



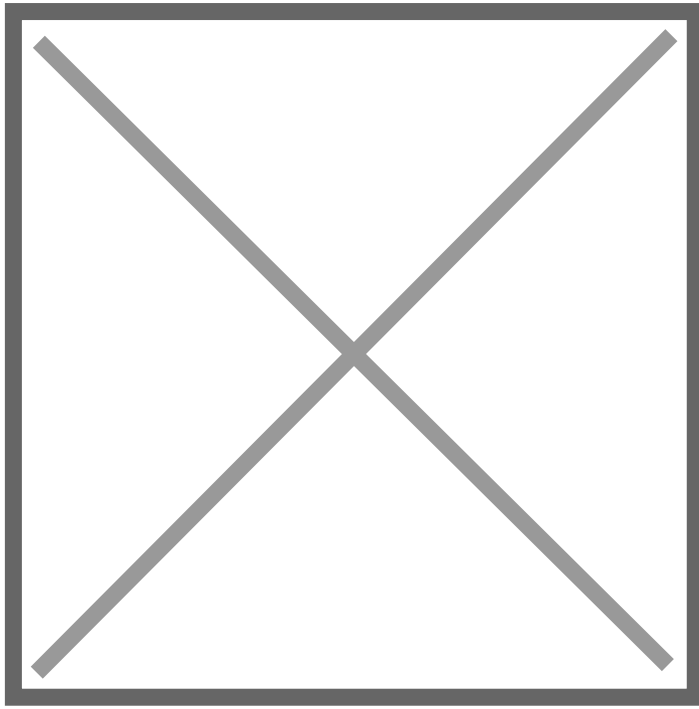
# BioSpect

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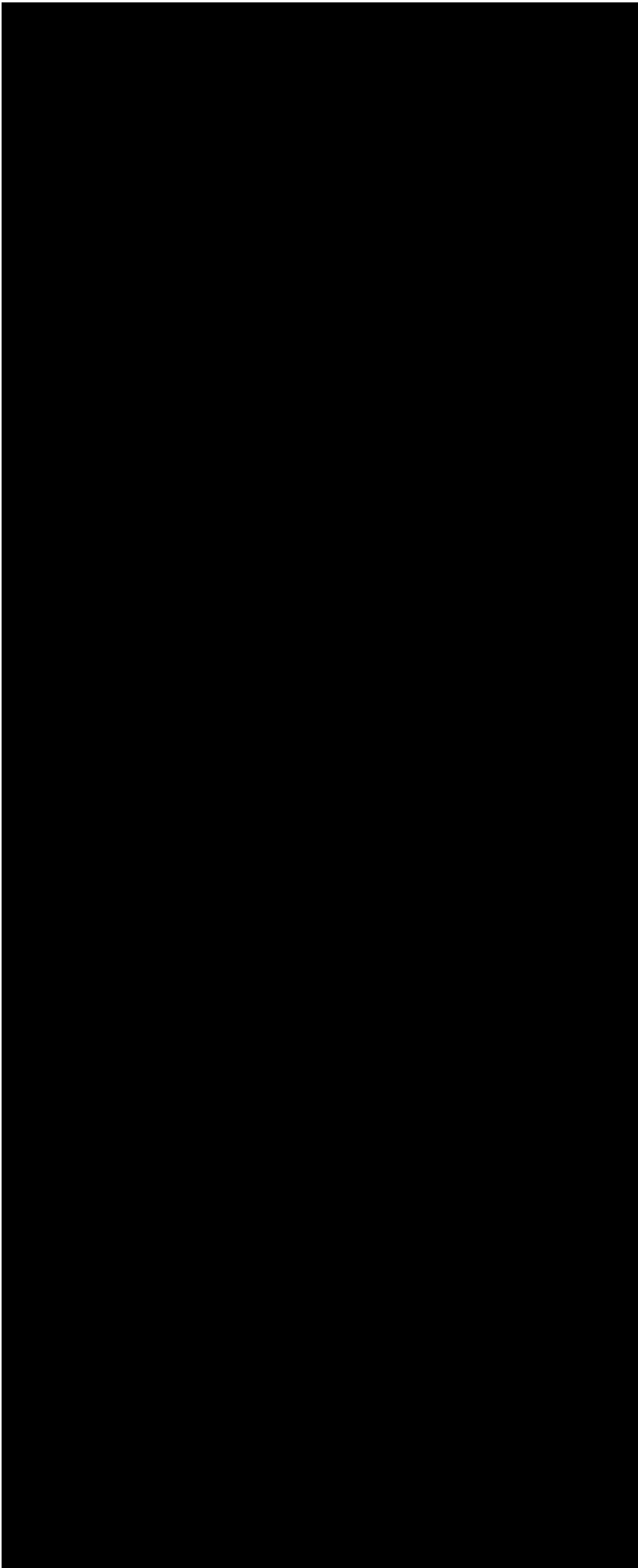
## **Novel Antibody, Several Firsts**

