3.4 Differences between Biosimilars and Generics

Biosimilars are thus more difficult to develop and manufacture than traditional generics for a number of reasons. First, it is almost impossible to produce an exact replica of a biologic because changes to the structure of the molecule can take place during the production process. Biosimilars, unlike generics, must therefore be subjected to additional clinical testing to ensure that they have similar pharmacokinetic profiles to those of the original products, and do not cause unexpected adverse responses or immune reactions. Second, the processes used to manufacture biosimilars are inherently much more complex than those used to manufacture generics. And, lastly, since biosimilars are injectable products which cannot be terminally steam sterilised, all processing must be performed under aseptic (sterile) conditions.

These challenges mean that it typically costs $10-40 million to develop a biosimilar, compared with just $1-2 million for a traditional generic. The gestation period for clinical development, regulatory approval and scale-up to commercial production is also much longer (typically, about seven years versus two or three years), so the risk to capital is much higher. The cost differential between a biosimilar and the original product is thus much smaller – a fact that some countries, such as Japan, have recognised by introducing differentiated pricing regulations for biosimilars and generics.

Moreover, since biosimilars are not easily shown to be bioequivalent to the original products (as traditional generics are), they are not normally interchangeable (i.e., a pharmacist cannot substitute a biosimilar for the original version). So any company that manufactures a biosimilar will need to employ a specialised sales force (or enter into a marketing agreement with a third party) to encourage physicians to prescribe it.

### 2.3.5 Differences in Regulation

The many differences between biologics and conventional drugs – and hence between biosimilars and generics – have resulted in very different criteria for regulatory approval. Small molecule bulk is approved based on analytical characterisation of the active moiety and identification of any impurities above a specified threshold. The formulated product is approved based on dissolution tests and/or bioequivalence/bioavailability studies in healthy volunteers. These are generally quick, relatively inexpensive and do not require a sophisticated clinical infrastructure.

However, all biosimilars currently require pre-clinical testing in animals (rodents, dogs or other relevant species) to Good Laboratory Practice (GLP) standards and clinical testing to Good Clinical Practice (GCP) standards to establish their pharmacokinetics, immunogenicity and comparative efficacy against the original product. Some countries (or groups of countries, like the European Union) also insist on clinical trials in their local populations or sourcing of the original reference product from the country or region concerned.

Fulfilling these stipulations is very time-consuming and expensive. It also requires clinical and bioanalytical expertise and infrastructure, and the use of clinical research organisations (CROs) with specific domain and country knowledge. Furthermore, the original product may not be one that is routinely prescribed in India. So only a few investigators and trial sites may have the clinical experience to comply with internationally accepted protocols.

There are other obstacles, too. It is relatively easy to implement most process changes, scale changes and site changes for small molecules by showing in-vitro characterisation data through high-performance liquid chromatography (HPLC), low molecular weight mass spectrometry and other such techniques. But there are not yet any guidelines for biosimilars in terms of defining which changes can be permitted through in-vitro testing and whether in-vitro testing can be permitted for "well characterised proteins" (which are mainly smaller proteins without complex glycosylation).

Sophisticated protein characterisation tools may be needed to justify use of in-vitro testing to establish comparability (e.g., mass spectrometry and high frequency nuclear magnetic resonance (NMR) spectroscopy for macromolecules, cell-based assays, affinity measurements, specificity to receptor binding, enzyme-linked immunosorbent assays (ELISA) and gel electrophoresis). The specifications for recombinant proteins and MAbs generally also include establishing limits for host cell proteins, host cell DNA and endotoxins, while products made using mammalian cell cultures have specifications on viral clearance. Performing the analysis and characterisation tests required to meet such specifications requires different skills from those involved in the analysis and characterisation of small molecules.

## 2.4 THE REGULATORY ENVIRONMENT

Regulatory pathways for approving original biologics have been created around the world. However, the member states of the European Union, Japan and Australia (which adopted the European system) are currently the only countries with established biosimilar market authorisation pathways. The US, which is the world's largest biologics market, has just passed legislation to create such a pathway, but some of the details still have to be finalised.

### 2.4.1 The Regulatory Environment in the US

In the US, original biologics gain access to the market through two regulatory pathways:

- The Public Health Service Act (PHS, 1944) – which covers the majority of biologics and is enforced by the FDA via two departments: the Center for Biologics Evaluation and Research (CBER), which mostly regulates blood products, cellular products and vaccines; and the Center for Drug Evaluation and Research (CDER), which mostly regulates biologics produced by biotechnological methods (e.g., MAbs and therapeutic proteins). Biologics falling under the PHS are approved through the Biological License Applications (BLA) procedure.

- The Food Drug & Cosmetic Act (FD&C, 1938) – which covers conventional pharmaceuticals and certain natural proteins (e.g., insulins and growth hormones) and is also enforced by the FDA. Biologics falling under the FD&C are approved through the New Drug Application (NDA) procedure.

At present, biosimilars can only be approved for originals authorised under the FD&C, which means that it is only possible to market a very limited range of biosimilars (the simpler proteins) in the US. Applications must be submitted to the CDER through the Abbreviated NDA (ANDA) pathway. Application data from the already approved reference product can be used in support of the biosimilar, although the FDA can request further documentation of the new product's safety and efficacy relative to the reference product (e.g., through clinical trials).

However, in June 2010, the US Federal Government passed the "Biologics Price Competition and Innovation Act" to create a regulatory approval pathway for biosimilar versions of more complex biologics approved under the PHS. The Act distinguishes between biosimilars and "interchangeable" biosimilars, and establishes a different burden of proof for each category; a biosimilar must possess no clinically meaningful differences in safety, purity and potency from the original product, whereas an "interchangeable" biosimilar must produce the same clinical result as the original product in any given patient and present no additional risk if a patient is switched from the original product to the biosimilar. The Act also includes a 12-year period of data exclusivity for all original products (with a six-month extension for products supported by paediatric studies) and introduces a new "patent information exchange" process, in which the biosimilar applicant is required to provide information about its manufacturing process to the innovator company and both parties are then required to identify the key patents they believe either need to expire or can be successfully challenged.

The FDA must still provide guidance on the clinical data it requires, although the nature of that guidance has not yet been specified. And the process is unlikely to provide a fast route to market; there is considerable scope for disagreement during the patent information exchange period, for example. Nevertheless, industry commentators widely regard the Act as welcome progress.

### 2.4.2 The Regulatory Environment in the European Union

Manufacturers of all pharmaceuticals, including biologics, can apply to the European Medicines Agency (EMA) for marketing authorisation in the 27 European Union member states. Approval is regulated through the 2001 Code for Human Medicines Directive (CHMD) and its subsequent amendments. The CHMD provides an abbreviated pathway for the approval of traditional generics and, following two amendments in 2003 and 2004, also covers biosimilars.

The EMA has issued various guidelines on the data biosimilar manufacturers need to supply with their applications, including specific guidelines for the approval of growth hormones, insulins, epoetin products and granulocyte-colony stimulating factors (G-CSF). It is still preparing guidelines for the approval of interferons and MAbs, but has already approved a number of biosynthetic growth hormones as well as biosimilar versions of epoetin and filgrastim.

The EMA assesses a biosimilar based on whether its safety, quality and efficacy are comparable to that of the original drug. The extent to which clinical trials have to be conducted to provide this information is at the agency's discretion. The regulations further stipulate that original drugs approved before 2005 enjoy marketing exclusivity for 10 years, if they were approved through the centralised European Union procedure. If they were approved in individual member states, varying marketing exclusivity periods apply. However, for original drugs approved after 2005, a data exclusivity period of eight years applies. An additional two years of marketing exclusivity – or three years, if the product is approved for a new indication with significant clinical advantages – can be granted.

### 2.4.3 The Regulatory Environment in Japan

The Japanese Ministry of Health, Labour and Welfare (MHLW) issued guidelines for the approval of biosimilars in March 2009. All manufacturers of biosimilars are required to support their applications with data from clinical trials, information on the manufacturing methods used and evidence of the product's long-term stability, as well as supporting data from use of the product in other countries.

The MHLW has now approved biosimilar versions of somatropin and erythropoietin. It has also introduced a reimbursement pricing regime specifically for biosimilars. Whereas all generics must be priced at no more than 70% of the price of the original drugs in order to be admitted to the National Health Insurance (NHI) list of reimbursable drugs, biosimilars command a 10% premium on this ceiling – and can thus be priced at up to 77% of the price of the original products.

# Overview of the Indian Biologics Sector

Chapter 3

**The Indian biopharmaceuticals market is currently worth nearly $2 billion a year and growing rapidly. Moreover, approximately 20 companies are already producing biosimilars, and about 50 such products (including imports and multiple brands of the same products) are already available on the domestic market. So India has made a good start.**

## 3.1 THE SIZE AND COMPOSITION OF THE INDIAN BIOLOGICS MARKET

The Indian biologics market consists primarily of vaccines, monoclonal antibodies, recombinant proteins and diagnostics. In the 2009/10 financial year, it was worth $1.9 billion – 62% of the $3 billion generated by the biotechnology industry as a whole (i.e., including bioagricultural and bioindustrial products, bioinformatics and bioservices). The top 15 biopharmaceutical companies accounted for nearly $1.2 billion of this sum (see Table 6).

**Table 6: The Top 15 Biopharmaceutical Companies Operating in the Indian Market**

| Rank in 2010 | Company | 2009-10 Revenues1 ($ millions) | 2008-09 Revenues1 ($ millions) | % Change |
|---|---|---|---|---|
| 1 | Biocon | 257.00 | 198.71 | 29.34 |
| 2 | Serum Institute of India[2] | 185.13 | 242.63 | -23.7 |
| 3 | Panacea Biotec | 153.15 | 130.06 | 17.76 |
| 4 | Reliance Life Sciences[2] | 98.01 | | |
| 5 | Novo Nordisk[2] | 74.49 | 71.87 | 3.64 |
| 6 | Shantha Biotech | 73.00 | 53.80 | 35.32 |
| 7 | Indian Immunologicals | 59.43 | 50.41 | 17.89 |
| 8 | Bharat Biotech | 59.17 | 52.50 | 12.70 |
| 9 | Eli Lilly | 40.73 | 35.72 | 13.85 |
| 10 | Bharat Serums | 38.12 | 30.50 | 25.00 |
| 11 | Hafkine Biopharma | 36.80 | | |
| 12 | Cadila Healthcare | 32.12 | 20.41 | 57.40 |
| 13 | GlaxoSmithKline | 26.86 | 18.18 | 47.75 |
| 14 | Intervet India | 26.48 | | |
| 15 | Intas Biopharma | 25.05 | 19.44 | 28.82 |

