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Eli Lilly: Leading the world with clinical trials

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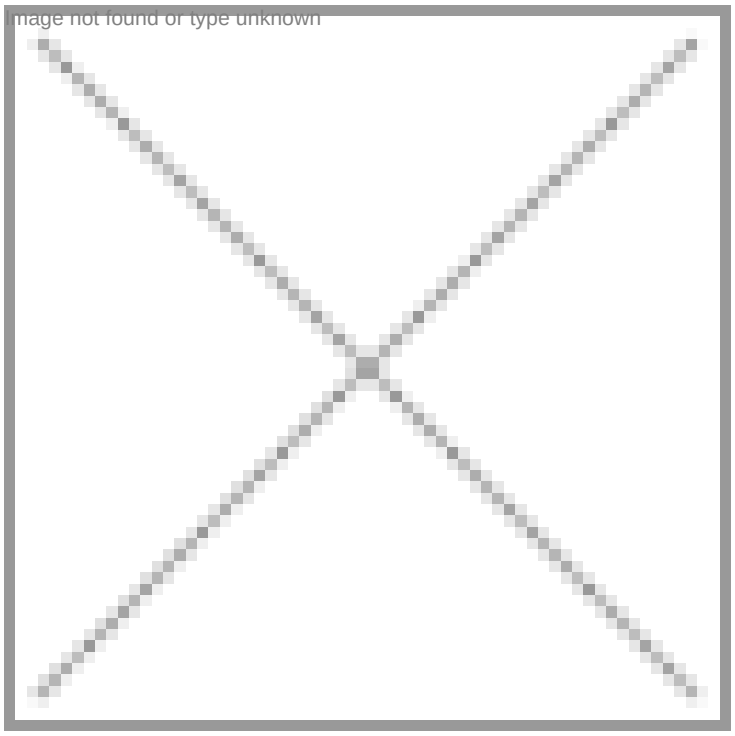

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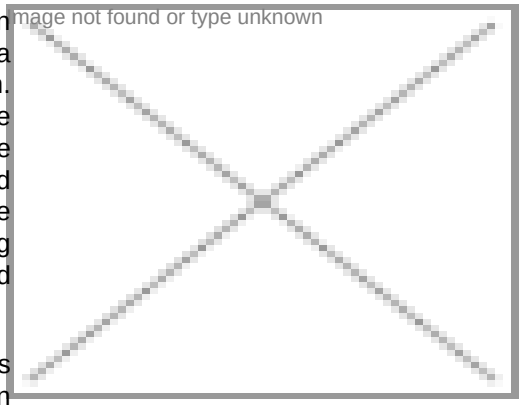

The pace of medical innovation is quickening, pushed by advances in biotechnology. The growing demand for healthcare too is forcing pharma companies to increase their product offerings. Eli Lilly is one among them. However, introduction of a new drug takes some 15 years to complete the laborious regulatory processes in most countries. Biotechnology has come to the rescue of pharma companies by reducing the time to market by a third and global leaders are making significant investments to broaden and quicken the clinical trial phase by moving it to countries like India and pulled by growing demand for healthcare. Completion of the Human Genome Project has provided a multitude.

American pharma giant Eli Lilly is a global leader in this new trend with emphasis on clinical trails. Eli Lilly with a presence in 179 countries employs more than 35,000 people worldwide and markets its medicines in 159 countries. Eli Lilly has major research and development facilities in nine countries and conducts clinical trials in around 70 countries. Within the company, around 6,000 employees are engaged in research and development activities. In India, Eli Lilly is mainly into the clinical trials activity.

Eli Lilly & Company (India) Pvt. Ltd [ELCIPL] is a 100 percent subsidiary of Eli Lilly & Company (ELC), USA. Eli Lilly came to

India in 1993 as a 50:50 joint venture between the Indian partner Ranbaxy and US based Eli Lilly & Company Inc. This venture was primarily set up for manufacturing and marketing of select drugs of Eli Lilly and Company and Ranbaxy Laboratories Ltd in the markets of India, Nepal, Sri Lanka, Bhutan and Maldives.

Later, Eli Lilly acquired the 50 percent equity stake of partner Ranbaxy Laboratories Ltd after the latter decided to sell its stake converting the joint venture into a 100 percent Lilly subsidiary, Eli Lilly & Company (India) Pvt. Ltd.

Eli Lilly and Co. (ELC), a Fortune 500 company, was founded in 1876, and is based in Indianapolis, Indiana. ELC is an innovation-driven pharmaceutical corporation, developing a growing portfolio of pharmaceutical products, by applying the latest research from its very own worldwide laboratories and from collaborations with eminent scientific organizations.