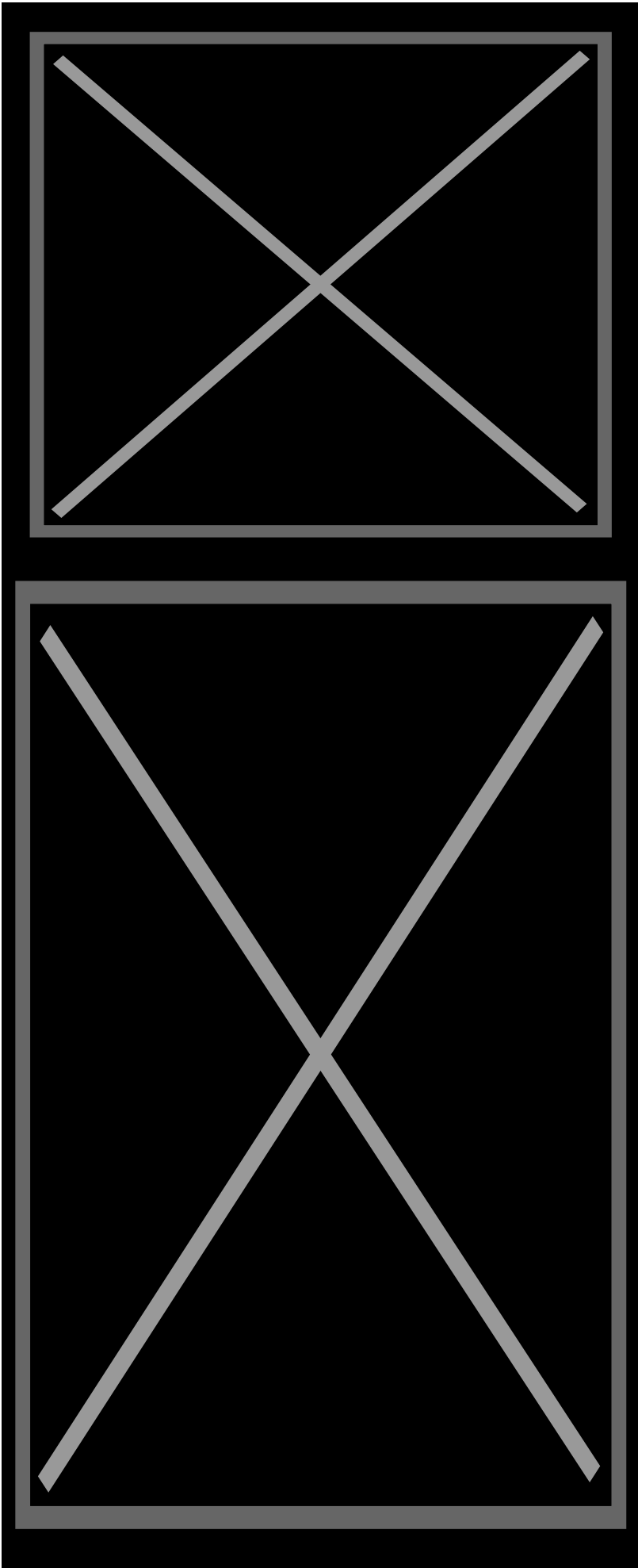
13 December 2007 | News



**Novel Antibody, Several Firsts**







*BIOMAb-EGFR, a therapeutic monoclonal antibody-based drug for treating solid tumors of epithelial origin such as head and neck cancers, clinically developed in India is the first by an Indian company. And patients in India are believed to be the first in the world to have access to a novel product.*