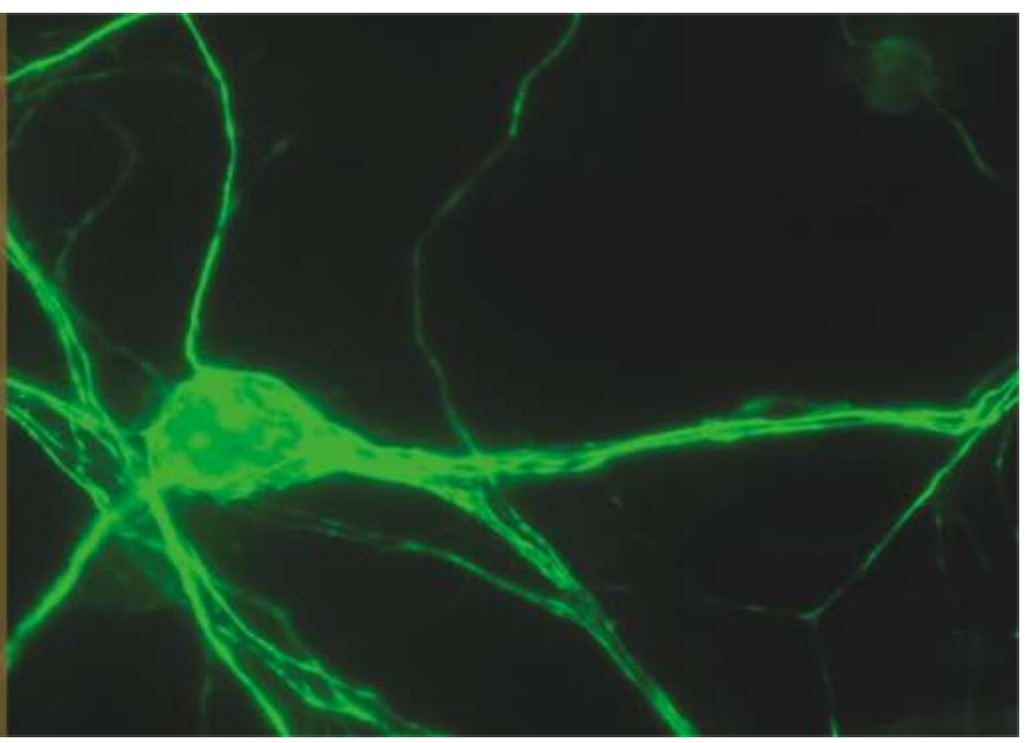
Source: BioSpectrum
Notes: (1) Revenues are for the Indian fiscal year, which runs from 1 April to 31 March; (2) BioSpectrum estimates.

### 3.1.1 Vaccines

The vaccines sector (including human and animal vaccines) represented the largest slice of the pie, with estimated sales of $475 million in 2009/10, up from $436 million the previous year. Human vaccines generated about 80% of this revenue, with domestic sales reaching $218 million and exports reaching $163 million. Sales of human vaccines are forecast to grow by 10-13% a year over the next five years, as better education and awareness about disease prevention, rising disposable incomes and government participation boost demand.

However, the market is clearly shifting from traditional "whole-cell" pertussis vaccines to combination vaccines and "acellular" preparations. Domestic players such as Bharat Biotech and Shantha Biotech (which was bought by Sanofi-Aventis for $783 million in July 2009) have already received massive orders for pentavalent vaccines from the GOI for immunisation programmes in the states of Himachal Pradesh, Kerala, Tamil Nadu, Jammu and Kashmir and Karnataka. Demand for newer products like the pneumococcal conjugate, meningococcal conjugate and human papillomavirus vaccines is also stimulating the paediatric and adolescent segment of the market, while flu vaccines will continue to play a big role in expanding the adult segment. And breakthrough products like Shanchol – the bivalent oral cholera vaccine jointly developed by Shantha Biotech and the International Vaccine Institute – will boost demand in the market as a whole.

**Oncology products are a very profitable line of business for many Indian biopharmaceuticals manufacturers because they address an area of high unmet need and thus command premium prices.**



### 3.1.2 Diagnostics and Targeted Therapeutics

The diagnostics and therapeutics sectors have also expanded in recent years. The diagnostics market is currently worth about $436 million, with molecular diagnostics accounting for sales of about $300 million in 2009/10. The market is growing at 15-20% annually, with revenues split equally between the multinationals – e.g., Roche, Siemens (which has acquired Bayer Diagnostics) and Abbott – and domestic players – e.g., Tulip Group, Transasia Biomedicals, RFCL (Diagnova), Span Diagnostics and Trivitron. Gradual acceptance of the concept of personalised medicine is driving much of this growth.

Meanwhile, the therapeutics sector accounted for 15% of India's biologics market in 2009/10, with cancer therapies clocking up sales of $68 million. Oncology products are a very profitable line of business for many Indian biopharmaceuticals manufacturers because they address an area of high unmet need and thus command premium prices. Uptake of such medicines is also increasing, as domestic producers make less expensive versions than those made by the multinationals and a growing number of Indian patients get medical insurance.

### 3.1.3 Oral Diabetes Drugs and Insulins

The oral diabetes market is currently worth about $338 million, while the insulin (and insulin analogues) market is worth about $133 million. Novo Nordisk dominates the latter, with more than 50% of all sales, followed by Eli Lilly with 22%. However, both markets are growing rapidly, as India becomes the "diabetes capital" of the world. Between 1995 and 2005, the number of patients with diabetes doubled from 20 million to 40 million, and it is projected to increase by another 70 million over the next 25 years. Demand for insulin analogues is growing especially rapidly; the market increased at a compound annual growth rate of 32%, measured in terms of value, in 2007-09. Novel delivery devices will also contribute to the expansion of the market in the future.

### 3.1.4 Biosimilars

About 20 Indian companies are already producing biosimilars. Dr. Reddy's Laboratories, Ranbaxy, Biocon, Shantha Biotech, Reliance Life Sciences, Panacea Biotec and Intas Biopharmaceuticals are among those that lead the way. But several other well-known companies have recently entered the field, including Glenmark, Cipla and Lupin Pharma. In June 2010, for example, Cipla announced that it was spending $65 million on stakes in two biotechnology companies – MabPharm and BioMab, based in India and Hong Kong, respectively – to bolster its presence in the global biosimilars space.

About 50 biosimilars have already reached the Indian market, and they are typically sold at discounts of as much as 85%, putting them within reach of the masses. In 2009/10, domestic sales of erythropoietin rose to $22 million while sales of c-GCSF rose to $11 million, sales of interferons rose to $22 million and sales of streptokinase rose to $15 million. Moreover, demand is likely to grow considerably, as India becomes more affluent. US investment bank Goldman Sachs estimates that the number of Indians with annual incomes of between $6,000 and $30,000 (measured in terms of purchasing power parity) will increase by 250-300 million during the next decade alone.

The global biosimilars market has even more potential for the most efficient Indian biosimilars manufacturers, since the market will be characterised by price competition, even when there are only a very limited number of rival products. That said, the manufacturers of branded products are likely to use second-generation products with more convenient administration schedules as a means of defending their territory. Some of these manufacturers may also try to crowd out the competition by producing their own biosimilars. So the competition is likely to be intense.

# Competitive Analysis

Chapter 4

**India's main national competitors in the biopharmaceutical space include China, Israel, South Korea, Singapore and Taiwan. These countries have initiated a number of infrastructure support and policy initiatives that provide an environment conducive to the growth of strong domestic industries.**

**Big BioPharma is not the only threat to India's biosimilars manufacturers. The industry is still in its infancy; however, a number of emerging economies have been actively building up their biopharmaceutical expertise, and some countries are clearly positioning themselves to capitalise on increasing demand for biosimilars. The following section provides an overview of India's key competitors. (We have treated Central and Eastern Europe, and Latin America collectively.)**

## 4.1 AUSTRALIA

Australia is one of the world's leading established centres of biopharmaceutical expertise (together with the US, Europe and Canada), thanks to a first-class research base and robust patent regime. The country is home to some 450 biotechnology companies and 600 medical technology companies. In March 2010, more than 150 biotechnology and healthcare companies with a combined market capitalisation of $47 billion were listed on the Australian Stock Exchange – by far the biggest being CSL, which specialises in pharmaceuticals, vaccines and plasma products.

### 4.1.1 Government Initiatives

The Australian Government is keen to maintain this lead. It allocated about $7 billion for investment in science and biotechnology in 2009/10, although the two sectors fared less favourably in this year's budget. The Commonwealth Scientific and Industrial Research Organisation (CSIRO) is the national body responsible for promoting scientific research in Australia. It oversees various initiatives, including the Cooperative Research Centres programme, which provides funding and other forms of support for long-term public-private collaborations aimed at commercialising scientific innovations.

In 2009, the federal government also launched "Commercialisation Australia", a new initiative to commercialise Australian research and ideas. The programme offers various forms of help, including up to $43,667 to pay for specialist advice and services; up to $174,670 (payable over two years) to assist with the recruitment of experienced executives; proof-of-concept grants of $43,668 to $218,338 to test the commercial viability of a product, process or service; and repayable early-stage commercialisation grants of $218,338 to $1.7 million to develop a new product, process or service to the stage where it can be taken to market.

Individual states have supplemented these initiatives with their own programmes. Queensland is particularly notable for its efforts; it has invested about $3 billion in the sector, and now has 90 core biotechnology companies employing 1,900 scientists as well as some 66 biopharmaceutical research institutes employing 5,700 researchers. Queensland will also host Australia's first major contract manufacturing facility for biologics, which is due to be completed in 2012.

### 4.1.2. Research Base

Australia has numerous world-class medical research organisations, including the Garvan Institute, Institute for Molecular BioScience, Menzies Research Institute, John Curtin School of Medical Research, and Australian Institute of Bioengineering and Nanotechnology.

### 4.1.3 Regulation

The Australian Therapeutic Goods Administration (TGA) is responsible for approving and regulating the marketing of medicines in Australia. The TGA has adopted the EMA's guidelines for regulating biosimilars.

### 4.1.4 Investment Incentives

The Australian Government offers tax concessions for biotechnology-related R&D. The existing system will be replaced in July 2010 with a new 45% refundable tax credit for companies with an annual turnover of less than $17 million. Companies with a turnover of more than $17 million can claim 40%.

## 4.2 CENTRAL & EASTERN EUROPE

The biotechnology sector in Central and Eastern Europe is smaller and less developed than it is in Western Europe. There are currently about 260 biotechnology companies in the region; 29 are engaged in developing medicines, 55 operate in other areas such as veterinary therapeutics and industrial biotechnology, and the remaining 176 provide biotechnology services like contract research, diagnostics, manufacturing and analytical services.

Hungary, Poland and the Czech Republic lead the way. Hungary has 67 companies engaged in developing human medicines or providing bioservices. Poland has 38 such companies, and the Czech Republic 29. We have therefore focused on these three countries in the details below.

### 4.2.1 Government Initiatives and Investment Incentives

In 2004, the Hungarian Government established a Research and Technology Innovation Fund to support the country's biotechnology efforts. It contributes half the fund's income; the rest comes from Hungary's 26,000 private companies, which are expected to pay at least 0.25% of their turnover into the fund as an "innovation contribution".

In 2005, the Hungarian Government also launched a five-year plan to develop the biotechnology sector, with corporate tax breaks for foreign direct investments and new companies. Tax credits are offered on R&D investments, and R&D corporate tax allowances are generous, particularly if a company locates its laboratory at a university or public research institute. Tailor-made incentive packages are available for biotechnology investments of more than $8 million that result in the creation of at least 10 new jobs, and highly educated students can be employed tax-free in educational and research activities.