The research division, Lilly Research Laboratories (LRL) is responsible for the discovery, development, and clinical evaluation of pharmaceutical products and for providing ongoing scientific support for marketed products. At the core of LRL's mission is discovering and developing innovative therapies for many of the world's unmet medical needs.

Lilly Research Laboratories

LRL comprises more than 6,000 people from a wide variety of scientific disciplines who work in laboratories in the US and at other locations around the world. R&D locations in the US include four sites in Indiana (Indianapolis, Greenfield, West Lafayette, and Clinton).

In 1994, Lilly acquired Sphinx's Pharmaceuticals (now Sphinx Laboratories), a division of LRL headquartered in Research Triangle Park, North Carolina. Sphinx's novel approach to drug discovery and development has provided the company with cutting-edge research tools to identify and optimize promising drug candidates more quickly and efficiently.

Outside the US, it operates research facilities in Belgium, Canada, England, Germany, Japan and Spain, Australia and Singapore. In addition, Lilly conducts clinical research in approximately 70 countries around the world.

Faiz Askari

Xigris - the first patented drug from Eli Lilly in India

Most global pharma companies have been reluctant to introduce their latest patented drugs in India in recent years due to the non-recognition of product patents in the country. They feared Indian companies would 'reverse engineer' such products and sell them at down to earth prizes and cut into their market. By and large, global companies had deferred the launch of new drugs till the product patent regime is introduced in India from 1 January 2005.

However, Eli Lilly chose not to wait till 2005 when it launched 'Xigris' for Sepsis (blood poisoning). Xigris is indicated for the reduction of mortality in adult patients with severe sepsis (sepsis associated with acute organ dysfunction) who have a high risk of death. Xigris is one of the newest drugs from Eli Lilly as it has received approval from the US Food and Drug Administration only on 21 November 2001 for the reduction of mortality in adult patients.

On 26 August 2002 the drug got the marketing authorization from the European Commission for introduction in all the 15-member states of the European Union. This novel, biotech therapy is approved for the treatment of adult patients with severe sepsis with multiple organ failure when added to best standard care.

Xigris is a genetically engineered version of the human Activated Protein C molecule, a naturally occurring protein in the body that helps to balance many of the major forces behind sepsis, including coagulation (blood-clotting) and suppression of fibrinolysis (the body's clot-busting system). Additionally, patients with severe sepsis treated with Xigris had a more rapid decline in interleukin-6 levels, a global marker of inflammation, consistent with a reduction in the inflammatory response. The drug is administered to patients as a one-time, 96-hour infusion within an ICU (intensive care unit) setting. The precise dosage depends on the weight of the patient.

Lilly's Indian market thrust

Eli Lilly is planning to introduce two major drugs in the Indian market in 2003. These are Forteo for Osteoporosis and Alimta & Affinitac in the area of Oncology. Forteo is claimed to be the only drug of its kind that builds bones.

Oncolology is a thrust area for the company. Said Dr Bhawana , a Clinical Research Physician (CRP), in Lilly: "We are conducting research in oncology and in the clinical development of a new molecule "Alimta" for malignant pleural mesothelioma and lung cancer, and looking at expanding the role of Gemcitabine in cancers of concern in India like cervical cancer, breast cancer, gall bladder cancer. "

"A new anti-sense molecule is being tested for lung cancer. In the field of critical care, we are conducting large-scale clinical research on the new molecule- Drotrecogin Alfa [activated] for patients of sepsis. In the diabetic patients, we are conducting research on insulins, "she added

"At present we are also conducting two clinical trials using Growth hormone: Humatrope, and completed a large (2000) patient study with human insulin that we are in the analysis phase and hoping to publish it soon. We are looking at conducting another clinical trial on analogue insulin to start in September. Work for that is in planning phase," the researcher said.

In addition, the company will be using the partnership and alliance route in India for growth. Eli Lilly already has three partnerships in India with Ranbaxy, Sun Pharma and Chennai based Shasun. Lilly and Sun Pharma are also planning to explore the possibilities of unveiling bulk drugs. Additionally Shasun will undertake contract research for three of Lilly's new drug molecules.

" We have 17 large and small clinical trials going in India"

A post graduate in pharmaceutical sciences from the Institute of Technology, Benaras Hindu University, Varanasi, and a post graduate in business management from the Indian Institute of Management, Ahmedabad, Rajiv Gulati started his career with Ranbaxy Laboratories Ltd in 1982. He is well known in the industry for some of the most successful product launches in the country. In 1992, he joined Eli Lilly and has been with the company since its Indian operation was launched. He has also worked for several years in Indianapolis and at the corporate headquarters of the company in diverse functions such as business development, strate-

gizing planning and human resources.