Rohit (name changed), a Bangalorean, was recently detected with an initial stage of neck cancer. He was then prescribed BIOMAb, a made-in-India product, which costs around Rs 40,000. He is being administered the drug every once in a week with 30 minutes infusion since the last two months. Rohit has not been getting any severe form of side effects as it is associated with other therapies and hopes to recover soon. BIOMAb is a new class therapy from Biocon for treating head and neck cancer and promises a lot of hope for the patients in India. Rohit and several other patients now have access to BIOMAb, which is cost-effective and affordable.

Globally there are very few monoclonal antibodies that have been approved and a majority of those are from companies in the US. Monoclonal antibodies, which are very complex large molecules, unlike aspirin, need a lot of scientific expertise to manufacture, characterize and even apply them in a clinical setting. These are not the kind of drugs that one goes to the pharmacy and picks up. Typically, they are applied in tertiary care settings where one goes to a specialist clinician who then prescribes this drug. It is fortunate that we have a molecule--BIOMAb EGFR from Biocon--that has been approved for use in India and is available for the Indian patients ahead of the patients in the rest of the world for managing head and neck cancer.

BIOMAb EGFR is a humanized antibody, a complex molecule approximately 1.5 lakh dalton in molecular weight. It targets a molecule called Epidermal Growth Factor Receptor (EGFR) that is present on epithelial cells. EGFR is present at particularly high levels on tumorous epithelial cells. When the BIOMAb EGFR binds this receptor, it helps to kill the tumor. According to Biocon, the clinical trials have indicated that patients respond extremely well to BIOMAb EGFR given in combination with traditional chemotherapy and radiotherapy.

These antibodies have complex secondary and tertiary structure that enable them to specifically target cancer cells as opposed to all cells; therefore the systemic toxicity is often very minimal. So one can almost get into a specialist clinic, get an infusion in an outpatient setting and walk away. This is not like typical chemotherapy where one has systemic toxicity because the drug targets specific receptors or signals in the body that causes the disease.

"This drug is also in clinical trials in Europe. They have very promising results in a very deadly form of brain cancer called pontine glioma in children. Many other trials are going around the world. There is a global meeting that occurs every once in a while where investigators meet. Here clinicians came from all over the world, including our clinicians, to share their experience about how this drug has worked," explained Dr Harish Iyer, head, R&D, Biocon.

BioMAb EGFR Nimotuzumab

The last few years have witnessed the approval of a number of chemotherapeutics and immunotherapeutics including various antibody based products for the clinical management of diverse cancers. The first MAb approved for cancer was rituximab, a chimaeric IgG1 kappa MAb, indicated for the treatment of lowgrade or follicular CD20+ non-Hodgkin's lymphoma (NHL) and is sold as MabThera/Rituxan by Biogen Idec, Genentech and Roche. The other monoclonal antibody from the same class is Cituximab from Merck which is also being widely prescribed for cancer patients in India.

The number of cancer cases is alarmingly high in India, about 100 per lakh, and the highest rates of head and neck cancers are reported in South Asian countries, The Indian sub-continent accounts for one-third of the world burden of head and neck cancers.

BioMAb-EGFR is available in a pack with a unit carton of four 10 ml vials each containing 50 mg.

Development of BIOMAb was a joint venture between Biocon and the Centre of Molecular Immunology (CIM), Cuba. CIM did the molecule research for the drug and also provided the initial human data. The drug is the first of its kind to be clinically developed in India and is the first anti-EGFR humanised monoclonal antibody for cancer and would be made available commercially anywhere in the world.

Kiran Mazumdar Shaw, chairman and managing director, Biocon, said, "It was interesting to bring the first true proprietary immunotherapeutics to the Indian market. Biomab-EGFR is competitively priced, making cancer treatment more affordable. It has the potential of be a billion-dollar product. Importantly, in terms of affordability and quality we score much higher than the multinationals and our mission is to bring innovative drug at an affordable price."