The Polish Government likewise provides grants for companies that conduct biopharmaceutical R&D, via the biotechnology division of the State Committee for Scientific Research. Grants typically range from $50,000 to $100,000. And the Czech Government supports biotechnology companies through CzechInvest, its investment and business development agency. CzechInvest has identified nine key areas of investment, including life sciences, medical devices and R&D – with particular emphasis on molecular biology,

biomedicine and biotechnologies, and the development of new materials designed to advance the life sciences.

### 4.2.2 Research Base

Most of the biotechnology-related R&D conducted in Central and Eastern Europe is performed at universities or institutes, and collaboration with industry is limited. Hungary has eight research institutes specialising in biomedical research, including a genetics and immunobiology department at Semmelweis University, Budapest. Poland has about 40 universities, hospitals and research institutes engaged in biotechnology-related R&D, as well as five technology parks. In December 2009, it also set up a new incubator, called Science2Business, to support the commercialisation of scientific discoveries and inventions. The incubator will cover five sectors: biotechnology, telemedicine, renewable energy, informatics and mobile technologies. The Czech Republic has 300 biotechnology institutes and 10 established technology parks and clusters. The government is currently building a new biotechnology park at Masaryk University, in Brno, and an international clinical research centre that it hopes will be able to compete with the top research hubs around the world.

### 4.2.3 Regulation

All the new European Union member states were required to bring their regulatory frameworks into line with the rules prevailing in the rest of the bloc during the accession process. They were also required to harmonise their patent protection laws with those in Western Europe, although full harmonisation will not occur until 2011-2019, depending on the country and product.

### 4.2.4 Access to Capital

There is very little private funding from venture capital sources and angel investors in Hungary, Poland and the Czech Republic. The majority of the funding for biotechnology-related research comes from state or European Union framework programmes and structural funds.

### 4.2.5 Access to Talent

All three countries have a highly educated workforce and labour costs are very much lower than they are in Western Europe. However, Hungary has clearly stated that it does not want to compete on the basis of low wages and is actively trying to woo talented Hungarian scientists working overseas back to their homeland.

## 4.3 CHINA

China's biopharmaceuticals sector is entering what has been called a "golden age", thanks to substantial investment from the central government, which wants to see it become one of the country's leading industries by 2020. A number of Chinese biopharmaceutical enterprises have entered into alliances with global biopharmaceutical research institutions and multinationals, primarily to develop therapeutic vaccines, MAbs and recombinant proteins. The central government is also promoting the development of stronger regulations, better enforcement of the patent protection laws and various other measures to support the industry.

### 4.3.1 Government Initiatives

China expressly stated in its National Medium- and Long-Term Science and Technology Development Plan Outline (2006–2020) that it aims to acquire expertise in various cutting-edge technologies in the biopharmaceutical space over the next 15 years. These include target discovery, drug molecule design, gene operation and protein engineering, stem cell engineering and a new generation of industrial biotechnology tools. The central government also issued a new regulation on the registration of drug technology transfers in August 2009, which should promote technological innovation, while the Chinese National Development and Reform Commission (NDRC) has secured an additional $65 million of funding to support advances in biological medicine, bio-breeding and biomedical engineering.

However, the government has already implemented 19 price-cutting initiatives for medicines and plans to make more cuts in the future. This may affect the country's biopharmaceutical revenue growth, but will benefit Chinese patients – and the overall increase in volume may be sufficient to offset the reduction in per-unit sales.

### 4.3.2 Protection of Intellectual Property

China is making significant efforts to improve the protection of intellectual property rights in compliance with the requirements of the World Trade Organisation. Several multinationals have now established R&D centres in China, indicating that there is growing global confidence in the country's patent-protection regime.

### 4.3.3 Regulatory and Funding Reforms

The Chinese State Food and Drug Administration (SFDA) is introducing new policies to encourage innovation, restrict imitation and encourage biopharmaceutical outsourcing. China is also in the process of establishing an effective venture capital system to attract foreign venture capital into the domestic BioPharma industry.

### 4.3.4 Biotechnology Clusters

China's central and local governments have built more than 100 biotechnology parks. Some of these parks have been very successful – e.g., Shanghai Zhangjiang High-tech Park, which has attracted numerous multinational and domestic companies, including Roche, Novartis Biomedical Research, Kirin Kunpeng Biopharma, Wuxi PharmaTech and Shanghai Lead Discovery. However, many parks still have high vacancy rates.

### 4.3.5 Enterprise Development

A number of Chinese biopharmaceutical companies have joined forces to enhance their overall strength. The biopharmaceutical giant CNBG is one such instance; it was formed by merging six major biological product institutes in Beijing, Shanghai, Changchun, Wuhan, Lanzhou and Chengdu with two biopharmaceuticals manufacturers (Beijing Tiantan and Chengdu Rongsheng). CNBG now employs 10,000 people across China.

### 4.3.6 Increasing Focus on R&D

Chinese biopharmaceutical companies are increasingly aware of the need to invest in R&D. Shenyang Sunshine Pharma, which invests 10% of its revenues in R&D, has developed several successful products, for example, and various other companies are now investing in technology platforms for upstream R&D and clinical studies. China's support bioservices subsector is also expanding rapidly. Several hundred CROs currently operate in China, offering integrated or specialised services, and some of these CROs are evolving from one-off study vendors into viable, strategic long-term players.

### 4.3.7 Greater International Collaboration

A growing number of Chinese nationals who have resided overseas are returning to their home country and taking important positions in the domestic BioPharma industry. They are using their connections to forge powerful international alliances.

## 4.4 ISRAEL

The Israeli biopharmaceuticals sector has grown impressively over the last decade, as a result of its strong track record in research. The country devotes 35% of its research activities to the life sciences and has the largest number of scientists per capita in the world. Its expertise in neurological disorders, cancer and autoimmune diseases is particularly noteworthy, but it is also a global leader in regenerative medicine and cell therapy. Moreover, with a high percentage of graduates in mathematics, physics and computer sciences, it is well placed to make an impact in interdisciplinary technologies such as bioinformatics and proteomics.

### 4.4.1 Government Initiatives

The Israeli Government declared the life sciences industry – and biotechnology in particular – a "preferred sector" in 2005. The Office of the Chief Scientist (OCS) of the Ministry of Industry, Trade and Labour is responsible for administering government policy regarding the support and encouragement of industrial R&D. It operates various support programmes, including grants of up to 50% of the approved budget for market-driven competitive R&D projects, up to 66% for start-up companies and advanced generic technology, and up to 85% for technology incubators. The OCS also participates in bi-national funding initiatives with the US, UK, Australia, Singapore, Canada and Korea; and recently launched a new funding route to bridge the gap between basic and applied research, with grants of up to $95,000.

### 4.4.2 Research Base

Biopharmaceutical research is carried out at seven universities, five colleges and 10 specialised institutes as well as the major hospitals. The leading universities also have commercial offices of technology transfer to facilitate the commercialisation of their research.

### 4.4.3 Technology Incubators

Israel has 23 high-technology incubators, one of which is dedicated to biotechnology and two to industry-related technologies. Each incubator houses up to 15 companies and provides funding of about $500,000 per company for the first two or three years of its life,

when the risk is highest and private funding is scarce. An estimated 1,000 high-tech companies have "graduated" so far, but a report submitted to the Knesset finance subcommittee for promoting and assisting high-tech technology suggests that the success rate has fallen in recent years. Between July 2006 and June 2009, only 100 companies managed to raise $500,000 or more. The subcommittee has now convened to consider a number of options, including extending the incubation period.

### 4.4.4 Regulation

Israel has aligned its regulatory framework with those in the US and European Union, and medications approved by the FDA or EMA are approved much more quickly than those that have not received such approval. The Israeli Ministry of Health and FDA have also signed a mutual recognition agreement to enable full acceptance and recognition by the FDA of clinical trials conducted in Israel for new drugs and medical devices. Israel's IP laws concerning technology-based products and services, pharmaceuticals and other emerging sectors likewise closely resemble those of the US and European Union.

### 4.4.5 Investment Incentives

The Israel Investment Centre (IIC) of the Ministry of Industry and Trade offers companies in knowledge-based industries and their investors various tax incentives and grants. Investors may apply for one of two incentives: government participation of up to 32% in capital investments for creating jobs in export industries; or accelerated depreciation and a tax holiday of up to 10 years on undistributed profits, based on the capital that has been committed to job creation in export industries. (The precise amount of the benefit depends on the location.)

### 4.4.6 Access to Capital

Israel has a robust financial infrastructure and well-developed venture capital industry. However, fledgling biopharmaceutical companies have had a hard time raising capital following the global downturn in the capital markets last year. In the first quarter of 2010, Israeli high-tech companies raised only $234 million from venture investors (both local and foreign), less than in any preceding quarter for the past five years. The life sciences sector attracted over a third of this money, but much of it was directed towards more developed businesses.

The Knesset finance subcommittee for promoting and assisting high-tech technology is now reviewing a number of proposals for supporting the sector. They include creating a private fund with state leveraging, offering incentives for venture capital investment in seed companies and establishing "second-stage incubators" to promote "industrialisation".

## 4.5 LATIN AMERICA

Latin America's biotechnology industry is growing at an impressive rate. Bioagricultural and bioindustrial applications (biofuels) account for most of this growth, but the BioPharma sector is also getting stronger. The most active countries in the region are Argentina, Brazil and Chile. Brazil has more than 100 biopharmaceutical companies, while Argentina and Chile have about 23 and 15 such companies, respectively. All three countries have also become centres for clinical research. In 2009, there were more than 425 trials in Chile alone.

### 4.5.1 Government Initiatives

The Argentinian Government has implemented several programmes to promote basic research and technological investment. In 2007, it also established a Ministry of Science and Technology specifically to encourage scientific and technological innovation. The Ministry administers two government-backed funds: the Fund for Scientific and Technological Research and the Argentine Technology Fund.

Brazil introduced a national biotechnology policy in the same year, and undertook to invest $5.8 billion over a 10-year period, with approximately 60% of the funds coming from public sources. Chile has likewise taken significant steps to incorporate biotechnology into its economy. The National Innovation Board for Competitiveness, which reports to the President, is responsible for coordinating the efforts of the government agencies concerned. These include the Chilean National Commission for Scientific and Technological Research (CONICYT), which supports basic research and the development of resources, principally by financing academic research and collaborations between universities and private firms; and the Chilean Economic Development Agency (CORFO), which promotes the commercialisation of new technologies and products.

### 4.5.2 Research Base

Argentina has more researchers per active person than any other country in Latin America, and over 115 Argentinian research institutes and universities are engaged in biotechnology-related research. But most of this work is in the field of bioagriculture. Brazil, by contrast, has a strong reputation in fundamental biopharmaceutical research, although it has been less successful in commercialising that research. It can call on several strong public research institutions specialising in health biotechnology, including the Oswaldo Cruz Foundation in Rio de Janeiro and the Institute Butantan in SãoPaulo.

