



Update

Hot Spots in the Pharmaceutical Pipeline

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High clinical development costs coupled with declining drug discovery success rates are causing productivity levels to fall in the global pharmaceuticals industry. The imminent patent expiry of several major blockbuster drugs and the related rise of cheaper generic alternatives is further exacerbating the situation. Despite this, the global pharmaceutical market, estimated at \$554 billion in 2004, is forecast to register an annual growth rate of 8.2% from 2004 to 2011 to reach \$967 billion, according to market research firm Frost & Sullivan, Inc. (Palo Alto, CA; www.frost.com).

However, for the expansion to occur, "It is essential for major pharmaceuticals companies to move from the blockbuster model and adopt new strategies that cater to specific diseases areas and populations," notes Frost & Sullivan healthcare analyst Phil Webster. Innovative products that focus on areas of unmet medical need and cover a broad range of disease indications are likely to underpin a strong, sustainable product pipeline. Also, the availability and implementation of novel techniques to identify toxic or ineffective drugs early in the development process, such as the use of biological models, bioinformatics and biomarkers, will drive down development costs, increase revenues and improve overall industry productivity, Webster notes.

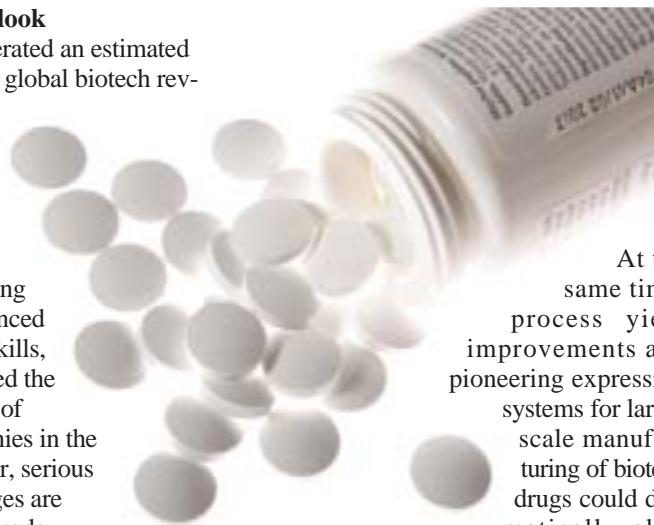
Accounting for over 70% of total revenues and R&D expenditure, the U.S. currently dominates the \$41.3 billion global biopharmaceuticals market. Europe is well entrenched in second place with nearly 20% share of global revenues and 22% share of R&D outlays. Sustained expansion in the region will require industry participants to effectively address funding deficits and concerns related to manufacturing capacity, according to Frost & Sullivan

European outlook

Europe generated an estimated \$8.30 billion in global biotech revenues with R&D expenditures totaling almost \$5 billion in 2002. Building on a tradition of strong R&D and advanced technological skills, the region hosted the largest number of biotech companies in the world. However, serious funding shortages are threatening to erode Europe's global market share. "In order for the 'cash-poor' companies to survive, they would have to look at means to reduce cost and be performance-oriented. This is to say, they should carry out effective research that will bring more products to launch and reduce the number of failures in clinical stages," says Frost & Sullivan's Oxford, U.K.-based biopharmaceutical analyst Raju Adhikari.

Another critical challenge for the industry as a whole has been the gap between demand and supply of manufacturing capacities. "In the short term, projected shortfall of supply in manufacturing capacities means companies are currently able to charge premium prices for providing this service. This could, however, change entirely in the long run as new facilities and expansions could mean that manufacturers will face more difficult market conditions," notes Adhikari.

Hectic expansion activity is currently taking place. A projected 2 million L/yr of manufacturing capacity for 2003 is set to increase to over 3 million L/yr in 2006. In particular, the 350-plus biopharmaceutical drugs undergoing clinical trials are expected to generate a sizable demand for capacity, while motivating more expansions.



At the same time, process yield improvements and pioneering expression systems for large-scale manufacturing of biotech drugs could dramatically alter

the capacity gap. For instance, transgenic technology has the potential to deliver large manufacturing capacities at much lower production costs than current expression systems.

On the other hand, if capacity supply exceeds demand, this would have important implications for the entire industry diluting the importance of the manufacturing function. "A reduction in charges from contract manufacturing organizations charges can be expected, which would affect their profit margins. However, the excess capacity would be beneficial in terms of higher product availability and easier access to capacity by R&D firms," adds Adhikari.