He is currently the chairman of the Pharmaceutical Council of the Indo American Chambers of Commerce, member of the executive committee of OPPI, Pharmaceutical Council of the Confederation of Indian Industry (CII), governing council of IMM and s[image not found or type unknown]rd of Pharmabiz. Excerpts from an interview with BioSpectrum:

"Eli Lilly has had the unique distinction and honor of launching the world's first biotechnology product, Human Insulin in 1982. This was followed by the launch of a growth hormone, *Somatropin* - the world's first Human insulin analogue, *Lispro*, the world's first approved treatment for severe sepsis, *Drotrecogin Alfa* [activated] and finally the world's first bone building agent for treatment of post menopausal osteoporosis, *Teriparatide*."

What is the focus of activities in India?

Lilly India is not involved in basic drug discovery research per se. This is an activity undertaken at Lilly's various R&D centers across the globe. In India, however, we have put in concerted efforts in conducting clinical research by partnering with key thought leaders and experts in the therapeutic areas of interest. We have conducted a clinical trial involving over 600 patients in partnership with numerous clinical investigators to help gather knowledge and share the experience of Human insulin and Insulin Lispro in varied settings.

How strong is the biotech activity of Eli Lilly?

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Human Insulin, Insulin Lispro, Som-atropin and Xigris are already available in India. Moreover, the company has filed for marketing permission of Teriparatide and we hope to launch the product to Indian patients within the next one year. Injection Teriparatide [Brand Forteo: for Osteoporosis] is the product which is in pipeline.

Could you give some details about the other activities in India?

At the moment we have 17 large and small clinical research projects running involving both phase 2 and phase 3 research. We are working with over 40 hospitals in India, including government and private hospitals.

The investigators that we work with in India have a positive attitude and are willing to learn and adapt and adhere to the guidelines of ICH (international commission on harmonization of clinical practice) and GCP (good clinical practice).

The infrastructure and training is an integral and ongoing part of the clinical research process. We invest significant time and resources for creating and maintaining the required standards.

The processes and sites are audited by the MQA (Medical Quality Assurance- an independent arm of Lilly Research Labs with focus on regulating the qualitative aspects of clinical trials) to ensure that the standards are adhered to the requirements.

At the same time, the challenges that confront are the unstructured environment in hospitals and government institutions, lack of GCP awareness amongst the large institutions, and regulatory environment which is not well defined for all aspects of research.

Do you think the Indian biotech industry will develop fast?

The country has all that it takes for becoming a major center for biopharma related trials. The size of opportunity is huge. Estimates show that drugs and vaccines that have biotechnology as their basis have already benefited greater than 250 million people. As per a new survey done by PhRMA (the American pharma association), many million more are expected to get the benefit in the future. The survey found 371 biotechnology medicines under development by 144 companies for nearly 200 diseases in the year 2002.

The number of biotechnology drugs approved by US FDA till date is 95. PhRMA statistics say that 178 products under development are in the cancer and related conditions, followed by 47 for infectious diseases in 2002. Another area to watch out is that of making copies of innovative drugs derived through biotech route, that is known as biogenerics.

What are the prospects of contract research and manufacturing sectors in India?

One more area under development is the contract research and manufacturing. Last few years has seen the advent of many large multinational CRO's (contract research orga-
nizaitons) that see India offering huge potential in this direction.

In the field of contract manufacturing, for example, Lilly has already started sourcing two products namely Nizatidine and Methohexital from a bulk drug manufacturer in South India to cater to its global requirements. India has the potential to be a major player in this sector. To make it happen, the need of the hour is to make sincere attempt to look at the existing challenges and find answers to these.

How are the regulatory mechanisms in the country?

There has been a long pending demand of the pharma industry to set up a single window clearance agency for biotech drugs. This is essential as the current process of going through a RCGM (review committee on genetic manipulation), GEAC (genetic engineering approval committee), DCGI's (drug controller general of India) approval etc takes a lot of time and is at times repetitive. Other than the time lag, the process is robust as such. We need to recognize the fact that as a good corporate citizen, it is incumbent upon everyone to ensure that our environment is protected from any form of pollutant.

The checks are by and large fine, it's the logistical process that can be hastened/ shortened. Also, the clause on having to conduct a clinical trial one phase lower than the developed world is the major cause of delay in bringing newer molecules to the Indian market. In this age of globalization, there should be no hindrance. Additionally, there is also a need to standardize the process for clinical trial related regulatory approvals, and transparency to be maintained consistently in implementing the same.