Meanwhile, Chile has 61 university research centres, 15 incubators and 10 technology transfer centres. It is also building a number of research nuclei as part of its Millennium Scientific Initiative, which has been partly funded by the World Bank. Five such nuclei have now been established, including the Millennium Institute for Advanced Studies in Cell Biology and Biotechnology, the Center for Scientific Studies and the Millennium Institute for Fundamental and Applied Biology. Again, however, human health accounts for a relatively small percentage of the country's biotechnology activities.

### 4.5.3 Regulation

Most Latin American countries (including Argentina, Brazil and Chile) have now aligned their local regulations with the Declaration of Helsinki, Council for International Organisations of Medical Sciences, and International Conference on Harmonisation-Good Clinical Practice (ICH-GCP) guidelines, and all have a regulatory agency responsible for pharmaceuticals, medical devices and clinical research. But there are still significant differences in the level of regulatory sophistication in the region.

### 4.5.4 Intellectual Property Protection

Argentina, Brazil and Chile are all signatories to the Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS). But although Chile scores highly for its enforcement of the rules on patent protection, Argentina and Brazil fare less well. The International Property Rights Index (2010) awards the latter two countries scores of 64 and 84, respectively (significantly below India's score of 53).

### 4.5.5 Investment Incentives

Argentina offers various incentives for biotechnology-related research under Law 26,270, including accelerated amortisation of income tax, early reimbursement of value-added tax (VAT) and tax credit bonds for services purchased from government-owned research institutes. Brazil has also enacted an "Innovation Law", which provides tax incentives for R&D, deductions on expenses related to patent filing and prosecution, and partial payment of the salaries of R&D scientists employed by biotechnology companies. Chile has adopted a similar approach, with tax incentives for R&D, subsidies of up to $30,000 to finance internships and subsidies of up to $730,000 to support innovation in the areas of goods, services, processes and organisational or trading methods.

### 4.5.6 Access to Capital

Latin America's venture capital industry is still undeveloped. However, experts anticipate that it will grow rapidly in Brazil and Chile (though not in Argentina) over the next few years. Brazil is one of the emerging countries with the greatest appeal for the investment community, thanks to the good economic management of successive democratic governments, the size of its domestic market, the strength of its industrial sector and the significant tax incentives available to venture investors. Chile also has a relatively strong economy, based on commodity production, and a dynamic, modern entrepreneurial class.

## 4.6 SINGAPORE

Singapore is well-known for being politically stable and business-friendly. It offers clear and consistent government guidelines, a reliable patent regime, a first-rate physical infrastructure and a favourable tax environment; indeed, in 2009, the World Bank dubbed it the world's "easiest place in which to do business". The city-state has also created a powerful biopharmaceutical nexus. More than 30 multinationals have established regional headquarters there, and Novartis chose Singapore as the home for its prestigious Institute for Tropical Diseases.

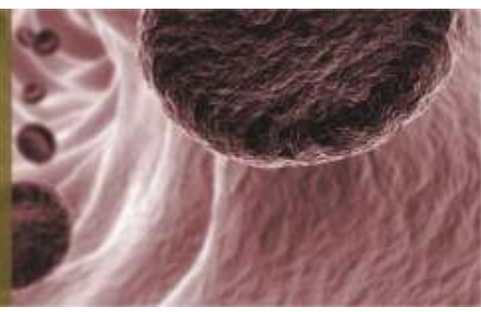
### 4.6.1 Government Initiatives

In the late 1990s, Singapore identified the biomedical sciences as an area with tremendous growth potential. Between 2000 and 2005, it put in place the key building blocks to establish a core biomedical research base. In the second phase of the initiative (2006-2010), it has been focusing on strengthening its capabilities in translational and clinical research. It has put serious money into these efforts, with a commitment of $9.8 billion for the four years ending December 2010.

### 4.6.2 Research Base

Singapore has established a strong scientific foundation with seven research institutes and five research consortia covering clinical sciences, genomics, bioengineering, molecular/cell biology, medical biology, bioimaging and immunology. It has also made significant progress in translational and clinical research; dedicated Investigational Medicine Units, many of them co-located with institutes of higher learning, conduct early-phase trials in public hospitals, while the Singapore Clinical Research Institute focuses on later-stage trials.

**Singapore's Health Sciences Authority (HSA) is actively involved in defining new regulatory frameworks and pursuing new areas of research in regulatory science.**



### 4.6.3 Biotechnology Clusters

Singapore has built a major biomedical research hub that co-locates public-sector institutes and private-sector corporate laboratories. It is currently expanding the Biopolis (as the hub is known), with a 460,000 square-feet expansion that will bring its total research space to more than three million square feet.

### 4.6.4 Regulation

Singapore's Health Sciences Authority (HSA) is actively involved in defining new regulatory frameworks and pursuing new areas of research in regulatory science. The HSA has forged strong links with many of the world's leading regulatory agencies. In October 2009, Singapore was also accepted into the OECD's Mutual Acceptance of Data framework, which means that data from GLP-compliant pre-clinical trials conducted in Singapore can be accepted by 30 OECD and non-OECD members, including the US, EU and Japan.

### 4.6.5 Manufacturing Expertise

Singapore has a strong track record in both small-molecule active pharmaceutical ingredient and secondary manufacturing. It is also building a substantial biologics manufacturing base. Baxter, GlaxoSmithKline Biologicals and Roche have already opened biologics manufacturing plants in Tuas Biomedical Park, and Lonza is currently constructing a cell therapy manufacturing plant which should be operational in 2011.

### 4.6.6 Access to Talent

Singapore has worked hard to develop its expertise in the biosciences. Some 4,000 researchers are now engaged in biopharmaceutical R&D, including about 1,200 foreign nationals. In 2001, Singapore's Agency for Science, Research and Technology (A*STAR) also launched a national scholarship programme to fund the education of 1,000 postgraduate students at the world's top universities. To date, the agency has awarded more than 500 biomedical sciences scholarships, and more than 100 recipients have returned to work in the city-state after completing their PhDs. A*STAR has likewise introduced various awards to attract bright young researchers and develop a cadre of local clinician scientists.

## 4.7 SOUTH KOREA

In the late 1990s, the South Korean Government launched a programme to make the country one of the top biotechnology powers by 2010. South Korea's life sciences industry is now the fourth largest in Asia. But the government is not resting on its laurels; in 2006, it announced a new initiative called "BioVision 2016" to invest another $14.3 billion in the industry, with the aim of turning it into a $60-billion market over the next 10 years.

### 4.7.1 Government Initiatives

In 2008, the government spent some $930 million supporting biotechnology research and commercialisation, as part of its BioVision 2016 programme. It had three key objectives: strengthening the scientific infrastructure to emphasise bioinformatics, nanobiotechnology and synthetic biology; fostering the globalisation of the biotechnology industry; and creating biotechnology clusters.

### 4.7.2 Regulation

The Korean Food and Drug Administration (KFDA) has established a clear regulatory approval pathway for biosimilars, with an amendment to the "Rules Governing the Approval and Examination of Biological Products" (effective as of July 15, 2009), which establishes the definition of a biosimilar, and the publication of guidelines for the evaluation of biosimilars on July 27, 2009.

### 4.7.3 Research Base

South Korea is still at the forefront of stem cell research, despite the setback that occurred in 2006 when one of the country's leading researchers was charged with using fraudulent data. It also aims to become a global leader in biosimilars. In July 2009, shortly after the regulatory pathway for biosimilars was established, South Korean electronics giant Samsung announced that it would invest $389 million in biosimilars over the next five years. Other significant developments include the successful completion of a South Korean clinical trial of a biosimilar version of Enbrel produced by Taiwanese drug development company Mycenax Biotech, and an agreement between US-based Hospira and Celltrion to develop and market eight biosimilars.

### 4.7.4 Biotechnology Clusters

South Korea is currently investing about $5 billion in the construction of two high-tech medical-industrial centres. The bigger of the two – the Osong Bio-Health Science Technopolis, based in Cheongju (about 60 miles south of Seoul) – is scheduled for completion in 2012. It will house the Korean Food and Drug Administration (KFDA), Korean National Institute of Health, Korea Centers for Disease Control and Prevention, and various other government bodies as well as private companies.

### 4.7.5 Clinical Trials Expertise

South Korea has earned a solid reputation as a place in which to perform clinical trials. It has highly trained physicians and a good IT infrastructure, as well as plenty of urban hospitals (which make it easy to recruit trial patients).

### 4.7.6 Investment Incentives

The South Korean Government offers foreign investors in high-tech companies a wide range of tax incentives, including tax credits on corporate and personal income tax, acquisition tax, registration tax, property tax and aggregate land tax. It also operates a number of free trade zones and free economic zones.

## 4.8 TAIWAN

The Taiwanese Government formulated a "Promotion Plan for the Biotechnology Industry" in 1995, under which it enacted various laws and regulations relating to biotechnology; and encouraged the private sector to invest in R&D, technology transfer, and the training and development of personnel. It has stepped up these efforts during the past decade, and a growing number of businesses are now focusing on the sector.


### 4.8.1 Government Initiatives

Between 2000 and 2008, the Executive Yuan's National Development Fund invested $394 million in the biotechnology industry. Then, in March 2009, the Executive Yuan launched the Taiwan Biotechnology Takeoff Package, aimed at boosting the sector and capturing a share of the global market. This package comprises four key elements: strengthening the country's translational research and commercialisation skills; establishing a biotechnology venture capital fund; founding a Food and Drug Administration; and creating an integrated biotech incubation centre.

### 4.8.2 Biotechnology Clusters

Taiwan is establishing a number of large science parks focusing on biopharmaceutical research and manufacturing. It aims to build two clusters: one in the Southern Taiwan Science Park (STSP) and the other in northern Taiwan's Hsinchu Biomedical Science Park (HBSP). The STSP is already open for business, with nearly 20 biopharmaceutical companies focusing on vaccines, bioagriculture, biomedical inspection and floriculture, as well as companies that manufacture medical equipment and devices. Construction of the HBSP started in October 2009 and, once the park is complete, it is expected to host about 30 biopharmaceutical manufacturers.

The government also plans to create an integrated incubation centre in a third park, to be called the National Biotechnology Development Park, in the Nangang District of Taipei City. This will contain an incubation centre, animal testing centre, biopharmaceutical R&D service centre and legal information centre.

### 4.8.3 Regulation

The Taiwanese Department of Health established a new Food and Drug Administration in January 2010 to improve the oversight of food and medicines, and link the standards of the local BioPharma industry more closely with those of the international market. Taiwan also set up an Intellectual Property Office in 1999, but it has relatively little experience in this area.

### 4.8.4 Investment Incentives

Companies in the biomedical and special chemical industries sectors meeting the criteria of the Incentive Programme for the Manufacturing and Technical Service Aspects of Major Emerging Strategic Industries may choose to take advantage of a five-year tax holiday or shareholder investment credit. The Taiwanese government has also established a series of tax breaks and other incentives to encourage local and overseas biopharmaceutical entities to invest in Taiwan. These include tax breaks for expenditure on R&D, training and automation, and energy-saving equipment; corporate and personal tax credits for investors in companies in newly emerging strategic industries; import tax exemptions for imported machinery and equipment; and tax exemptions for certain kinds of income, where a company sets up its headquarters in Taiwan.