Opportunity in the "new EU"

In contrast to subdued growth in the pharmaceutical markets of the former 15-state European Union (EU), pharmaceutical markets in the "new" EU accession markets are expanding vibrantly. While the former has been increasing at 8%/yr, the latter has been growing at 16.5%/yr over the past five years. The pharmaceutical market in the new EU countries — Cyprus, the Czech Republic, Estonia, Hungary, Latvia,

Lithuania, Malta, Poland, Slovakia and Slovenia — represents about 8% of the EU15 market.

Propelled by the twin advantages of low costs and easy patient recruitment, the new EU also offers tremendous scope for conducting clinical trials. Already, large multinational pharmaceutical and biotechnology companies from Western Europe and from U.S. are carrying out clinical trials on rare diseases and diseases relevant to large worldwide markets. Coordination and swift completion of clinical trials in the new EU have been facilitated by easily accessible, large and relatively under medicated patient populations, as well as more structured healthcare systems.

Moreover, with hourly wages in the new EU countries pegged at a quarter that of western countries, pharmaceutical companies have been able to avoid their single largest cost — the opportunity cost of a delay in getting a drug to the market. This is particularly pertinent since delays can amount to a daily loss of \$1 million.

Identifying potential growth segments in the new EU markets, Adhikari says, “Mirroring the changing disease burden of the west, the anti-infectives market share has declined, whereas cardiovascular, central nervous system (CNS) and metabolic disease categories have taken over. Huge growth opportunities in asthma and oncology also exist and companies with products in these diverse areas are likely to be more successful in the ‘new’ EU markets.”

However, the “new” EU market does face a significant obstacle — parallel trade. Estimated at \$3.8 billion, parallel trade is projected to last for a minimum of another five years. This practice is expected to wane when there is a single EU25 market (when price differences narrow sufficiently). Several international drug companies have attempted to tackle parallel trade by applying restrictions to wholesalers, seeking to prevent export using legal loopholes, or removing or reducing the ex-manufacture price differentials of their products across the various EU states. Others, such as Schering AG, have attempted to limit parallel trade through a consistent European pricing policy and setting prices within a narrow band.

Asia enters the picture

Other emerging markets, such as Brazil and Mexico, exhibit strong development potential, but perhaps the most exciting growth prospects are forecast for two Asian powerhouses — India and China. High domestic pharmaceutical consumption levels coupled with their importance internationally as a supplier base for active pharmaceutical ingredients (APIs) and intermediates have made India and China a magnet for pharmaceutical and biotechnology companies. Furthermore, both countries offer the benefits of low-cost R&D, and a strong scientific base coupled with a large and skilled labor pool.

Underlining the growing appeal of these two countries, several pharmaceutical/biotechnology companies are looking to expand their presence. Swiss pharmaceutical company Hoffmann-La Roche intends on making India one of its larger sourcing hubs for APIs and bulk intermediates. Novartis is investigating clinical trial opportunities in both countries, while big pharmaceutical companies such as Eli Lilly and Pfizer have established their clinical trial programs in India.

However, each country has distinct challenges, such as invariable bureaucratic delays, along with the prospect of less transparency in China. Such hurdles are being offset by several encouraging trends. The market for over-the-counter drugs is expanding. Industry participants and the government are increasingly displaying a global vision, demonstrated by the enhancement of patent protection legislation. An improved patent protection situation is expected to favor foreign entry, even as government initiatives to attract foreign direct investment (FDI) gain momentum. Licensing opportunities offer another incentive to enter these regional markets. “Overall, the large and rapidly expanding economies of India and China are set to have a positive ripple effect on both pharmaceutical and biotechnology sectors,” says Frost & Sullivan industry analyst Himanshu Parmar.



BUSINESS NEWS

Lonza's Clinical-Scale Mammalian Cell Culture Capacity Gets a Boost

A \$10.75 million enhancement is underway at Lonza's (Basel, Switzerland; www.lonza.com) clinical-scale mammalian manufacturing site (MMS) in Slough, U.K. Plans include the installation of a 500-L stirred-tank bioreactor system with accommodations for inoculum expansion, media preparation and primary recovery, and the addition of two new purification suites. The purification systems are being commissioned to handle enhanced downstream requirements caused by the bioreactor and the additional product titers resulting from Lonza's GS expression technology. These processes are projected to be online in the fourth quarter of 2006. Lonza is also installing a 20,000-L bioreactor train at its MMS in Portsmouth, NH, which it hopes to launch in 2006. Moreover, the organization is building a biopharmaceutical manufacturing facility in Visp, Switzerland, equipped with two 15,000-L microbial production trains.



Lonza's main chemical plant in Visp, Switzerland, will soon host a biopharmaceutical manufacturing facility.