"We are today the largest selling monoclonal antibody in the country and we aim to be the leader in cancer care. The product has already been launched in Pakistan and Sri Lanka a couple of months back"

-Rakesh Bamzai, head, marketing, Biocon

She added, "The company made an investment of approximately Rs 150 crore on BIOMAb EGFR including the clinical development programs and the manufacturing facility. The investment in the clinical development program is still in progress for other cancers and each clinical trial is costing around Rs 15-20 crore."

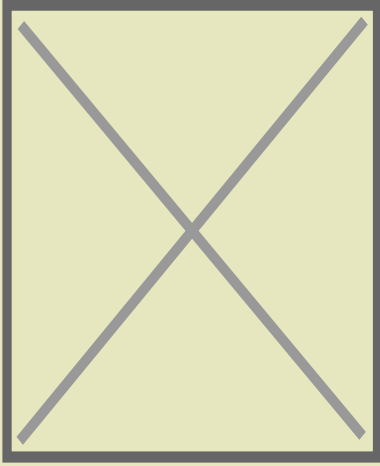
The product has shown consistent response in clinical trials initiated both in India and globally and is produced at its manufacturing facility at Biocon Park. BioMAb-EGFR is indicated for use in combination with radiation therapy or chemotherapy.

The pathbreaking monoclonal antibody, BioMAb EGFR was granted regulatory marketing and manufacturing approval and was launched in India in September 2006. The company is expecting it to get approved in Europe by next year.

Commenting on BIOMAb EGFR's success, Rakesh Bamzai, head, marketing, Biocon, said, "We are today the largest selling monoclonal antibody in the country and we aim to be the leader in cancer care. The product has already been launched in Pakistan and Sri Lanka a couple of months back."

"Our manufacturing rights are more compared to our marketing rights. We have at present the marketing rights for almost 25 countries and we will be marketing the product across these markets based on the regulatory approvals. We are looking at marketing the drug to these markets through alliance partners and distribution channels," he added.

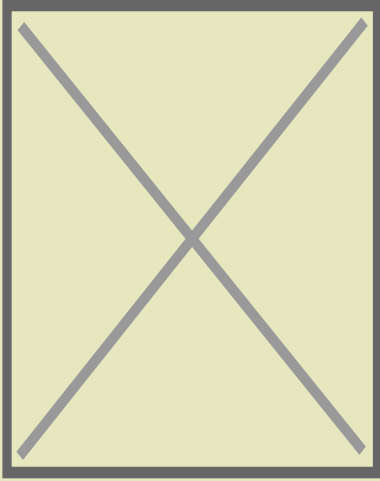
The total number of registered patients for BIOMAb is almost 1,000 in India which is much higher than any other similar product from the multinational companies, according to Bamzai. The drug indicated for head and neck cancer is also being studied in global clinical trials for colorectal, lung cancer, glioma (brain cancer) and pancreatic cancers.



"My main objective was to see how to get into innovation and new drugs. The question then was how to develop the products as developing new products or medicines involved a very high risk component. Further, as there was little access to new drug development in India then, we had to look outside of India for any kind of innovation. Antibodies were a new class of therapies and Cuba was doing R&D and innovation in this area. Since we needed to be innovative, we took the risk of partnering with CIM as we believed in the cutting edge work being done there and they had human data. We joined hands for developing the product, invested in the clinical development, invested in the technology for antibody production and finally brought it to the Indian market at a very affordable price.

Cancer is a very challenging area. Most of the cancer drugs are not billion-dollar drugs. Because not all drugs work for all cancers, there are a fewer number of patients. Therefore, it is a high-price low-volume segment".