### 4.8.5 Access to Capital

The government plans to create a $1.9 billion biotechnology venture capital fund to attract private capital to the sector and give financial assistance to start-ups. The Executive Yuan's National Development Fund will contribute 40% of the funding, with the remaining 60% to come from private investors.

### 4.8.6 Access to Talent

Various Taiwanese universities have established life sciences departments to cultivate the highly educated professionals the BioPharma industry needs. The Academia Sinica (Taiwan's foremost research institute), National Health Research Institutes, Industrial Technology Research Institute, Development Centre for Biotechnology and other related organisations also provide training. The number of university graduates with degrees in the biopharmaceutical and biotechnological sciences has risen accordingly; it was 53,283 in 2008, with 12,660 having obtained masters or Ph.D. degrees. However, the country is still very short of trained personnel, particularly those with international experience.

# Key Recommendations for the Medium Term (2015)

Chapter 5

**If India's biopharmaceutical players are to compete effectively on the global stage and capture a significant share of the biopharmaceuticals market, they will need to make a substantial investment in building new manufacturing capacity. However, the GOI will also need to play its part by providing the necessary enabling environment.**

**India already has a strong pharmaceutical manufacturing base. It is thus well positioned to capitalise on the opportunities arising from the "patent cliff" and growing demand for biosimilars. But the domestic market will remain relatively small in the near term, so India's efforts should be directed towards becoming a global manufacturing hub.**

**If India is to capture 10% of the global biosimilars market by 2020 – the goal for which we believe it should aim – the private sector will have to invest a considerable amount of capital in building the necessary manufacturing capacity and skills base. The GOI will also need to provide the environment required to enable that expansion. This chapter covers the infrastructure improvements, fiscal incentives, regulatory changes and policy initiatives that we believe will be crucial. We estimate that they will require an investment of at least $1 billion over the next five years. We have divided our recommendations into six sections: R&D; manufacturing and commercialisation; human capital; the regulatory framework; innovation; and intellectual property.**

## 5.1 RESEARCH & DEVELOPMENT

### 5.1.1 Build Protein Characterisation Laboratories and GLP-Certified Animal Study Facilities

Foreign regulators require evidence that the product development process has been performed to the applicable standards as part of the regulatory submission. The product development process includes both the method of manufacture and high-end bioanalytical product characterisation to verify that the method being used delivers a product that is consistently comparable in quality to the original drug. The product that is manufactured through such a "validated" process must then be tested in a "GLP-certified" animal laboratory and the data from these tests must be submitted, together with data on the process and analytical characterisation of the product, to the regulator for permission to conduct a clinical trial.

India currently has very few GLP-certified animal laboratories and only one GLP-certified protein characterisation laboratory at the National Centre for Biological Sciences (NCBS) in Bengaluru. The industry needs at least four more such laboratories, all of which will have to be GLP-certified. The GOI should therefore fund the construction of the necessary facilities in national scientific institutions and laboratories as well as in CROs. This would not only support two of the most crucial stages in the biopharmaceutical product development cycle, it would also help to promote collaboration between academia and industry.

In addition, the GOI should offer duty waivers or other incentives to encourage existing service providers to branch into biologics development, using the Research-as-a-Service (RaaS) model – which would, in turn, attract multinationals wanting to outsource such activities and improve revenue generation. India's public institutions are not equipped to provide such services because they do not have sufficient understanding of the regulatory requirements.

### 5.1.2 Create a National Animal Breeding Facility

India needs a "National Animal Breeding Facility" to produce high-quality animals for pre-clinical studies and to generate certified data that meet international standards and scrutiny. The Chinese Government has set up two dozen primate breeding facilities, but many Indian firms are currently breeding their own animals. In January 2010, the GOI announced plans to establish a large centre to breed dogs and monkeys for use in clinical research, and the Department of Pharmaceuticals has invited expressions of interest from both public and private institutions with relevant biomedical expertise. However, at least one rodent facility and two large-animal facilities are required to develop MAbs and biosimilars, and it takes at least two years to build a rodent facility, so the GOI should start creating this infrastructure immediately.

It should also set up quarantine centres for imported animals at the places where they are imported and make provision for inspecting these facilities properly. The Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), acting under the aegis of the Department of Forestry, currently controls all animal facilities, including registrations. But it lacks the expertise to conduct proper scientific inspections and is under-staffed. The GOI should therefore equip the CPCSEA to match international standards.

### 5.1.3 Expand Viral Testing Facilities

India does not have enough facilities for testing and evaluating the viral safety of biologics derived from characterised cell lines of human or animal origin, in compliance with International Conference on Harmonisation guidance ICH Q5A (R1). The GOI should therefore support the construction of more such facilities. The Indian regulatory agencies should likewise start requiring viral clearance as a pre-condition for approval of all domestic biomanufacturing plants.

### 5.1.4 Provide Financial Assistance for Ensuring Compliance with Global Standards

All facilities for characterising proteins, breeding animals, conducting animal studies and performing viral testing will need to operate to international standards. So the GOI should also provide financial assistance with the cost of hiring consultants to advise on the global regulations.

### 5.1.5 Promote the Development of Pre-clinical Service Providers

Very few centres for offering services such as outside toxicology and bioanalysis currently exist – and they are too few to cater for the increasing number of early drug candidates being developed by companies that want to outsource these activities. One senior industry analyst estimates that the market for toxicology and bioanalytical services is worth about $12 billion, and that only 15% is outsourced. The GOI should thus provide soft loans to help pre-clinical service providers establish such facilities, as well as ensuring that subsidised infrastructure support is available.

### 5.1.6 Provide Practical Support for Clinical Trials

Any Indian biosimilars company that wants to sell a biosimilar in a regulated market will be required to conduct clinical trials of that biosimilar against the reference product in the country concerned. This represents a major financial risk, so the GOI should provide assistance in engaging consultants to design and execute world-class trials.

### 5.1.7 Simplify the Procedures for Importing and Exporting Biologics

The procedures for importing comparator drugs, test materials, Genetically Modified Organisms (GMOs) and Living Modified Organisms (LMOs) into India for research purposes, and for exporting biologics out of India, for clinical studies in other countries, are currently very cumbersome. India also lacks cold storage facilities (and most biologics are heat-sensitive).

The GOI should therefore simplify the process for importing biological samples and participate in negotiating government-to-government treaties for handling biologics (which would make it easier to export biosimilars that are manufactured in India). In addition, it should encourage the construction of cold storage throughout the supply chain and mandate faster clearance times at Customs to avoid loss of material in transit.

## 5.2 MANUFACTURING & COMMERCIALISATION

The domestic market is too small to sustain a significant amount of manufacturing capacity by itself, and most Indian biopharmaceutical companies are not yet ready to launch their products in developed countries with highly regulated markets. So the best way for India to become a manufacturing hub is to encourage multinationals to set up manufacturing facilities here, both by building the necessary physical infrastructure and by providing a commercially attractive environment.

Various kinds of infrastructure are essential to support the manufacturing of biologics. They include an uninterrupted power supply (since power failures can result in the contamination or death of the production organism or other process deviations); potable water to maintain sterility and yields; common effluent treatment plants so that individual sites need only invest in primary treatment (rather than zero discharge); and good road and rail freight links, especially in semi-urban and rural areas.

### 5.2.1 Create a Single-Window System for Approvals and Clearances

A biopharmaceutical company that wants to establish a manufacturing site in India must secure various approvals and clearances governing land use, access to power and potable water, and so forth. Different local state authorities may administer these regulations, and different states may have different tariff structures. The GOI should ensure that the format, content and interpretation of all such regulations is common throughout the country and introduce a single-window system for securing all clearance and approvals from the various central and state agencies.

### 5.2.2 Introduce Flexible Pollution Controls

Under the current rules for controlling pollution, a biopharmaceutical manufacturer must secure approval from the local pollution control board whenever it changes its product mix or yield, even if there is no net increase in the total amount of effluent. However, biopharmaceutical products typically generate easily biodegradable, aqueous effluents. The regulations should therefore be revised to allow for flexibility in terms of changes in product mix, especially when those products use the same process flows and generate the same amount of effluent.

### 5.2.3 Invest in Better Transport Links and Cold-Chain Facilities

The GOI should also invest in constructing more roads and ports, especially in areas of intensive biopharmaceutical manufacturing such as Mumbai, Pune, Goa, Hyderabad and

Bengaluru, and in creating a distribution network for the temperature-controlled transportation of biologics throughout the supply chain. At present, only a few airports like Chhatrapati Shivaji International Airport in Mumbai and Bengaluru Airport have temperature-controlled areas, and Indian pharmacies frequently suffer from power cuts or shortages.

### 5.2.4 Provide Fiscal Incentives

Any biologics manufacturer planning to enter the highly regulated markets must have a plant that is capable of meeting foreign regulatory standards, but such factories are much more expensive than normal chemical plants. The GOI should therefore endeavour to attract such companies (as well as manufacturers of ancillary products like Heating, Ventilating and Air Conditioning (HVAC) systems, Water For Injection (WFI) systems, sterilisers, process tanks and purification systems) by providing investment incentives, either on a standalone basis or through dedicated special economic zones and industrial parks. This would help to build India's future manufacturing capacity.


However, financing is not the only challenge for companies investing in more expensive manufacturing facilities to match Western expectations. The additional expenditure means that it is more difficult for such organisations to compete in cost-conscious markets like India and other emerging countries. So the GOI should consider extending the weighted tax deduction of 200% on expenses incurred for in-house R&D to cover expenses incurred from outsourcing to CROs. It should also expand the definition of R&D expenditure to include incidental costs, whether incurred in India or elsewhere (e.g., consultancy fees for patents and product registrations in foreign countries).

In addition, it should permit accelerated depreciation on capital expenditure incurred in constructing R&D laboratories or manufacturing facilities that are either accredited by international certification agencies or approved by foreign regulators like the FDA and EMA. It should also re-set the clock on tax holidays, so that they start at the point when a company moves into profit (as is the case in Malaysia, for example), rather than at the date of commissioning; favour companies that make a material investment in the Indian BioPharma industry (be they indigenous or foreign-owned) in government tenders; and reduce import duties on high-end equipment purchased from international manufacturers to encourage the creation of state-of-the-art bioanalytical facilities.

## 5.3 HUMAN CAPITAL

India's BioPharma industry faces several workforce challenges, including a shortage of skilled job candidates and difficulties in retaining employees who possess the right skills because there are too few opportunities for growth. More and better-educated graduates and postgraduates, and better training programmes, are essential to overcome these problems – and both will require closer collaboration between academia, the industry and government.

### 5.3.1 Expand India's Capability in Toxicity Studies

India's strength in toxicological studies is limited; it needs to create a pool of some 1,000 well trained toxicologists. The GOI should therefore borrow from best practice elsewhere and set up training institutes in toxicity studies. (We estimate that the cost of training 100 people per year at CRO sites would be about $500,000 annually.)

### 5.3.2 Foster a Trilateral Relationship between Industry, Academia and Government

Collaboration between the industry, academia and government has recently improved, but more work is required to create clear lines of communication and coordinate the sharing of resources, thereby reducing the duplication of expenditure and effort. Stakeholders from all three sectors should meet regularly to keep each other informed about their activities in this regard. The GOI should also help Indian companies form partnerships with foreign universities.

### 5.3.3 Improve and Expand the Workforce Development Pipeline

India's universities should offer interdisciplinary undergraduate programmes covering the physical sciences, information sciences, translational research and other related subjects, as well as a core specialisation, since many of the new skills required to be innovative combine two or more disciplines (e.g., bioinformatics). They should also involve the industry in designing these programmes; place greater emphasis on laboratory skills, problem-solving skills and independent learning; and provide more tutoring and mentoring. The GOI can play a key role here by providing organisations like the National Institute of Pharmaceutical Education and Research (NIPER) with modern equipment. Meanwhile, the industry itself should support academia's efforts by providing internships to give students hands-on experience and prepare them more effectively for work life.

### 5.3.4 Establish Exchange Programmes, "Finishing Schools" and Scholarships

The GOI should establish exchange programmes with foreign training institutes and professional bodies [like International Society for Pharmacoepidemiology (ISPE) and Drug Information Association (DIA)] for local graduates. It should also create "finishing schools" to impart industry-specific skills – e.g., vocational training in biopharmaceutical plant operations, quality control and cGMP regulations – and devise an accreditation programme for the purposes of quality control, drawing on the industry for guidance. In addition, it should set up scholarships for new recruits to help defray in-house training costs, and absorb half their salary costs during the training period.

### 5.3.5 Increase Public Awareness about Career Opportunities in the Industry

Academia and the industry should collaborate to increase public awareness about the industry and the career opportunities it offers by holding careers fairs and job fairs, and creating and distributing literature on these opportunities – e.g., brochures, fact sheets and newsletters.

### 5.3.6 Provide More Training for Existing Employees

The industry is rapidly evolving, with the result that employees must constantly maintain and update their expertise. Training programmes should therefore be developed so that employees can acquire and strengthen the technical and soft skills they need to advance. Tax relief should also be provided on all expenditure on training made by biosimilars manufacturers.

## 5.4 THE REGULATORY FRAMEWORK

India is becoming an increasingly attractive place in which to conduct clinical trials, thanks to its large patient population, well-trained investigators and relatively low costs. It is also building a regulatory regime based on the International Conference on Harmonisation guidelines for GCP. However, before making any changes in policy, it is important to evaluate the lacunae in the existing policies. Very often, it is not a particular policy that is deficient but, rather, its implementation and enforcement. Patent law reforms and regulatory reforms both require knowledgeable people to implement or enforce them, for example. Hence the importance of building both capability and capacity in the various regulatory agencies.


### 5.4.1 Simplify the Procedure for Approving Biologics

The Drug Controller General of India (DCGI) and Central and State Drugs Control departments like the Central Drugs Standard Control Organisation (CDSCO) and Drug Regulatory Authorities (DRAs) are responsible for regulating most aspects of most biopharmaceuticals. However, in certain cases – e.g., where a product is developed or manufactured using recombinant-DNA technology – the approval of various other agencies or committees is essential. These include the Genetic Engineering Approval Council (GEAC), Recombinant DNA Advisory Committee (RDAC), Review Committee on Genetic Manipulation (RCGM), Institutional Biosafety Committee (IBSC) and many more such committees, at the state and district levels.

The approvals procedure is also very cumbersome. In most countries, a single central body is responsible for reviewing the data from animal studies and granting permission to start clinical trials. In India, by contrast, the IBSC reviews the data before forwarding it to the RCGM for additional reviewing and approval. The GOI should therefore review and rationalise the roles and responsibilities of the IBSC, RCGM and DCGI in order to streamline and simplify the approvals procedure.

### 5.4.2 Create an Independent Inspection Facility

The GOI should establish an independent inspection facility to audit the manufacturing and containment facilities of all companies involved in the production of recombinant drugs. This would help to ensure that Indian rDNA products are acceptable in the global marketplace. Establishing strong agencies for providing GLP and GCP accreditation, and monitoring compliance with the rules would likewise help to create a reliable network of service providers, which would in turn help to lower costs and attract foreign investment in domestic product development and manufacturing facilities.

### 5.4.3 Modify the Regulations on Process Validation

Under the current system, process validation batches must often be supplied prior to (or during) the clinical development phase. Large-scale batches are also needed to supply representative samples for clinical trials and export registration. These large-scale production lots are taken prior to receipt of a local manufacturing licence, which is issued only once a drug has been approved. However, biopharmaceutical products have long manufacturing cycle times. The regulations should therefore be changed to permit the use of product from validated batches for commercial launch in India after receipt of the manufacturing license, provided that the product is within its established shelf life. This would reduce development costs and time-to-market, and make the products more affordable.

## 5.5 INNOVATION

For every dollar India invests in innovation, China invests as much as 10 times that amount. The Chinese public sector also plays a key role in biopharmaceutical innovation, whereas, in India, the burden falls almost exclusively on the private sector. If India is to compete with China and other such emerging economies, and attract investment from the multinationals, it must adopt a much more proactive stance.

### 5.5.1 Provide Seed Funding for Innovation

The GOI should invest more money in setting up "venture" funds specifically to support all companies that create innovation in India, be they foreign-owned or locally owned. It should also encourage more innovation by providing seed funding to help indigenous biopharmaceutical companies license new technologies and intellectual property from other countries and build on them. Such funding could take the form of mixed grants and loans, with repayment of the loan element contingent on success.

The existing funding programmes provide support for companies that have products in the later stages of development, but there is a crippling paucity of risk capital for early-stage innovation. Moreover, assuming that such innovation will only be performed at academic institutes is too restrictive an approach. Start-up biotechnology companies can be effectively groomed to conduct directed research that yields useful insights into disease biology and novel targets with validation screens, but this does require substantive grant support from government funding agencies.

### 5.5.2 Construct Biotechnology Clusters

Setting up biotechnology clusters would also help to improve the sector's productivity and competitiveness by leveraging the synergies of common areas of research and technology, supporting industries and human capital. Clusters foster innovation through increased ease of experimentation with new activities and asset configurations, and facilitate the commercialisation of research by increasing the visibility of opportunities.

India will probably need about five biotechnology clusters, each containing a molecular sciences facility, analytical laboratories, pilot production facilities and laboratories for pre-clinical work and nanotechnology research.

### 5.5.3 Promote Translational Research

The GOI should create incentives for academic institutions and companies working on translational research, and allocate funding for providing grants to encourage further work in this field.

### 5.5.4 Provide Financial Support in Specific Areas of Innovation

The GOI should provide grants or soft loans for expenditure incurred in filing patents in foreign countries.

## 5.6 INTELLECTUAL PROPERTY

India has made genuine efforts to develop an intellectual property rights regime that meets international criteria. It has adopted an approach which aims to balance the need for a regime that encourages investment in scientific and technological innovation with the performance of its social responsibilities, including the protection of public health, biodiversity and traditional knowledge. The creation of a clear framework is particularly important for the BioPharma industry, since lack of clarity often results in wasteful litigation.

### 5.6.1 Protect Innovation

The GOI has implemented various measures to ensure that India complies with the TRIPS Agreement. However, from an international perspective, further improvements are needed. These include resolution of the legal situation regarding data exclusivity (i.e., whether data submitted to the regulatory authorities for testing for approval should be protected); and government-funded training to strengthen the Indian Patent Office.
Addressing these issues would encourage the manufacturers of branded products to shift some of their production to India. A number of companies have already set up secondary manufacturing operations outside their home countries. Ireland and Singapore have already become global manufacturing hubs, for example, and India should aim to do likewise.

### 5.6.2 Approve the Bill Liberalising the Commercialisation of Intellectual Property generated in State-Funded Institutions

A revised draft law on the intellectual property rights of state-funded institutions was re-submitted to parliament for discussion in June 2010. The revised bill introduces relaxed norms for patenting inventions and also gives the GOI more control over the non-exclusive licensing of the intellectual property to third parties, if this is deemed to be in the public interest.

The bill – which was originally introduced as the "Indian Bayh-Dole Act" in 2008 – has gone through considerable changes during the consultation process. However, it is hoped that the bill will have the same effect as the original Bayh-Dole Act did in the US, in encouraging investigators and institutions to commercialise the intellectual property generated from state-funded research with direct financial benefits flowing to both parties. Biotechnology research often emanates from the laboratories of such state-funded institutions in India, so the lowering of the legal barriers to the commercialisation of that research can only be good. It would be particularly useful if the Department of Pharmaceuticals and the Department of Biotechnology could launch awareness programmes alerting the technology transfer officers of state-funded institutions to the new statute, once it is passed, so that they can advise their researchers on the resulting opportunities.

# Key Recommendations for the Longer Term (2020)

Chapter 6

**India will not only need to build a robust biopharmaceutical infrastructure, it will also need to become a source of innovation. There are at least five initiatives the GOI could implement to help the domestic BioPharma industry leverage its unique advantages.**

**We have made a number of suggestions for strengthening India's biopharmaceutical resources over the next five years. But will these be sufficient to help the country realise its aspirations? We believe not. If India is indeed to become the world's leading provider of affordable biopharmaceutical products by 2020, it cannot simply count on biosimilars and vaccines; it must also become a source of innovation. More specifically, it should aim to have at least 10 original biologics on the local market and at least two on the global market by 2020.**

**In other words, India cannot simply learn to play the game better; it must also change the game. We have identified five longer-term initiatives that we think would help it to do this – and we recommend that the GOI make an additional $1 billion available over the next 10 years to provide for them.**

## 6.1 CREATE A FRAMEWORK FOR INTELLIGENT REGULATION

India should be bold and create a completely new framework for regulating biopharmaceutical products. The current regulations do not meet the standards of many foreign regulatory authorities – and the obvious answer would be to harmonise them with the regulations in the US or other developed countries. However, history has played a large part in shaping those regulations and it is sometimes difficult to put history aside, even when conditions have changed dramatically. The current paradigm of clinical development, with its reliance on double-blinded, randomised control tests, is one such instance. It was devised in the wake of the Thalidomide tragedy but has altered very little since then, despite the fact that it is inefficient and, arguably, unethical (in its use of placebos).

Two changes, in particular, will have a major bearing on how biopharmaceutical products should be regulated in the future:

- The development of diagnostic tests for distinguishing between patients with related but different disease subtypes. More than 40 such "companion diagnostics" are already on the market, and there are many more tests in the pipeline.

- The development of sophisticated remote monitoring technologies (e.g., ingestible microchips and implantable devices that can be connected to a wireless network).

These advances will enable healthcare providers to diagnose patients much more accurately and monitor them continuously, eliminating the need for some of the precautions that are currently required. The GOI should therefore establish a special committee to formulate a new framework for regulating biopharmaceutical products intelligently in an intelligent age. That committee should include experts in biostatistics, public health, pharmacovigilance, genomics and molecular diagnostics, and healthcare informatics.