-Kiran Mazumdar Shaw, chairman and managing director, Biocon

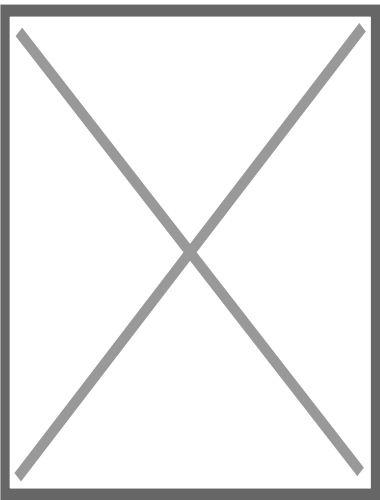


"When we have any new drug or any molecule to be used for patients the first thing we need to look at is the safety issue and then the efficacy. BioMAb EGFR from Biocon is a humanized molecule that belongs to the category of Nimotuzimab. Now every drug has some side effects but the degree of side effect varies. So, any treatment that we prescribe to the patients should not be worse than what they are suffering from. The most common forms of side effects, which occur with this category of drugs, are skin rashes and diarrhoea. With this drug, this side effect has been found to be less than 2 percent in patients. It doesn't need any extra treatment and is very safe".

-Dr K Govind Babu, medical oncologist, Curie Centre of Oncology

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"The major challenge was that nobody had done it before in India"



-Dr Harish Iyer, head, R&D, Biocon

Biocon's BIOMAb EGFR is a novel molecule that has been developed for the first time in India. Dr Harish Iyer, head, R&D, Biocon, shares with BioSpectrum the trials and tribulations that Biocon underwent in developing this product.

How did you come up with the idea for developing BIOMAb EGFR?

During one of her visits to Cuba, Kiran Mazumdar-Shaw found scientists at the Centre of Molecular Immunology (CIM) doing very interesting work with antibodies. Kiran always focuses on being at the cutting edge of technology. And since they had

some human data available, we took the decision to make the connection and that got us started on this project.

This was also an opportunity to make very advanced therapies available to patients in India. This is one of my personal motivations to undertake this work and I believe many of our employees feel this way as well. Before BIOMAb EGFR, all antibodies in the Indian market were imported. So they are very expensive. Now that India is developing strong indigenous capabilities, you can think about how to make it available to the patients at a more affordable price.

**Which are the other companies in this space?**

There are very few companies in this segment as it is a complex and expensive business. In India, we have Dr Reddy's, but most other companies are global players like Amgen, Bristol-Myers Squibb, Genentech, Johnson & Johnson, and Roche.

**What are the advantages and disadvantages of the product?**

There are lots of advantages including a significant survival benefit. It is a very good drug. The side effects are very minimal as it is a highly targeted immunotherapy. The systemic toxicity is minimal with no serious incidence of rashes. I cannot really think of any disadvantages.

**What were the challenges that you faced in the development process?**

The major challenge was that nobody had done it before in India. We were blazing a new trail at every step-on process development, characterization, manufacturing, clinical development. Nobody in India has done trials in a novel antibody, while there was very little experience outside. We had Indian doctors using the therapy for the first time and not having done it elsewhere.

We had developed a lot of methods internally to characterize the molecule and understand its mechanism of action.

**How many years did it take to develop BIOMAb EGFR?**

When we started we had some preliminary data from Cuba. Once we set up the joint venture, it took us about five years (the product was approved in 2006) to finally come out with it. Now, we manufacture the product in Bangalore and market it in India and other countries. BIOMAb EGFR is also being developed in other countries including Canada, China, Germany, and Japan.

**Can you briefly tell us about your team that developed the product here?**

I was a part of the team that helped with the process and analytical development and absorbing the technologies from CIM. We had a manufacturing, quality and regulatory team headed by Srinivasan Raman, Tara Jayaram and Sriram Akundi. The clinical trials were done by Arvind Atignat and his team from Clinigene. Rakesh Bamzai was looking after the business development and marketing.

Of course, we had consultations with our partners in Cuba and the two of the key people from Cuban side were Dr Patricia Sierra and Dr Joaquin Villan who are both stationed here in Bangalore.

**After the success of this drug, what is the next step forward?**

We have a pipeline of very exciting products. Our next antibody in clinical trials is T-cell inhibitor that we are testing in RA and is showing promise in other autoimmune disease. We also have an antibody that blocks TNF-alpha and another that target lymphomas by depleting B-cells (by targeting CD20). So, it is a very rich pipeline that has the potential to change the pharmaceutical landscape within India for many serious diseases.

Jahanara Parveen

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