### 6.2 INVOKE "MARKET PULL"

Various healthcare studies have documented the impact of "market pull" in stimulating the creation of world-class healthcare systems in emerging economies. Affluent patients in these countries typically have health insurance, suffer from many of the same chronic diseases as patients in the mature economies and are abreast of the latest medical advances. Venture capitalists and private equity players are therefore interested in reaching them, as are global vendors with local manufacturing, sales and delivery facilities.

India already has experience of this phenomenon; several high-profile physician-entrepreneurs are currently creating first-rate healthcare infrastructures in urban centres. But the GOI could boost the effect if it started investing much more heavily in the public health system, as China is doing. Providing healthcare for its citizenry should be motivation enough. However, such a move would have a welcome secondary effect in stimulating the market for biopharmaceutical products. (It is worth noting that China plans to spend nearly $500 billion a year on healthcare by 2017, and that the domestic biopharmaceuticals market is forecast to reach $61 billion in 2013, making it the third-largest market in the world.)

Public health in India remains a huge developmental challenge that needs serious attention from the nation's most strategic thinkers, and the support of political giants to ensure implementation. The Ministry of Health's flagship programme, the National Rural Health Mission (NRHM), is a step in the right direction, but it needs to be scaled up massively. The central government allocated $3.86 billion for healthcare in its annual budget in fiscal 2009, of which $2.3 billion was earmarked for the NRHM. Nevertheless, India's citizens still bear most of the financial burden, with public resources covering less than 20% of overall healthcare costs.

The mega-healthcare establishments serving the urban centres have proved that extraordinary economies of scale can be leveraged to make healthcare affordable at levels unimaginable in the West; take the case of Narayana Hrudalaya, which performs paediatric cardiac operations for just $1,400. These models must be taken to the countryside. The spread of India's telecommunications connectivity must also be leveraged to make the practice of telemedicine much more routine. Lastly, the logistics of healthcare delivery must be addressed with the same efficiencies the fast-moving consumer goods (FMCG) sector achieves today. Suitable infrastructure and financial incentives should be provided to those who lead the way.

**The mega-healthcare establishments serving the urban centres have proved that extraordinary economies of scale can be leveraged to make healthcare affordable at levels unimaginable in the West...**

### 6.3 SEEK OPPORTUNITIES FOR GROWTH THROUGH ACQUISITIONS

Indian companies in various sectors (e.g., steel manufacturing, automotive manufacturing and telecommunications) have shown great skill in acquiring surplus manufacturing capacity from other organisations, integrating it with their own operations and managing it profitably. The consolidation of the global BioPharma industry may present more such opportunities, as the leading manufacturers dispose off surplus plants – enabling the Indian BioPharma sector to acquire capacity in markets that are attractive.

The DoP could therefore contract an international consultant to scope out the opportunities on behalf of the indigenous industry. It could also offer Indian entrepreneurs financial assistance through guarantees, "round-off" capital and other debt instruments, where necessary.

### 6.4 ENCOURAGE HIGHLY SKILLED EXPATRIATES TO COME HOME

The BioPharma sector should capitalise on the "Indian Diaspora" by encouraging expatriate Indians with the relevant expertise to return to their home country. The IT sector has been very successful in attracting highly qualified professionals of Indian origin back to their homeland by holding "job fairs" in Silicon Valley and other regional clusters of IT expertise. The BioPharma industry should emulate these tactics.

The GOI can play a valuable role in helping organisations like ABLE and the Federation of Indian Chambers of Commerce (FICCI) create targeted seminars in high-density locations such as the UK, and US East and West Coasts, to advise professionals of the opportunities in India. The global consolidation of the industry – and the instability it is causing in some of these careers – should also weigh in India's favour.

### 6.5 LEVERAGE INDIA'S EXPERTISE IN HOLISTIC AND TRADITIONAL MEDICINE

Lastly, India should leverage its expertise in herbal and nutritional therapies, and other forms of traditional medicine. The Department of Ayurveda, Yoga and Naturopathy, Unani, Siddha and Homoeopathy (AYUSH) and the Council for Scientific and Industrial Research (CSIR) have jointly created a database to codify this knowledge. The Traditional Knowledge Digital Library (TKDL) now contains nearly 805,000 Ayurvedic formulations, 98,700 Unani formulations and 9,970 Siddha formulations – information that could be invaluable in developing new biologics.

## Conclusion

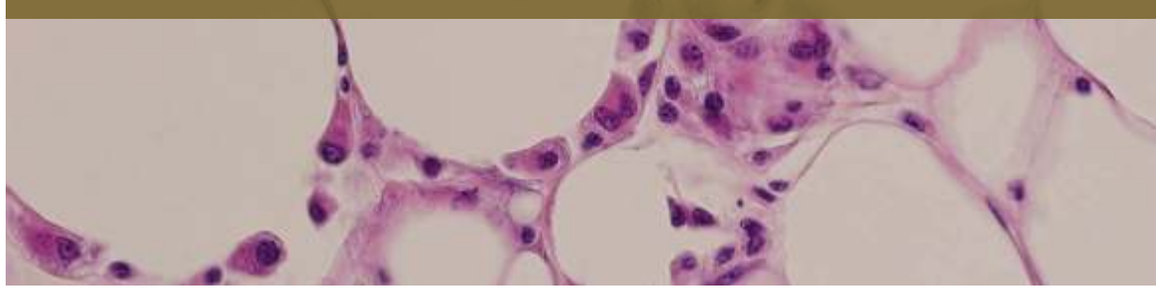
The future of medicine lies in biologics and diagnostics. Conventional drugs will continue to play an important role in the treatment of disease, but many of tomorrow's most innovative therapies will be biopharmaceutical packages comprising biologics and companion diagnostics.

India has a unique opportunity to make its name in this space. It can leapfrog over an entire generation of technologies and compensate for what it missed in the field of chemistry by making targeted investments to create the infrastructure required for researching, developing and manufacturing large molecules.

There are a few pockets of excellence in the public domain but, on the whole, the physical infrastructure for R&D remains minimal. There are critical gaps in the facilities required for everything from basic research to clinical development. So, if the domestic BioPharma industry is to succeed in securing 10% of the global biosimilars market and becoming one of the world's top five biosimilars producers – as we believe it should aim to do – it will need to make a substantial investment in new manufacturing capacity. However, the creation of physical assets cannot be seen in isolation from the ecosystem that is necessary to foster an expertise in biopharmaceuticals.

We have outlined the key steps we believe the GOI should take to help the country attain its vision of becoming the world's leading producer of biopharmaceutical products by 2020. Fulfilling this vision will take capital and commitment. But if India succeeds, it will not only generate significant additional revenues, it will also be serving a global population desperately in need of good, affordable medicines.

**India has a unique opportunity to make its name in the biopharma space. It can leapfrog over an entire generation of technologies and compensate for what it missed in the field of chemistry by making targeted investments to create the infrastructure required for researching, developing and manufacturing large molecules.**



**Appendix 1: Exchange Rates**
All currency conversions were calculated using the average exchange rate on 21 June 2010, as follows:

| | | |
|---|---|---|
| **Australia** | 1 AUD | = 0.87335 USD |
| **China** | 1 CNY | = 0.14666 USD |
| **Euro Zone** | 1 EURO | = 1.23988 USD |
| **India** | 1 INR | = 0.02178 USD |
| **Israel** | 1 ILS | = 0.26221 USD |
| **Korea** | 1 KRW | = 0.0008381 USD |
| **Singapore** | 1 SGD | = 0.72314 USD |
| **Taiwan** | 1 TWD | = 0.03113 USD |

**Appendix 2: The Global Pipeline for Biosimilars**
The table below provides details of some of the biosimilars currently in development.

| Biologic Drug Class | Biosimilar | Development Company | Stage of Development |
|---|---|---|---|
| Monoclonal Antibodies | Bevacizumab | Biocon | In development |
| | Trastuzumab | Biocon | In development |
| | Rituximab | GTC Biotherapeutics and LFB Biotechnologies | Preclinical |
| | Rituximab | Ranbaxy/Zenotech | In development, along with other monoclonal antibodies |
| | Various | Dr. Reddy's | Various biosimilars in development including monoclonal antibodies |
| | Four monoclonal antibodies against lung cancer, melanoma and pancreatic and breast cancer | Shantha Biotech | In development in the US |
| Insulin | Gensulin/SciLin | Bioton/SciGen | Marketed in Poland and Russia. Launches expected in Asian and Pacific markets, including China |
| | Human insulin and insulin analogues | Biocon | Marketed in India. Launches planned in Europe and the US |

| Biologic Drug Class | Biosimilar | Development Company | Stage of Development |
|---|---|---|---|
| Erythropoietin | JR-013 | Kissei | Submitted for regulatory approval in Japan |
| | MK-2578 (darbepoetin alfa) | Merck & Co. | Phase 1 of clinical testing |
| Interferons | Biferonex (Interferon beta-1a) | BioPartners | Submitted to EMA as new drug but rejected |
| | CinnoVex ( Interferon beta-1a) | CinnaGen | Marketed in Iran. Launches planned in European markets |
| | Interferon beta-1b | Merck BioVentures | In development |
| | Alpheon (Interferon alfa-2a) | BioPartners | Submitted to EMA but rejected |
| | Pegylated Interferon alfa-2b | Shantha Biotechnics | In development |
| CSF Drugs | Tevagrastim (filgrastim) | Teva | Approved by EMA in 2008. Launched in Germany, further launches expected including US in 2010 |
| | Nufil (filgrastim) | Biocon | Launches planned in Europe and the US |
| | Nugraf (filgrastim) | Ranbaxy/Zenotech | Regulatory submissions planned in European markets |
| | Neukine (filgrastim) | Intas/Apotex | Phase I in Europe completed |
| | Filgrastim | Stada | Phase I |
| | Filgrastim | Wockhardt | In development |
| | INS-20 (pegfilgrastim) | Merck BioVentures | Phase I |
| | Neupeg (pegfilgrastim) | Intas/Apotex | In development |
| | Macrogen (molgramostim) | Ranbaxy/Zenotech | Regulatory submissions planned in European markets |
| Growth Hormones | Valtropin (somatropin) | LG Life Science/BioPartners | Currently marketed (South Korea) Approved (EU and US) Phase III (once-a-week, sustained release) |

Source: visiongain

**Appendix 3: Biologics with Patents due to Expire between 2010 and 2020**

The following table lists all biologics with patents due to expire during the next decade. We have ranked them by date and, where the same product is made by more than one company, we have included details of the revenues generated by each company.

| Product | Generic Name | Company | Therapeutic Subcategory | 2009 Sales [$ millions] | Patent Expiry | Patent Expiry [ex US] |
|---|---|---|---|---|---|---|
| NovoSeven | eptacog alfa | Novo Nordisk | Anti-fibrinolytics | 1,324 | 15-11-2010 | 28-02-2011 |
| BeneFIX | nonacog alfa | Pfizer | Anti-fibrinolytics | 98 | 11-02-2011 | |
| Enbrel | Etanercept | Amgen | Other anti-rheumatics | 3,493 | 23-10-2012 | |
| Enbrel | Etanercept | Pfizer | Other anti-rheumatics | 378 | 23-10-2012 | 28-02-2015 |
| Neupogen | Filgrastim | Amgen | Immunostimulants | 1,288 | 12-03-2013 | 22-08-2006 |
| Humalog | insulin lispro | Eli Lilly | Anti-diabetics | 1,959 | 07-05-2013 | |
| Avonex | interferon beta-1a | Biogen Idec | MS Therapies | 2,323 | 30-05-2013 | 31-12-2005 |
| Epogen | epoetin alfa | Amgen | Anti-anaemics | 2,569 | 20-08-2013 | |
| Procrit/Eprex | epoetin alfa | Johnson & Johnson | Anti-anaemics | 2,245 | 20-08-2013 | |
| Cerezyme | Imiglucerase | Genzyme | Other therapeutic products | 793 | 27-08-2013 | |
| Rebif | interferon beta-1a | Merck KGaA | MS Therapies | 2,142 | 31-12-2013 | |
| NovoMix | insulin & insulin aspart | Novo Nordisk | Anti-diabetics | 1,216 | 06-06-2014 | 31-12-2015 |
| NovoRapid/ NovoLog | insulin aspart | Novo Nordisk | Anti-diabetics | 1,825 | 07-12-2014 | 31-12-2017 |
| Rituxan | Rituximab | Roche | Anti-neoplastic Mabs | 5,620 | 31-12-2014 | 31-12-2013 |
| Kogenate | octocog alfa | Bayer | Anti-fibrinolytics | 1,238 | 31-12-2014 | 14-04-2009 |
| Prevnar | Pneumococcal vaccine | Pfizer | Vaccines | 287 | 01-01-2015 | |
| Lantus | insulin glargine | Sanofi-Aventis | Anti-diabetics | 4,293 | 12-02-2015 | 30-09-2013 |
| Actemra | Tocilizumab | Roche | Other anti-rheumatics | 44 | 07-06-2015 | |
| Gonal-F/ Gonalef | follitropin alfa | Merck KGaA | Fertility agents | 678 | 16-06-2015 | |
| Neulasta | Pegfilgrastim | Amgen | Immunostimulants | 3,355 | 20-10-2015 | 02-08-2015 |
| Nimotuzumab | Nimotuzumab | YM BioSciences | Anti-neoplastic Mabs | | 17-11-2015 | 22-05-2016 |
| Norditropin SimpleXx | Somatropin | Novo Nordisk | Growth hormones | 824 | 15-12-2015 | 31-12-2017 |
| Helixate | octocog alfa | CSL | Anti-fibrinolytics | 563 | 31-12-2015 | 14-04-2009 |
| Humira | Adalimumab | Abbott Laboratories | Other anti-rheumatics | 5,488 | 31-12-2016 | 10-02-2017 |
| Zostavax | herpes zoster vaccine | Merck & Co. | Vaccines | 277 | 31-12-2016 | |
| Tysabri | Natalizumab | Elan | MS Therapies | 509 | 26-04-2017 | |
| Tysabri | Natalizumab | Biogen Idec | MS Therapies | 544 | 26-04-2017 | |
| Provenge | sipuleucel-T | Dendreon | Immunostimulants | | 30-06-2017 | 23-12-2016 |
| Victoza | Liraglutide | Novo Nordisk | Anti-diabetics | 13 | 22-08-2017 | |
| Cervarix | Human papillomavirus (HPV) vaccine | GlaxoSmith Kline | Vaccines | 293 | 06-10-2017 | 31-12-2019 |

| Product | Generic Name | Company | Therapeutic Subcategory | 2009 Sales [$ millions] | Patent Expiry | Patent Expiry [ex US] |
|---|---|---|---|---|---|---|
| Avastin | Bevacizumab | Roche | Anti-neoplastic Mabs | 5,744 | 26-02-2018 | |
| Apidra | insulin glulisine | Sanofi-Aventis | Anti-diabetics | 191 | 18-06-2018 | |
| Forteo/Forsteo | teriparatide acetate | Eli Lilly | Bone calcium regulators | 817 | 08-12-2018 | |
| Remicade | Infliximab | Johnson & Johnson | Other anti-rheumatics | 3,088 | 31-12-2018 | |
| Remicade | Infliximab | Merck & Co. | Other anti-rheumatics | 431 | 31-12-2018 | |
| Xolair | Omalizumab | Roche | Other respiratory agents | 572 | 31-12-2018 | |
| Xolair | Omalizumab | Novartis | Other respiratory agents | 338 | 31-12-2018 | |
| Gardasil | Human papillomavirus (HPV) vaccine | Merck & Co. | Vaccines | 1,119 | 24-01-2019 | |
| RotaTeq | rotavirus vaccine | Merck & Co. | Vaccines | 522 | 19-02-2019 | |
| Erbitux | Cetuximab | Merck KGaA | Anti-neoplastic Mabs | 971 | 13-05-2019 | |
| Erbitux | Cetuximab | Bristol-Myers Squibb | Anti-neoplastic Mabs | 683 | 13-05-2019 | 31-12-2016 |
| Levemir | insulin detemir | Novo Nordisk | Anti-diabetics | 978 | 17-06-2019 | 31-12-2018 |
| Elaprase | Idursulfase | Shire | Other therapeutic products | 353 | 03-09-2019 | |
| Orencia | Abatacept | Bristol-Myers Squibb | Other anti-rheumatics | 602 | 14-10-2019 | 31-12-2017 |
| Herceptin | Trastuzumab | Roche | Anti-neoplastic Mabs | 4,862 | 31-12-2019 | |
| Pegasys | peginterferon alfa-2a | Roche | Interferons | 1,528 | 31-12-2019 | 22-05-2017 |
| PEGIntron | peginterferon alfa-2b | Merck & Co. | Interferons | 149 | 31-12-2019 | |
| Vectibix | Panitumumab | Amgen | Anti-neoplastic Mabs | 233 | 08-04-2020 | 12-04-2022 |
| Lucentis | Ranibizumab | Novartis | Eye preparations | 1,232 | 30-06-2020 | 31-12-2022 |
| Lucentis | Ranibizumab | Roche | Eye preparations | 1,106 | 30-06-2020 | |
| Botox | onabotulinumtoxinA | Allergan | Muscle relaxant, peripheral | 1,310 | 21-07-2020 | |
| Bapineuzumab (AAB-001) | Bapineuzumab | Pfizer | Nootropics | | 28-11-2020 | |
| Synflorix | Pneumococcal vaccine | GlaxoSmith Kline | Vaccines | 114 | 31-12-2020 | 31-12-2020 |
| Replagal | agalsidase alfa | Shire | Other therapeutic products | 194 | 31-12-2020 | 31-12-2020 |

Source: EvaluatePharma

| | |
|---|---|
| A*STAR | Agency for Science, Research and Technology |
| ABLE | Association of Biotechnology Led Enterprises |
| ABT | American Board of Toxicology |
| ANDA | Abbreviated New Drug Application |
| AUD | Australian Dollars |
| AYUSH | Department of Ayurveda, Yoga and Naturopathy, Unani, Siddha & Homoeopathy |
| BLA | Biological License Application |
| CAGR | Compound Annual Growth Rate |
| CBER | Center for Biologics Evaluation and Research |
| CCH | Central Council of Homeopathy |
| CCIM | Central Council of Indian Medicine |
| CDER | Center for Drug Evaluation and Research |
| CDSCO | Central Drugs Standard Control Organisation |
| CEE | Central and Eastern Europe |
| cGMP | Current Good Manufacturing Practices |
| CHMD | Code for Human Medicines Directive |
| CNBG | China National Biotec Group |
| CNY | China Yuan Renminbi |
| CONICYT | Chilean National Commission for Scientific and Technological Research |
| CORFO | Chilean Economic Development Agency |
| CPCSEA | Committee for the Purpose of Control and Supervision of Experiments on Animal |
| CRO | Clinical Research Organization |
| CSIR | Council for Scientific and Industrial Research |
| CSIRO | Commonwealth Scientific and Industrial Research Organisation |
| CSL | Commonwealth Serum Laboratories |
| DABT | Diplomate of the American Board of Toxicology |
| DBT | Department of Biotechnology |
| DCGI | Drug Controller General of India |
| DIA | Drug Information Association |
| DNA | Deoxyribo Nucleic Acid |
| DoP | Department of Pharmaceuticals |
| DRA | Drug Regulatory Authorities |
| ELISA | Enzyme Lined Immuno Sorbent Assay |
| EMA | European Medicines Agency |
| EPO | European Patent Office |
| EU | European Union |
| FD&C | Food Drug and Cosmetic Act |
| FDA | Food and Drug Administration |
| FDI | Foreign Direct Investment |
| FICCI | Federation of Indian Chambers of Commerce |
| FMCG | Fast Moving Consumer Goods |
| GCP | Good Clinical Practices |
| G-CSF | Granulocyte Colony Stimulating Factor |
| GEAC | Genetic Engineering Approval Council |
| GLP | Good Laboratory Practices |
| GMOs | Genetically Modified Organisms |
| GOI | Government of India |
| HBSP | Hsinchu Biomedical Science Park |
| HPLC | High Performance Liquid Chromatography |
| HSA | Health Sciences Authority |
| HVAC | Heating, Ventilating and Air Conditioning |
| IBSC | Institutional Biosafety Committee |
| ICH | International Conference on Harmonisation |
| ICH-GCP | International Conference on Harmonization-Good Clinical Practices |
| IIC | Israel Investment Centre |
| ILS | Israeli New Shekel |
| INR | Indian Rupees |
| IP | Intellectual Property |
| ISM&H | Indian System of Medicine and Homeopathy |
| ISPE | International Society for Pharmacoepidemiology |
| IT | Information Technology |
| KFDA | Korean Food and Drug Administration |
| KRW | Korea (South) Won |
| LMOs | Living Modified Organisms |
| Mabs | Monoclonal Antibodies |
| MALDI | Matrix Assisted Laser Desorption Ionization |
| MCB | Master Cell Bank |
| MHLW | Ministry of Health, Labour and Welfare |
| NCBS | National Center for Biological Sciences |
| NDA | New Drug Application |
| NDRC | National Development and Reform Commission |
| NHI | National Health Insurance |
| NMR | Nuclear Magnetic Resonance |
| NRHM | National Rural Health Mission |
| OCS | Office of the Chief Scientist |
| OECD | Organization for Economic Cooperation and Development |
| PHS | Public Health Service |
| PwC | PricewaterhouseCoopers |
| Q-TOF | Quadruple Time Of Flight |
| R&D | Research and Development |
| RaaS | Research-as-a-Service |
| RCGM | Review Committee on Genetic Manipulation |
| RDAC | Recombinant DNA Advisory Committee |
| r-DNA | Recombinant DNA |
| SFDA | State Food and Drug Administration |
| SGD | Singapore Dollars |
| SME | Small and Medium Enterprise |
| STSP | Southern Taiwan Science Park |
| TGA | Therapeutic Goods Administration |
| TKDL | Traditional Knowledge Digital Library |
| TRIPS | Trade Related Aspects of Intellectual Property Rights |
| TWD | Taiwan New Dollars |
| US | United States |
| USD | United States Dollars |
| VAT | Value-Added Tax |
| WCB | Working Cell Bank |
| WFI | Water for Injection |

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